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Meningioma Encasing the Internal Carotid Artery

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Occult Type 2 Dens Fracture

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ABSTRACT

Vestibular schwannomas (VS) are benign tumors of the vestibular division of cranial nerve VIII. The initial presentation of intra-tumoral hemorrhage in a vestibular schwannoma is uncommon. The clinical sequela after such event is still being elucidated and the treatment approach to these has not been clearly defined. We report a case of a 39-year-old female referred to our care after being diagnosed with a 22mm left-sided hemorrhagic cerebellopontine angle mass. She initially presented with left ear pain, nausea, vomiting, and balance problems. Mild hearing loss was found on initial audiogram. The patient had progressive improvement of symptoms and elected to continue with observation rather than intervention for the VS. Ten months after initial onset, she developed sudden worsening of her hearing that did not improve with corticosteroids. Brain MRI did not reveal recurrent hemorrhage. The patient underwent a retrosigmoid approach for gross total resection of a WHO grade I vestibular schwannoma with evidence of prior hemorrhage and had a satisfactory post-operative course. Details of this case report as well as a review of the risk factors, radiographic and pathologic findings, possible mechanisms, and outcome for hemorrhagic vestibular schwannomas that may influence decision-making is also presented.

INTRODUCTION

Vestibular schwannomas (VS) are histologically benign tumors that most commonly arise from the superior division of the vestibular nerve (CN VIII) in the Obexerter-Redlich transition zone. They comprise 8-10% of all intracranial tumors in most series and represent approximately 85% of tumors of the cerebellopontine angle (CPA). While the vast majority of VS are sporadic, 5% of cases are associated with neurofibromatosis type 2. The most common symptoms are sensorineural hearing loss (98%), tinnitus (70%), dysequilibrium or vertigo (67%), and headache (32%). Larger tumors will cause symptoms related to compression of the brainstem and adjacent cranial nerves. Facial pain is present in 10% of patients.2 The course is variable, from clinical dormancy for many years, to a slow chronic progression of the above-mentioned symptoms, or on an acute onset with associated ataxia or rapid neurological decline. Tumor size is variable at presentation, however, with increased access to magnetic resonance imaging (MRI) a recent trend is to find tumors smaller in size.20 While 3.9 - 11% of intracranial tumors present with intratumoral hemorrhage (ITH), less are included in the differential diagnosis, such as high grade glioma, osteosarcoma, metastasis, or chordoma.3,4 Due to the progressive improvement of her symptoms, close observation and short interval brain MRI was recommended as initial treatment to monitor for blood product resolution as well as rule out any progression of the lesion that would suggest a more aggressive pathology.

In subsequent visits at 2, 4, and 6-months, the patient had progressive resolution of left otalgia, improved tinnitus, and improved balance. She never developed vertigo. Her hearing remained stable and she was able to continue use of telephone on both ears. There were no limitations of her daily activities. Repeat brain MRI scan at these intervals revealed progressive resolution of intratumoral hemorrhage as well as stable to slightly decreased size of the tumor. The worsening edema or developing hydrocephalus was seen. During these visits, the patient wished to continue with observation in view of stable decreasing size of tumor, lack of symptoms, and reasonably preserved hearing. Ten months after her initial hemorrhage, the patient developed a sudden onset left-sided balance loss that was treated with a course of corticosteroids. Her audiogram after treatment showed improvement. However, the patient did not notice any symptomatic improvement of her hearing loss, she reported inability to use the phone on her left ear. She also described worsened tinnitus. On evaluation, she denied headache, vertigo, nausea, or balance problems. Decreased finger rub perception on her left side was noted. No facial palsy, nystagmus, or gait problems. A new brain MRI did not reveal new hemorrhage or increasing size of the tumor (Figure 2). After discussion with the patient regarding treatment options including stereotactic radiation versus microsurgical resection, the patient elected surgery. A left-sided retrosigmoid cranietomy was performed with drilling of the interpeduncular and AICA. Intraoperatively, the tumor had gross appearance consistent with a vestibular schwannoma. Gross total resection was achieved. No damage to the facial nerve (CN VII) was appreciated intraoperatively and suggested with neurophysiologic monitoring. There were no intra- and post-operative complications. Post-operative brain MRI revealed gross-total resection (Figure 3). The patient was discharged on post-operative day 1. On follow up, the patient was found without significant imbalance, vertigo, nausea, or nystagmus. The patient had non-functional hearing on her left side, yet there was no facial palsy or any other additional cranial neuropathy. Pathology revealed a WHO grade I schwannoma with predominance of Antoni A areas as well as scattered areas of focal hemosiderin deposition, consistent with a vestibular schwannoma with chronic hemorrhage.

DISCUSSION

We describe a case of a VS with the rare presentation of acute ITH. To our best knowledge, under 38 cases have been reported in literature since the first documented by Mc Coy et al in 1974.11,13 This demonstrates the rarity of this presentation. Vestibular schwannomas most commonly present with slowly progressive growth and development of symptoms related to CN VIII dysfunction as well as CN VII or other adjacent cranial nerves.12 In VS that have presented with ITH, the symptoms are sudden and most commonly associated with headaches or otalgia.16,17 In patients with a prior diagnosis of VS, ITH is found after an acute worsening of their prior symptoms and associated headaches.18,19 The prevalence of facial palsy is increased from 6% to 31% when compared to VS that do not present with ITH.20 Given the acute presentation, the mortality rate, however poorer outcome is suggested in hemorrhagic VS compared to non-hemorrhagic.12

On brain imaging, findings on both CT and MRI will be consistent with acute hemorrhage in a CPA lesion. CT scans usually show
prior microhemorrhages in cases of VS with subacute (hyperintense on T1, hypointense (isointense on T1, hypointense on T2) or Hemorrhage within the mass will commonly 2.5 x 2.5 cm. Rapid growth can be secondary to repeated microhemorrhages or growth of the cystic component in cases of VS. In the latter, it has been suggested that their cystic components could represent prior hemorrhages. When the imaging index is not specific to cystic VS, their growth is most likely secondary to enlargement of the cystic component.

Risk factors non-specific to VS that have been reported to be associated with recurrent hemorrhage are large tumor size on presentation, rapid increase in size, prior SRS, history of anticoagulant use, trauma, and cocaine use. The mechanisms suggested include hypervascularity and abnormal vasculature that predispose to hemorrhage.

A recent review by Niknafs et al showed that 17.9% of VS with ITH were previously treated with SRS. The presence of these events was due to an increased risk of ITH after SRS or whether these events were due to the tumor size at presentation.

In our case, the patient had initial conserva- tive treatment, and the tumor presented to our care 1 week after onset, had progressive resolution of symptoms with preserved hearing, no limitation in daily activities, and a small moderate size of tumor. Additionally, given the low rate of ITH in VS, currently reported as a 15%, close follow-up should rule out other malignancies (ie, malignant glomus, metastatic, other tumor) that would alter treatment options was chosen. Despite close follow-up that included short interval MRIs to monitor blood resolution and tumor growth pattern, as well as serial audiological tests to monitor hearing, the patient developed sudden hearing loss 10 months after initial presentation. Subsequent follow-up showed that the hemorrhage or acutae size increase was not found on imaging. This could indicate that sudden hearing loss can occur without recurrent hemorrhage. This case decision to treat either surgically or with SRS should not be made on the occurrence of this event. Despite the sudden hearing loss, the patient had a good clinical outcome as, therefore, with non- hemorrhagic VS, any sign of neurological deterioration should prompt intervention.

CONCLUSION

In this report we present a rare case of a VS with an initial presentation of ITH. A review of existing literature indicates that these may represent a more aggressive kind of VS with a slightly increased risk of devel- oping facial palsy and poorer outcome. Risk factors suggested include large tumor size on presentation, rapid increase in size, prior SRS, history of anticoagulant use, trauma, and cocaine use. The mechanisms suggested include hypervascularity and abnormal vasculature that predispose to hemorrhage. There is a significant risk of recurrent hemor- rhage in VS with PTH and acute worsening of symptoms. VS that present with ITH warrant close observation and lack of documented recurrent hemorrhage in the setting of worsening symptoms should not be withheld intervention.

REFERENCES


Benign Meningioma Encasing the Internal Carotid Artery

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A 47-year-old woman presented with an incidental finding of an extra-axial brain tumor on MRI. (A) Gadolinium-enhanced MRI of the brain showed that the tumor encased the left intracranial internal carotid artery (ICA). (B) T2-weighted MRI confirmed that the flow void (black dot) in the tumor was the left ICA. (C) The intraparenchymal mass demonstrates smooth, intact, and homogeneous hyperintense areas on T2W imaging, consistent with a meningioma. (D) After resection of the tumor, the left ICA is seen with all of its smaller branches intact. The third cranial nerve is seen to the left. (E) Postoperative MRI confirmed gross total resection. (F) Cerebral angiography showed that the occlusion of the ICA was mildly narrowed by the tumor.

Unique Imaging Characteristics of P16+ Squamous Cell Carcinoma of the Oropharynx

Victor Carlson, BA1; Steven Finden MD2

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Department of Neuroradiology, Thomas Jefferson University
June 7, 2013 – August 16, 2013

ABSTRACT
The increasing rate of human papillomavirus (HPV) infection is responsible for the rising incidence of oropharyngeal (OP) malignancy in tonsil and base of tongue tumors. Early HPV detection can guide treatment and reduce metastasis to the base of the skull and cranial nerve subsites. Currently, there are no non-invasive techniques to determine HPV positivity. The aim of this study was to investigate the correlation between HPV+ tumors and lymph node imaging. Pretreatment images of 126 patients (102 male, 24 female; age range, 41-90) were evaluated for cystic foci, size, and matting. HPV status was determined using immunohistochemistry (IHC) for p16 and confirmed with in situ hybridization (ISH). Out of the total sample size, 93 were HPV+. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated. Initial data (19 patients) showed 42.9% sensitivity, 80% specificity, 85.7% PPV, and 33.3% NPV for cystic focus. Matted lymph nodes showed 85.7% sensitivity, 40% specificity, 80% PPV, and 50% NPV. Morphologically normal small (<1.5) lymph nodes with cystic focus showed 84.3% sensitivity, 100% specificity, 100% PPV, and 29.4% NPV. Early results suggest correlation between morphologically normal small lymph nodes with cystic foci and HPV+ malignancy. These findings warrant evaluation of the remaining images.

BACKGROUND
The oropharynx (OP) is the anatomical region in the upper respiratory tract containing the tonsillar pillars, base of the tongue, soft palate, and pharyngeal walls.1 Lined predominately by non-keratinized2 squamous epithelium,3,4 the OP shares many characteristics of the cervix including inflammatory activity and susceptibility to the human papillomavirus (HPV).5-7 HPV infection markedly increases risk of squamous cell carcinoma (SCC)5 in OP crypts.6 HPV-related SCC accounts for 25% of head and neck cancers and the majority of oropharyngeal cancers.7 The most common sites of oropharyngeal tumor development are the tonsils followed by the base of the tongue.8

In up to 96.1% of reported HPV-OPSCC cases, HPV-16 is the infecting virus;9, 10 other high-risk strains such as HPV-18 account for the remaining cases.10 HPV+ tumors have distinct molecular, pathologic, and clinical characteristics.11-13 HPV oncogenes E6 and E7 drive tumor formation14-16 by respectively degrading the master cell regulator p53 and inactivating Rb.10,16,17,18 Viral integration into genomic DNA reinforces dysplasia and triggers malignant transformation.19

In light of intact apoptotic pathways, HPV+ tumors respond enthusiastically to radiation and chemotherapy.20,21 Many studies, including a meta analysis by Bagin et al, reported increased survival in HPV+ patients who undergo surgery, chemotherapy, or radiation treatment.22,23,24 Reduced risk of recurrence was also evident.24

In addition to HPV status, the most influential prognostic factors of head and neck cancers are smoking and nodal staging.25 HPV+ SCC demographics differ from OPSCC associated with smoking. Data indicates increased representation of white males, higher socioeconomic status, decreased age, and better performance status.26 Increased marijuana rates are also associated with HPV+ OPSCC,27 however increased tobacco and alcohol rates are not.28 Reflecting the rise in HPV prevalence, OPSCC tonsil rates increased 1.3% annually and base of the tongue rates increased 6% annually from 1971-2004.29 Smoking rates decreased by half during the same time period implying significant increase in HPV associated tumors.30

Clinically, HPV+ patients are more likely to present with small, poorly differentiated, stage III or IV primary tumors31,32 and are less likely to have synchronous or metachronous second primaries.32 Unusual patterns of metastases and longer latent intervals following therapy are also more likely and warrant a thorough patient work-up.33 Metastatic routes include direct extension along bone, lymphatics, and neurovascular bundles to the skull base and cranial nerves.33 Basaloid morphology, defined as nests of cells with dense hyperchromatic nuclei and a high nuclear to cytoplasmic ratio also correlates strongly with HPV positivity.34,35 Surrogate markers for HPV infection include p16 over expression, EGFR amplification, and c-myc expression5 without cyclin D amplification.36-38 Testing for p16 identifies all HPV+ high risk HPV+ straws with a reported sensitivity of 100% and specificity of 79%.39 A tumor is designated HPV+ when at least 75% of cells have strong and diffuse,
nuclear and cytoplasmic immunohistochemical (IHC) staining for p16.

HPV status significantly influenced outcomes and prognostic implications. Early HPV+ detection, particularly in base of tongue OPSCC, can significantly reduce mortality with HPV status being a determinative factor in treatment

This retrospective study aims to evaluate the potential role of HPV status in OPSCC and to determine the characteristics and HPV+ OPSCC using an adequate sample size. If nodal cystic focus provides high specificity or sensitivity for HPV positivity, then nodal imaging can be used to determine HPV status.

Methods Pretreatment

HPV status was determined using IHC for p16 and confirmed with in-situ hybridization (ISH). According to standard protocol, IHC for p16 was performed on representa-
tive 4-μm sections cut from formalin-fixed, paraffin-embedded tissue blocks using a monoclonal antibody to p16 (M7050; DAKO, Carpentaria, CA). The IHC staining was scored as negative, weakly positive, or positive based on the intensity of staining. Positive staining was defined as nuclear staining with an intact membrane. Negative staining was defined as a lack of staining or staining of the cytoplasm only. Weakly positive staining was defined as staining of the cytoplasm and the nucleus. Positive staining was defined as staining of the cytoplasm and the nucleus with a more intense nuclear staining. The results were recorded as negative, weakly positive, or positive based on the intensity of staining.

RESULTS

Initial data analysis showed 42.9% sensitivity, 80% specificity, 85.7% PPV, and 33.3% NPV for cystic focus.

Table 2. Cystic focus Cystic focus HPV Status

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Our study examined nodal imaging as potential means to determine HPV status in OP cancers. Preliminary data suggest smaller lymph nodes with low attenuation

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Occult Type II Dens Fracture Diagnosed on Repeat Imaging: A Case Report for Standardizing CT Imaging Techniques in Spine Trauma

George M. Ghotrial, MD1, Richard T. Dalai, MD2; Peter M. Ghotrial2,3; James Harrop, MD1,2
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ABSTRACT

Introduction

Many spine traumatic fractures are referred to multidisciplinary tertiary care centers for definitive management. We highlight a case of an acute type 2 dens fracture that failed to be identified using CT reformatted imaging with 3mm axial images.

Clinical Course

A fifty-eight year-old man was witnessed to fall from standing. He had evidence of a myocardial infarction and required cardiosurgical resuscitation (CPR). On arrival to the outside ER he had minimal responsiveness to deep stimulation but required no emergent cardiac intervention since he was hemodynamic stable. A CT of the cervical spine was performed due to the history of a fall demonstrated a “chronic odontoid ‘osseous abnormality’” and with an acute Jefferson-type fracture variant. Upon transfer for definitive cardiac and spine care, the patient had a repeat CT scan with 1.25 mm axial images of the cervical spine demonstrating a type 2 dens fracture. MRI of the cervical spine confirmed an acute type-2 dens fracture.

Conclusion

The use of thin cut axial images improved the quality of reformatted images, thus repeat images with thinner cut images may be required to define anatomy with greater accuracy.

Key Words

Spine, odontoid, computed tomography, trauma, occult

INTRODUCTION

To the effort to reduce cost in the emergency room and trauma setting, concern for missing occult spine fractures is still a common concern among clinicians. The NEXUS and CCR criteria are two widely accepted algorithms for cervical spine scanning by the American College of Radiology, which sets ‘Appropriateness Criteria’ for the diagnostic imaging for several hours apart. Despite the effort to reduce cost in the trauma setting today, seen in as high as 15% of cervical spine fractures, a growing number in the aging population. The typically accepted treatment is immobilization or surgical stabilization with instrumentation. Factors potentiating a high incidence of nonunion of type 2 odontoid fractures were fracture gaps greater than one millimeter, posterior displacement greater than five millimeters, and failure to initiate treatment within 4 days. Today, many spine fractures are referred to multidisciplinary subspecialty institutions (i.e. ‘spine centers’) for definitive management. Theoropoulou, et al found that the added risk from radiation of CT scanning for cervical spine fracture is counterbalanced by the increased sensitivity for detecting cervical spine fractures and increasing that patient’s likelihood for treatment. Speciality centers typically employ high resolution helical/spiral CT scanners to maximize resolution of imaging and provide high-quality multimodality reconstructions to rapidly aid in evaluation of the spine. Williams, et al evaluated 192 patients, nearly 20% of which were diagnosed with osseous thoracic compression fractures, finding only 5% accurately diagnosed. Given the increased prevalence of type 2 dens fractures in the elderly population, recognition of the possibility of underreported occult fractures is a real issue. We present at our institution a specific case of an occult type 2 dens fracture, where the diagnosis hinged on repeat CT scanning with high resolution axial images.5-12 Factors portentiating a high incidence of nonunion of type 2 odontoid fractures were fracture gaps greater than one millimeter, posterior displacement greater than five millimeters, and failure to initiate treatment within 4 days. Today, many spine fractures are referred to multidisciplinary subspecialty institutions (i.e. ‘spine centers’) for definitive management. Theoropoulou, et al found that the added risk from radiation of CT scanning for cervical spine fracture is counterbalanced by the increased sensitivity for detecting cervical spine fractures and increasing that patient’s likelihood for treatment. Speciality centers typically employ high resolution helical/spiral CT scanners to maximize resolution of imaging and provide high-quality multimodality reconstructions to rapidly aid in evaluation of the spine. Williams, et al evaluated 192 patients, nearly 20% of which were diagnosed with osseous thoracic compression fractures, finding only 5% accurately diagnosed. Given the increased prevalence of type 2 dens fractures in the elderly population, recognition of the possibility of underreported occult fractures is a real issue. We present at our institution a specific case of an occult type 2 dens fracture, where the diagnosis hinged on repeat CT scanning with high resolution axial images.5-12 Factors portentiating a high incidence of nonunion of type 2 odontoid fractures were fracture gaps greater than one millimeter, posterior displacement greater than five millimeters, and failure to initiate treatment within 4 days. Today, many spine fractures are referred to multidisciplinary subspecialty institutions (i.e. ‘spine centers’) for definitive management. Theoropoulou, et al found that the added risk from radiation of CT scanning for cervical spine fracture is counterbalanced by the increased sensitivity for detecting cervical spine fractures and increasing that patient’s likelihood for treatment. Speciality centers typically employ high resolution helical/spiral CT scanners to maximize resolution of imaging and provide high-quality multimodality reconstructions to rapidly aid in evaluation of the spine.
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**BACKGROUND**

A fifty-eight year-old man had a witnessed syncopal episode, and subsequent fall from standing, with trauma to the head and neck.

Cardiopulmonary resuscitation (CPR) was initiated for ten minutes and then upon arrival by EMS, ACLS protocol was initiated prior to rapid sequence intubation en route to the emergency department. Upon arrival at the emergency room the patient was noted to be with pulseless electrical activity; CPR was administered for ten minutes, with return of circulation. A STEM was diagnosed by twelve-lead electrocardiogram. Given a poor neurological exam with minimal responsiveness, no emergent cardiac intervention was attempted. Upon stabilization, a CT of the head was obtained, which was normal. A CT of the cervical spine demonstrated a ‘chronic odontoid’ ossous abnormality” and Jefferson-type fracture variant. Upon stabilization of arrhythmia by the cardiac intensive care unit, a repeat CT of the cervical spine was obtained. 1.25mm thick images were reformatted in multiple planes; these demonstrated an acute Jefferson variant fracture of the arch of C1. In addition, an acute type 2 dens fracture was evident on sagittal reformations, with minimal retrolesion, and a fracture line approximately 1 millimeter wide. No canal violation was noted (Figure 2). On post injury day 4, a diagnostic MRI brain and cervical spine was obtained to demonstrate an underlying cause of the failure of neurologic improvement. At this point, minimal trace upper and lower extremity movements to deep painful stimuli were observed, felt to be spinal reflexes. The MRI of the cervical spine demonstrated further dislocation of the odontoid process, a thin epidural hematoma underlying the fracture, with cord hyperintensity signal from the obex to C4 (Figure 3). An MRI of the Brain without gadolinium found no underlying strokes or evidence of global anoxia. T2 hyperintensity of the obex was noted. On post injury day 3 spontaneous eye opening was noted, as well as signs of brainstem function, and minimal spinal reflexes only in the lower extremities.

**DISCUSSION**

The impetus for transition from plain film to CT radiography in the evaluation of the unresponsive trauma patient has been the low sensitivity and negative predictive value.12 Link, et al evaluated plain films and CT radiographs for 234 trauma patients with multiple injuries, finding 44 cervical fractures by xray, 20 of which were of C2. When compared to available CT evidence, CT diagnosed nearly twice the number of cervical spine fractures. Achenes, et al evaluated 160 patients with 136 fractures, finding 99% by CT while 47% was detected by plain radiography alone.12 Additionally, the diagnostic significance of sagittal reconstruction in CT imaging has been likewise established.7 When compared to available CT evidence, CT demonstrated further dislocation of the odontoid process, a thin epidural hematoma underlying the fracture, with cord hyperintensity signal from the obex to C4 (Figure 3). An MRI of the Brain without gadolinium found no underlying strokes or evidence of global anoxia. T2 hyperintensity of the obex was noted. On post injury day 3 spontaneous eye opening was noted, as well as signs of brainstem function, and minimal spinal reflexes only in the lower extremities.

There are few studies in the literature investigating disparities between various modalities of CT scanning devices, as well as slice thickness, and a minimum standard of clinically acceptable imaging quality. With the advent of spiral CT scanning, improved spatial resolution and the ability to routinely utilize multiplanar reformatted images have been demonstrated over older, more conventional CT technology.18,19 Even with conventional CT technology, cases in the literature may be found involving occult spine fractures in patients with diseases of bone mineralization such as ankylosing spondylitis.20 While the concern for occult fracture in the trauma patient with osteoporosis and other bone demineralizing states is recognized, this case report highlights the more prevalent issue where variance in CT protocol can lead to undetectable fractures in the healthy, aging population. In this particular case of a 58 year-old male presenting in a comatose state, imaging is of vital importance for a witnessed trauma. The referral institution had used the GE Ultra Lightspeed® (GE Healthcare, Waukesha, WI) to conduct scans with a minimum reformatted slice thickness of 3mm, as compared to a Philips (Phillips Healthcare, Andover, MA) 64 slice scanner utilizing a routine minimum reformatted slice thickness of 1.25mm. At our tertiary facility, 1.25mm slice thickness slices are reformatted to optimize the quality of 3-dimensional reconstructions. While few may argue that CT scanning of the trauma patient is acceptable given a witnessed trauma, there is little consensus on the appropriate slice thickness, radiation dose, and number of reformatted sequences obtained to achieve a clinically acceptable imaging series of a particular set of anatomy. Regarding a 2009 statement by the American College of Radiologists, there is not a consensus on the specific radiation dose accepted, as well as a specific algorithm for implementing CT. There are general recommendations regarding slice thickness, however. Given the nature of dens fractures in the transverse plain, they have proposed a lateral radiograph of C2 to supplement ‘thick-cut’ axial CT scans greater than 3 mm slice thickness of the cervical spine.23 The AJR instead suggests that this is unnecessary and that slice thicknesses of 2.5 mm should be adequate in detecting these injuries.24 This patient presents a tough challenge to the clinician. The clear and apparent injury to the patient was evident on EKG as a STEMI, which explains the syncopal episode. Given the traumatic fall and GCS of 1 upon arrival, the concern for cerebral hypoperfusion/ anoxia as well as spinal cord injury are real.
REFERENCES


Osteoporosis: Morbidity, Perioperative Implications, and a Review of the Management in Spinal Surgery

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ABSTRACT

Osteoporotic spinal fractures are a major cause of morbidity and mortality. Spinal surgery are often the initial healthcare providers to encounter a newly diagnosed osteoporosis, in the form of vertebral osteoporotic compression fractures. Osteoporosis is highly prevalent, with a significant cumulative lifetime expense. The initial treatment of osteoporosis is medical management, with targeted biological therapies aimed at the osteoblast/osteoclast complex with a goal of restoring or maintaining bone mineral density. Many randomized controlled trials have demonstrated the advantages of vertebroplasty and kyphoplasty in post-operative pain relief and improved quality of life in patients with osteoporotic compression fractures. However, much heterogeneity exists in the literature, and compression fractures are largely considered a non-operative disease. Raising awareness of this disease and its need for urgent management needs to be a priority for all physicians, including spinal surgeons.

Key Words: Osteoporosis, spinal surgery, vertebroplasty, balloon kyphoplasty, minimally invasive surgery

Core Tip

Osteoporosis carries a significant morbidity and mortality and is unfortunately the most common cause of compression fractures of the spine in the elderly. It is often a disease where preventative care is underplayed at both the primary care and tertiary care level. Surgical treatments for compression fractures such as vertebroplasty and kyphoplasty can dramatically reduce pain and achieve immediate postoperative ambulation in the elderly patient. While the literature is heterogenous, recent data in is support of the benefits of these surgical interventions.

INTRODUCTION

With a national (USA) prevalence of 10 million and a worldwide prevalence estimated to be 300 million, osteoporosis is becoming increasingly more common. Other estimates place vertebral osteoporotic compression fractures (VOCFs) at an incidence of 1.4 million new cases per year.1,2 Osteoporosis is referred to as either primary (type 1), or secondary (type 2). Primary osteoporosis, which has a prevalence of 30% are male, and therefore gender should not be underplayed. Generally, osteoporosis is defined as a disease of the elderly population. They occur at a rate of approximately 700,000 per year and are the most common type of osteoporotic fracture.1 More than half of women and one-third of men will suffer from a VCF in their lifetime, with between 50 and 80% of them being incidentally diagnosed on chest radiographs.3,4 Longitudinal studies show that up to one in fifth of these patients are unfortunate enough to have a second VCF, heightening the need for prompt preventative treatment.5 Several surveys of US Spinal surgeons have been conducted regarding the frequency of osteoporotic fractures in evaluation of fracture etiology. The poor results are surprising, suggesting a need for a heightened awareness of the importance of addressing bone mineral density in the elderly on a routine basis.6,7 In this manuscript the authors summarize the literature regarding the recommendations for preventative treatment for spinal osteoporosis and perioperative management of osteoporotic spinal fractures.

MEDICAL MANAGEMENT

Bisphosphonates

Bisphosphonates are a class of agents traditionally targeted at osteoblasts and osteoclasts.8 Spine surgeons should keep this in mind since these are the target cells for agents in this class. However, in the only human clinical study performed assessing bisphosphonates in spinal fusion, there was no clinically significant difference between the treatment and the control arm.
with regards to fusion. This study, however, did find a 95% fusion rate in the arthrodesis group versus 65% in the vitamin D control group treated for one year after surgery (P=0.025). Aside from this randomized controlled trial, the restorative potential of animal studies demonstrating histological support that bisphosphonate result in a relatively rapid resorption of bone with only one human trial of less than 40 patients in favor of bisphosphonate use to improve fusion results in single level posterior lumbar interbody fusions, there appears to be no consensus on the optimal medical management of osteoporosis in patients undergoing spinal surgery.

Parathyroid Hormone
Parathyroid Hormone (PTH) is secreted by the parathyroid glands in response to low calcium, wherein the net effect is elevation of serum calcium. PTH is antagonistic to calcitonin, a hormone that lowers the serum calcium concentration and is produced by the thyroid gland. A preponderance of the available animal literature shows that PTH chemotherapeutic may aid calcium balance, however, the same cannot be said for clinical practice. Many clinical studies have been shown to build bone mineral density. Recent systematic reviews and meta-analyses have shown benefits of pain relief in the acute period with either balloon kyphoplasty or vertebroplasty versus nonsurgical management. It is commonly witnessed in patients with PTH as well as cancer-related compression fractures to note dramatic pain relief and ambulation on the same day after intervention. More recently, evidence shows that PTH can have an advantage over vertebroplasty and vertebroplasty in the reduction of subsequent fractures and in the reversal of kyphosis.13

Novel Therapies
New medical devices for the treatment of osteoporotic compression fractures have risen out of the drive for competition over a lucrative market share. These new devices are typically small modifications of the proven systems. Many of these involve the placement of a graft in the vertebroplasty to be a means of maintaining restoration of vertebral height. For example, vertebroplasty stent which is not decreasing the loss of height that may occur after a balloon kyphoplasty where intravertebral settling may occur. Additionally, an expandable stent is placed after the balloon re-expansion of the vertebral column. This is then followed by percutaneous kyphoplasty which has this therapy has been available for several years, its additional use has limited its widespread use in place of BKP. In addition, a recent randomized controlled trial found no major differences in the reduction of kyphosis for vertebroplasty when compared to the use of BKP.14

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8. Wu I, Lipiec J, Seabrook D, et al. Vertical白雪山板式、Kyphoplasty/Vertebroplasty versus nonsurgical management of vertebral compression fractures. Balloon kyphoplasty and vertebroplasty are commonly used as treatment options for acute osteoporotic compression fractures, as mentioned above. Recent systematic reviews and meta-analyses have shown benefits of pain relief in the acute period with either balloon kyphoplasty or vertebroplasty versus nonsurgical management. It is commonly witnessed in patients with PTH as well as cancer-related compression fractures to note dramatic pain relief and ambulation on the same day after intervention. More recently, evidence shows that PTH can have an advantage over vertebroplasty and vertebroplasty in the reduction of subsequent fractures and in the reversal of kyphosis.13

CONCLUSION

Spinal surgeons are increasingly on the front line of the diagnosis of osteoporosis, as OVDs are the most common initial fracture leading to its diagnosis. Osteoporosis is highly prevalent, with a significant cumulative incidence and impact in the social and economic burden of this disease and options for its management is a priority for all physicians, including spinal surgeons.
Cerebrovascular

Myotic Aneurysm Management

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ABSTRACT

The management of myotic aneurysm has always been subject to controversy. The aim of this paper is to review the literature on the intracranial infected aneurysm from pathogenesis till management while focusing mainly on the endovascular interventions. This novel solution seems to provide additional benefits and long-term favorable outcomes.

Intracranial infectious aneurysms (IIA) or myotic aneurysms are a rare entity and represent 0.7 to 5.4% of all cerebral aneurysms. The name myotic originated from the fact of infection or abscesses formation following endovascular surgery.

This theoretical fear exists in spite of the absence of reports in the literature on persistent infection or abscesses formation following endovascular surgery. A recent review of the literature examined 287 cases of cerebral mycotic aneurysms (CMA) found no postprocedural infection or abscesses formation following endovascular surgery. The prevalence have decreased from 86% after the advent of antibiotic era. The most common sources of infectious bacteremia remain intravenous (IV) drug abuse and poor dental hygiene. Direct invasion of the vascular wall from a nearby infectious focus, such as cavernous sinus thrombophlebitis and bacterial meningitis are also common cause of IAA. The median age tends to vary from 25 to 60 years. Some studies reported a higher male predominance while the pooled cohort done by Ducruet et al revealed that 65% of patients with IIA have an underlying endocarditis.

INTRODUCTION

Intracranial infectious aneurysms (IIA) or myotic aneurysms are a rare entity and represent 0.7 to 5.4% of all cerebral aneurysms. The name myotic originated from the fact of their resemblance to fungal vegetation. Although they can be caused by fungal pathogen, they are most commonly due to bacterial infection. Historically the management of myotic aneurysms relied on surgery and antibiotics with limited use of endovascular therapy fearing the risk of overwhelming infection by introducing a foreign body to an infected region.

This theoretical fear exists in spite of the absence of reports in the literature on persistent infection or abscesses formation following endovascular surgery. A recent review of the literature examined 287 cases of cerebral mycotic aneurysms (CMA) found no postprocedural infection or abscess formation following endovascular surgery. This theoretical fear exists in spite of the absence of reports in the literature on persistent infection or abscesses formation following endovascular surgery.

The safety and efficacy of these techniques are published in case-series and case-reports. Therefore, endovascular treatment remains an individualized therapy with no standard guidelines. Given the inconsistency in IIA evolution, response to treatment, and the lack of randomized controlled trials (RCTs), there has not been any widely accepted standard management. The purpose of this article is to briefly review cerebral mycotic aneurysms while focusing on the endovascular approach for their management.

METHODOLOGY

We performed a literature review using MEDLINE. The following meshwords were used individually or in combination: mycotic, cerebral, infectious, intracra- nial, aneurysm, endovascular, treatment, management, and only. We managed to find 3 articles on the use of onyx in the treatment of IIAs. Other articles were included in our study using a more extensive search to briefly review the pathogenesis of the disease and to evaluate other alternative management. The search was limited to studies published in English.

EPIDEMOLOGY

IIA’s represent 5% of all intracranial aneu- rysms. Currently there are no rigorous population-based epidemiological studies, but an analysis of a pooled cohort by Ducruet et al revealed that 65% of patients with IIA have an underlying endocarditis. The prevalence have decreased from 86% after the advent of antibiotic era. The most common sources of infectious bacteremia remain intravenous (IV) drug abuse and poor dental hygiene. Direct invasion of the vascular wall from a nearby infectious focus, such as cavernous sinus thrombophlebitis and bacterial meningitis are also common cause of IAA. The median age tends to vary depending on the reviews between 35-53 years. Some studies reported a higher male predominance while the pooled cohort done by Ducruet et al showed similar proportions of both genders (52% males and 48% females).

PATHOLOGY AND PATHOGENESIS

The process is the result of a developing infec- tious process involving the arterial wall.
The acute inflammation leads to neutrophil infiltration followed by degradation of the internal elastic lamina and proliferation of the intima. The weakened vessel wall in combination with the pulsatile pressure in the vasculature leads to an aneurysm formation and consequent growth. The acute inflammation leads to neutrophil infiltration followed by degradation of the intima. The weakened vessel wall in combination with the pulsatile pressure in the vasculature leads to an aneurysm formation and consequent growth. Most of the authors prefer the term pseudoaneurysm, although, both are widely used. Many processes may contribute to the development of IIAs; septic emboli lodging at distal branches, spreading infection involving the vasa vasaum and periarterial lymphatic and vascular manipulation precipitating infection, all of which leads to focal polymorphic neutrophil infiltration with enzymes and pro-inflammatory cytokine secretions. Consequently, the inflammatory reaction contributes to vessel friability, weakening and pseudoaneurysm formation. Grossly, the aneurysm appears friable, have a thin-wall, and wide or absent neck. This predisposes the aneurysm to rupture and consequent bleeding. If it ruptures, the mortality rate can be extreme, as high as 80%-90%. Even though a fusiform morphology points toward a mycotic pseudoaneurysm, a saccular morphology does not exclude it, as it has been shown that approximately 41% of mycotic aneurysms in the literature are saccular. Even though virus and fungi can cause IIAs, bacterial infection remains by far the most predominant cause. The most commonly reported bacterial pathogens are Staphylococcus and Streptococcus species. IIAs have been described following viral infection such as HIV-1 and ZEV (20), and fungal infection such as Candida and Aspergillus. IIAs can be formed at distal branching points when the infectious agent spread by hematogenous route, as seen in endocarditis, or it can be formed near the infected foci when the infectious agent spreads by direct invasion of the arterial wall from the extravascular site. The latter is more commonly seen in immunocompromised patients. The most common location of IIA seems to be the anterior circulation, mainly the MCA and its distal branches, contributing to as much as 50-75% of all IIAs. 

CLINICAL MANIFESTATIONS AND DIAGNOSIS
IIAs natural history is somewhat unpredictable, but linked to significant mortality ranging from 30% to 80% if rupture occurs. Some studies reported rupture as the most common presentation of IIAs, and most of the studies reported that headache followed by fever are the most common symptoms. However, a recent review found septic infarct to be more common than intraparenchymal hemorrhage (IPH), and focal neurologic deficit to be a more common initial presentation than fever. The bleeding can be subarachnoid, intraparenchymal, or intraventricular. Other signs and symptoms of IIAs are due to the underlying etiology, such as septic emboli, fever and chills, or to the mass effect of the aneurysm. Silent IIAs are not uncommon and can present up to...

Figure 1. Management Algorithm
A patient with a history of intravenous drug abuse was admitted to an outside hospital for treatment of endocarditis. MRI at this time demonstrated multiple cortical septic emboli and mycotic aneurysms (A-42). Two weeks after initiation of antibiotics, the patient had a significant headache and CT scan demonstrated new hemorrhage in the superior parietal lobe (B). The patient was transferred to our hospital for further care, and CTA and MRA at this time demonstrated 3 persistent mycotic aneurysms with hemorrhage surrounding the third aneurysm arising from the distal cortical branch from the middle cerebral artery (C-D). The patient required a cardiac valve replacement and would receive full anticoagulation and had a hemorrhage 2 weeks after initiation of antibiotics, the intervention of the ruptured aneurysm was considered the best course of therapy. Due to the distal nature of the aneurysm, microsurgical removal was deemed the best therapy (Figure 2, intraoperative image). Intraoperative angiogram demonstrated complete occlusion of the cortical based aneurysm with only the single aneurysm remaining (E-K). Follow CTA demonstrated resolution of the final remaining aneurysm. Proximal aneurysm and those arising from cavernous ICA tend to be treated more by a direct approach using coiling, SAC, or Onyx. Follow CTA demonstrated resolution of the final remaining aneurysm. Proximal aneurysm, a saccular morphology does not exclude it, as it has been shown that approximately 41% of mycotic aneurysms in the literature are saccular. 

Figure 2.
The diagnosis of mycotic aneurysms relies on a predisposing infectious process with an aneurysm documented by vascular imaging. Some literature even recommend screening patients with bacterial endocarditis for intracranial aneurysms given the strong correlation between the two. Digital Subtraction Angiography (DSA) continues to be the gold standard for the diagnosis of mycotic aneurysms. CT angiography and Magnetic Resonance imaging can be used: some of the findings on DSA that points toward IIA are: the fusiform shape, the multiplicity, the distal location, and the change in size on follow-up angiography. Positive culture from the wall itself can confirm the diagnosis. Other indicators are positive blood culture (only found in 35%), leukocytosis, elevated erythrocyte sedimentation rate (ESR), and elevated C-reactive protein (CRP). In the case of aneurysms that are distal in location such as those arising from cavernous ICA tend to be treated more by a direct approach, while both approaches are used for aneurysms that are in distal location such as those arising from MCA and perforating (see Table 3). The advantages and disadvantages of the different agents used are summarized in Table 2.

Endovascular coiling has been attempted by Androu et al and Chapot et al with successful outcome, without any rupture or death (Table 3). In these settings, the endovascular approach seems to have replaced surgery as the standard of care in treatment of IIA, and the optimal treatment paradigm remains controversial.

Endovascular Management
The advantages of endovascular therapy over surgery are a decreased risk of anesthesia particularly in patients with impaired valve function, rapid and effective anticoagulation therapy, and shortening of the delay between aneurysm treatment and cardiac surgery. The delay can be reduced from 2-3 weeks to as little as 1 day.4-10 A major indication for endovascular therapy would be a patient with high surgical risk, a patient candidate for cardiac surgery, and a surgically inaccessible or multiple IAs. Current strategies in endovascular therapy include an indirect approach by parent artery occlusion (PAO) using coils or liquid embolic agents (Onyx, etc), and direct approach by the aneurysm using coils, stent-assisted coiling (SMC), flow diverters, and LEAs.10-12 PAO is attempted when the aneurysm is distally located, dysplastic, involving the whole circumference of the parent vessel, and has a complex morphology.

Mycotic aneurysms are seen in patients with intracranial infection. Both PAsO and endovascular treatment are commonly used to treat aneurysms. The treatment involves antimicrobial agents, surgery, endovascular approach and or a combination of them. As a role, IAs management depends essentially on whether it has ruptured or not. The aneurysm characteristics and the overall health status of the patient. For unruptured IIA in patients with high surgical risk, conservative treatment with antibiotics is the main therapy. Antibiotics are guided by blood and cerebrospinal fluid (CSF) cultures. If the results were negative, empiric treatment based on suspected pathogens is continued. A period of four to six weeks of antimicrobial therapy is generally recommended.26 An aneurysm has a high surgical risk if there is a circumferential vessel involvement, if the location is proximal, or if parent artery sacrifice cannot be done due to considerable neurological deficits. These characteristics render the surgery or the endovascular therapy difficult and unsafe. Follow-up angiography is necessary to assess the risk of rupture, which is always present even with appropriate medical therapy.3 Conservative management yields different outcomes in terms of change in size or disappearance of the aneurysm. The outcome with conservative management is worse than that of invasive treatment when the latter is indicated.9-21 Table 1 summarizes some of the outcomes after conservative management. Resistance to conservative treatment is suspected when the aneurysm size increases or remains the same, and/or when other aneurysms developed while the patient was on the appropriate antibiotics. In this case, invasive management is warranted.11 However, some authors advise for hemicranial or surgical management whenever the aneurysm is accessible, regardless of the rupture status.

In the case of unruptured aneurysm without high surgical risk, endovascular or surgical treatment is advised irrespectively of the size because of the high risk of rupture and the weak association between size and rupture.20 Ruptured aneurysms on the other hand should be immediately secured by surgical or endovascular means. The success of endovascular or surgical treatment depends mostly on the aneurysm morphology, the co-morbidities of the patient and the presence of an associated intracerebral hematoma.21 The choice between endovascular and open surgical approach is complex and should be individualized.

Table 1. Response of aneurysm to medical treatment

<table>
<thead>
<tr>
<th>Disappearance</th>
<th>Decrease in size</th>
<th>No Change in size</th>
<th>Increase in size</th>
<th>Additional aneurysm development</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bartaske S et al</td>
<td>29%</td>
<td>18.5%</td>
<td>15%</td>
<td>22%</td>
</tr>
<tr>
<td>Cor P et al</td>
<td>33%</td>
<td>17%</td>
<td>33%</td>
<td>17%</td>
</tr>
</tbody>
</table>

Table 2. Characteristics of different agents used in embolization

<table>
<thead>
<tr>
<th>Agent</th>
<th>Properties</th>
<th>Advantages</th>
<th>Inconvenience</th>
</tr>
</thead>
<tbody>
<tr>
<td>NBeCA</td>
<td>Non absorbable, adhesive</td>
<td>Rapid polymerization</td>
<td>High risk of giving the micro catheter (infectant polymerization)</td>
</tr>
<tr>
<td>Detachable coil</td>
<td>New generation soft coil</td>
<td>Hydrophilic (vs old-generation coil)</td>
<td>Risk of rupture (transient increase in pressure while deployment)</td>
</tr>
<tr>
<td>DSA</td>
<td>Non absorbable, adhesive</td>
<td>Slow polymerization</td>
<td>Requires familiarity</td>
</tr>
<tr>
<td></td>
<td>- First injection from single catheter</td>
<td></td>
<td>Requires special catheter</td>
</tr>
</tbody>
</table>

Table 3. Aneurysm coiling with or without stent

<table>
<thead>
<tr>
<th>SSD (al)</th>
<th>Modality of treatment</th>
<th>Response</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yen PS et al</td>
<td>- Helicent 3.5mm + GDC for left cavernous carotid</td>
<td>Complete occlusion</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Helicent 4mm + GDC for right cavernous carotid</td>
<td>No complication</td>
<td></td>
</tr>
<tr>
<td>Nakaoa et al</td>
<td>3.2mm PICA, ultrafast GDC</td>
<td>Complete occlusion</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- 5.7mm distal left ACA, ultrafast GDC, treated by PAO</td>
<td>No complication</td>
<td></td>
</tr>
<tr>
<td>Chapot et al</td>
<td>- Non-selective cyanoacrylate</td>
<td>Complete occlusion</td>
<td></td>
</tr>
<tr>
<td>(18 cases)</td>
<td>- Coil-embolization</td>
<td>Complete occlusion</td>
<td></td>
</tr>
</tbody>
</table>

10% of autopsy cases29. It is noteworthy that in contrast to saccular aneurysms, size does not seem to predict the risk of rupture.23 When the GMA is intracranial, the presentation tends to be different. When this is the case, the most common presentation is a pulsatile mass, which may compress the cranial nerves resulting in dysphasia and dysphonia24. If left untreated, it may rupture causing a hemorrhagic shock, or may deliver septic emboli to the anterior circulation of the brain.25 The diagnosis of mycotic aneurysms relies on the presence of a predisposing infectious process with an aneurysm documented by vascular imaging. Some literature even recommend screening patient with bacterial endocarditis for intracranial aneurysms given the strong correlation between the two. Digital Subtraction Angiography (DSA) continues to be the gold standard for the diagnosis of mycotic aneurysms. CT angiography and Magnetic Resonance imaging can be used. Some of the findings on DSA that points toward IIA are: the fusiform shape, the multiplicity, the distal location, and the change in size on follow-up angiography. Positive culture from the wall itself can confirm the diagnosis. Other indicators are positive blood culture (only found in 35%), leukocytosis, elevated erythrocyte sedimentation rate (ESR), and elevated C-reactive protein (CRP).
was effective and safe (Table 3 and 4). For management algorithm, please refer to Figure 2.

At our institution, Thomas Jefferson University Hospital, 4 mycotic aneurysms, 3 of which were associated with arteriovenous malformation and 1 with Marfan syndrome, were successfully treated. Complete aneurysm obliteration was achieved in all patients by using Onyx 18 to occlude the aneurysm or to trap the parent vessel, with a procedural related mortality and morbidity rate of 0%. Unfortunately, 2 of our patients died from cardiac complications caused by their endocarditis. The technique that seemed to provide additional safety was the injection just proximal to the aneurysm, limiting thus the distal migration while the filling is taking place. There were neither instances of reflux nor accidental migration of embolic material. There were no recanalization or rebleeding on follow-up. We conclude that parent vessel trapping with Onyx 18 offers a simple, safe, and effective means of achieving obliteration of distal challenging aneurysms. Avoiding the need for aneurysm catheterization reduces intraprocedural manipulation, and thus practically eliminates the risk of aneurysm perforation. Figure 2 illustrates a case of IA that was treated by Onyx 18.

CONCLUSION
IAs have a rupture risk of less than 2%. Nevertheless the mortality rate post rupture could reach as high as 80%.[10] In the last decade the flourishing advances in endovascular techniques expanded the scope of its application and have transformed it from a rescue procedure to a first line treatment as recommended by many authors.[10,11,15] The majority of the patients with IAs are quite ill with multiple comorbidities. Therefore, an endovascular approach would be a more suitable treatment option.[16] Unruptured IAs can be treated with antibiotics and follow-up imaging in 1-2 weeks after therapy. If the size of the aneurysm decreased in size or resolved, then the patient most likely will not need an invasive therapy. Continuation of the antimicrobial in that case would be appropriate, while noting that a decrease in size does not correlate with a decrease in the risk of rupture.[17] If the aneurysm is increasing in size or remaining the same, invasive procedures become mandatory.

The choice between open surgery and endovascular management depends on a multitude of factors already described above, but the most important are the following: the morphology and location of the aneurysm, whether it is possible or not to sacrifice the parent artery, whether the patients needs or has received valve replacement surgery, and lastly the patient overall health status. Even though there is no head to head RCTs comparing endovascular and open surgery, most infectious aneurysms are being treated by endovascular method.[18,19] The IAs of patients considered “strongly immunocompromised” such as those with AIDS, those on chemotherapy or on immunomodifying drugs, have higher rates of growth and rupture.[20,21] The prognosis of these patients depends on the prompt recognition and early aggressive treatment. Both endovascular and surgical techniques are safe and effective options that have been shown to increase survival when compared to conservative management alone.19

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Intra-Operative Visualization of Prior Stroke

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Racemose Neurocysticercosis

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The patient is a 41-year-old right-handed female with a history of stroke at age 24, in the distal right middle cerebral artery territory. Of note, when the patient had the stroke she was a cigarette smoker and simultaneously on oral contraceptives. She presented to our institution in early 2013 with medically intractable epilepsy, for surgical evaluation due to worsening of her seizures. The patient had experienced seizures for the past 16 years, and failed multiple anti-epileptic drugs. She underwent placement of a vagal nerve stimulator in 2007. Further work-up at Jefferson Hospital for Neuroscience revealed the patient to be a surgical candidate for her epilepsy.

She underwent an extended temporal-parietal lobectomy with intraoperative electrocorticography. The above images (Figures 1A, B) were taken from the initial exposure of the brain, and show the area of brain where her strokeoccurred 17 years ago. The patient remained at neurological baseline post-operatively.

Figure 1 A, B

Intraoperative visualization of a middle cerebral artery territory stroke during exposure for a right temporal lobectomy indicated for medically intractable epilepsy.

ABSTRACT

Neurocysticercosis (NCC) is an invasive parasitic infection of the central nervous system (CNS) caused by the larval stage of the tapeworm Taenia solium. The clinical manifestations of NCC depend on the parasitic load and location of infection as well as the developmental stage of the cysticerci and host immune response, with symptoms ranging from subclinical headaches to seizures, cerebrovascular events, and life-threatening hydrocephalus. Racemose NCC represents a particularly severe variant of extraparenchymal NCC characterized by the presence of multiple confluent cysts within the subarachnoid space and is associated with increased morbidity and mortality as well as a decreased response to treatment. In this report, we describe a patient recently emigrated from Mexico with racemose NCC and hydrocephalus and review the clinical, diagnostic, and therapeutic features relevant to the management of this aggressive form of NCC.

INTRODUCTION

Neurocysticercosis is a common parasitic infection of the central nervous system caused by the tapeworm Taenia solium. Infection is typically characterized by the presence of intraparenchymal cysts within the cerebral hemispheres at the grey-white junction and NCC is the most frequent cause of acquired epilepsy in developing countries.1 Parasitic infestation is endemic to South and Central America, Southeast Asia, China, and Sub-Saharan Africa2 and is of increasing importance in the United States due to the high volumes of immigration from these endemic areas.2-4 Extraparenchymal NCC is less common than the intraparenchymal form and is defined as neurocysticercosis involving the subarachnoid, meningeal, and intraventricular space. Extraparenchymal NCC presents unique diagnostic and therapeutic challenges compared to the intraparenchymal form. The racemose variant of extraparenchymal NCC represents a particularly aggressive infection and is associated with relatively increased morbidity and mortality and decreased responsiveness to medical treatment. The variant is characterized by the presence of multiple lobulated confluent cysts within the basal subarachnoid space that appear “grape-like” both radiographically and pathologically.2 In this report, we describe the successful management of a patient with extensive racemose NCC and hydrocephalus treated with cerebrospinal fluid (CSF) diversion and prolonged administration of albendazole and corticosteroids with complete radiographic and clinical resolution of infection.

CASE REPORT

A 39 year old male presented to the emergency room with complaint of worsening headaches and visual decline. The patient emigrated from Mexico 13 months prior to presentation and reported no other significant medical history. He described diffuse headaches that had progressed over a one month period with new onset bilateral visual impairment and nausea for the last week. His neurologic exam was non-focal, however, ophthalmologic evaluation revealed bilateral papilledema and diminished visual acuity. He was afebrile on presentation and without meningeval irritation signs. Initial laboratory findings indicated a normal white blood cell count of 7400/mm3 with 73% polymorphonuclear leukocytes, 21% lymphocytes, and 1% eosinophils. A head computed tomography (CT) scan demonstrated hydrocephalus with transependymal flow and a multi-lobulated hypodense mass in the basal cisterns. Subsequent magnetic resonance imaging (MRI) was performed which demonstrated the presence of too numerous to count non-enhancing, T2-hyperintense cystic lesions in the lateral ventricles and subarachnoid spaces including the bilateral sylvian fissures and cerebellopontine angles as well as the suprasellar, interpeduncular, and prepon
tine cisterns with the largest cyst measuring 21mm in diameter and exerting mild mass effect upon the brainstem (Figure 1). Minor sylvian fissure enhancement was noted bilaterally, however, magnetic resonance angiography (MRA) showed no large vessel stenosis or occlusion. A screening MRI of the spine demonstrated a small subarch-
noid cystic lesion at the level of the conus and multiple septations at the S1-S2 level. A lumbar puncture was performed and an elevated opening pressure was documented. Cerebrospinal fluid (CSF) analysis revealed a mild lymphocytic pleocytosis with 60 white blood cells/mm3 (96% lymphocytes, 4% eosinophils). The initial CSF protein level was 106 mg/dL with a glucose level of 74 mg/dL. CSF cysticercus antibody ELISA testing was positive and a diagnosis of racemose NCC was made based on the immunouassay results, neuroimaging findings, and history of recent emigration from Mexico. After extensive discussion between the neurosurgical and infectious diseases teams, we elected to proceed with placement of a ventriculoperitoneal shunt to ameliorate his elevated intracranial pressure and communicating hydrocephalus. High-dose dexamethasone (4mg QID) was initiated.
and he was able to be slowly weaned off of disorder that responded well to steroids treatment. He maintained a mild headache suprasellar, prepontine, and foramen magnum cisterns.

Figure 1.

followed by administration of prolonged albendazole (10mg/kg/day) treatment. The patient experienced immediate relief of his visual deficit following the CSF diversion treatment. He maintained a mild headache disorder that responded well to steroids and he was able to be slowly weaned off of this medication over a 12 month period. MRI scan performed at that time revealed complete radiographic resolution of his subarachnoid, spinal, and intraventricular cystic lesions with very mild persistent meningial enhancement (Figure 2). A serum cysticercus-antigen ELISA test was nonreactive and albendazole was discontinued.

DISCUSSION

Cysticercosis is the most common helminthic infection of the central nervous system with infection occurring primarily through the ingestion of eggs of the parasitic tapeworm Taenia solium. The eggs hatch within the digestive system and the released oncospheres penetrate the intestinal mucosa to enter the circulation. The oncospheres are then passively transported to various tissues including the brain, muscle, and arachnoid over the parasitic larval cysts, or cysticerci. Extraparenchymal NCC occurs as the cysticerci reach the ventricular space through the choroid plexus where they may pass freely or become attached to the ependyma. Intraventricular infection appears to be more frequent than previously believed with recent series documenting the presence of parasitic cysts in up to 30% of patients with NCC.13 Displacement of the cysts from the ventricles via the CSF may lead to infection within the basal cisterns, subarachnoid spaces, and cortical and spinal subarachnoid spaces. Excessive basal subarachnoid infection involving numerous parasitic membranes and enlarged vesicular cysts accompanied by a relative lack of scolices is termed racemose NCC, although no definitive diagnostic criteria for this rare but severe variant have been described.1

The diagnosis of racemose NCC is typically based on imaging (CT, MRI) and laboratory evaluation, and clinical epidemiologic data including immigration from or frequent travel to disease endemic areas. Contrast-enhanced MRI is the imaging modality of choice for detection of extraparenchymal NCC as CT has limited sensitivity for identification of intraventricular and small subarachnoid cysts. Lesions typically appear as hyperintense T2 cyst sequences and provide clear delineation of the cyst wall and presence of obstructive or communicating hydrocephalus. Contrast evaluation is important to determine the extent of the host inflammatory response including ependymitis and basal arachnoiditis as well as the evolutionary stage of the parasite. While the clinical and neuroimaging findings are of great importance, serologic testing may provide additional data especially in patients without an appropriate epidemiologic history. Peripheral eosinophilia is a common but nonpathognomonic finding with NCC.14 Similarly, the presence of CSF eosinophilia is frequently indicative of NCC and is a helpful in differentiating NCC from other forms of infectious chronic meningitis, although this finding has been reported to occur in only 15% of patients.15 The most common CSF abnormalities observed with NCC are a mild-moderate lymphocytic pleocytosis and increase in protein with the levels varying according to parasitic burden and location of infection. Positive serum and CSF immunassays for detection of anti-cysticercal antibodies are highly suggestive of NCC infection in the appropriate clinical setting, although false-negative results are a well-recognized limitation.16 The sensitivity of these immunassays has not been established for the racemose variant but would be expected to be increased given the robust inflammatory reaction typically elicited with subarachnoid infection.

The intraventricular and cisternal forms of NCC typically manifest in a more clinically aggressive manner than parenchymal infection and frequently cause intracranial hypertension due to CSF outflow obstruction or inflammatory basal arachnoiditis.10 Cysts within the ventricular cavities may be free floating and cause obstruction at the foramina of Monro, subarachnoid aqueduct, or fourth ventricle and may present with rapid clinical deterioration secondary to acute hydrocephalus. These cysts may also become attached to the ependymal wall of the ventricle and result in ependymitis following cyst degeneration that may lead to intraventricular loculation and make CSF diversion more problematic. Similarly, cyst degeneration within the subarachnoid space may elicit an accompanying host inflammatory response with basal arachnoiditis, vasculitis, elevated intracranial pressure, and subacute to chronic hydrocephalus requiring CSF diversion. In 2002, DeGiorgio demonstrated that patients with heavy cyst burdens and hydrocephalus carried the highest risk of mortality with NCC, primarily because of elevated intracranial pressure and shunt-related problems.10 Similarly, Colls et al reported a 30.8% mortality in patients who required placement of a ventriculoperitoneal shunt due to a greater than 90% rate of shunt failure secondary to shunt obstruction due to proteinaceous debris.11 In addition to hydrocephalus, the active inflammatory process may lead to vasculitis and cerebro-vascular complications. Angiography or magnetic resonance angiography (MRA) may reveal segmental narrowing or occlusion of large vessels within the basal cisterns and subarachnoid spaces, with the majority of infarcts occurring in the lenticulostrate artery distributions.12 Basal meningitis may also cause cranial nerve dysfunction due to fibrous encasement.13 Callacondo et al. recently described that extension of infection to the spinal subarachnoid space is very common in racemose NCC, with spinal involvement documented in 17 of 28 patients in their prospective study leading the authors to recommend that screening MRI of the spine be performed in basal subarachnoid disease to document spinal involvement, prevent complications, and monitor for recurrent infection.17 No consensus exists regarding the optimal treatment of racemose NCC including the duration of anthelmintic treatment and the role of surgical intervention. In patients presenting with hydrocephalus, the priority is relief of raised intracranial pressure.13 Obstructive hydrocephalus due to intraventricular cysts is best managed endoscopically via cyst removal or drainage and often obviates the need for permanent shunt placement.18 Intraventricular cysts may be freely mobile and imaging immediately prior to neuroendoscopic intervention is recommended to confirm the location of the cyst. A relative contraindication for endoscopic removal of intraventricular cysts is the presence of significant ependymal enhancement as this typically indicates dense adhesion between the parasitic cyst and the ependymal wall with attempted cyst removal associated with neurologic injury and intraventricular hemorrhage.14,19 A role for endoscopic surgical removal of subarachnoid cysts within the basal cisterns and subarachnoid spaces is less established due to the relatively high cyst burden and widespread subarachnoid distribution and inflammatory response. Giant (>5cm) subarachnoid cysts with associated mass effect and intracranial hypertension are most often managed surgically, although Pravda et al. demonstrated complete resolution of giant cysts in 19 of 33 patients treated medically with prolonged multi-course anthelmintic and corticosteroid therapy.20 Couldwell et al. suggested that surgical therapy be reserved for extrarenal forms of NCC if initial medical management fails or experiences neurologic decline as conventional microsurgical approaches have been associated with significant morbidity, likely due to the presence
of arachnoiditis with adherence of the cyst walls to cranial nerves and arteries. More recently, several authors have described minimally-invasive keyhole or endoscopic approaches to the basal cisterns to achieve cyst drainage, although the utility of these approaches for extensive subarachnoid disease has yet to be established. Fortunately, spillage of cyst contents with these approaches has not proven to exacerbate the inflammatory response in the postoperative period, although careful attention to this concern and copious intraoperative irrigation are recommended.33,35

In our patient with hydrocephalus and relatively rapid progression of visual loss, given the bilateral sylvian fissure involvement and absence of any dominant cystic lesion or focal neurologic deficits, we elected to proceed with placement of a ventriculoperitoneal shunt prior to initiating therapy directed against the invasive infection. Delayed exacerbation of intracranial hypertension frequently occurs several days following administration of cystidal agents as a result of cyst degeneration and subsequent host inflammatory reponse with release of proinflammatory cytokines. For this reason, steroids should be administered concomitantly with anesthetic therapy to reduce the inflammatory response. Subarachnoid cysts are considered less responsive to pharmacologic therapy compared to intra-parenchymal lesions, with albendazole the preferred drug for treatment of racemose NCC due to its superior CSF penetration compared to praziquantel. Additionally, the CNS distribution of albendazole is less effected by steroid administration.22 The dose and duration of treatment must be individually tailored to each patient depending on their parasitic burden and clinical and radiographic response to treatment with the treatment course frequently longer than that prescribed for parenchymal disease. Aggressive medical treatment has been shown to decrease the incidence of shunt malfunction which has been directly linked to poorer clinical outcome.45 For patients with giant cysts, Proaño et al. achieved excellent results with a four week course of albendazole, although more than half of their patients required more than one treatment course to achieve cyst resolution. Four of the 33 patients in their study required three or more months of therapy and ten patients also received praziquantel following a failure of the cysts to respond to albendazole.57

CONCLUSION

In our patient, we report the successful clinical resolution of racemose NCC following CSF diversion and prolonged anthelminthic therapy and corticosteroid administration to prevent development of chronic subarachnoid inflammation. No shunt complications or revisions occurred and a complete radiographic response was observed. Racemose NCC represents a fortunately rare but aggressive form of extraparenchymal NCC often resulting in basilar arachnoiditis, vasculitis, and cranial neuropathy. Proper recognition of this infection and appropriate management with careful consideration of the deleterious effects of the attendant host inflammatory response to cyst degeneration is necessary to reduce patient mortality and morbidity. Racemose NCC accompanied by intra-cranial hypertension and hydrocephalus is associated with poorer clinical outcomes, often related to ventriculoperitoneal shunt infection and malfunction. Vigilant clinical and radiographic monitoring of response to treatment is imperative to reduce neurologic sequelae and infection relapse as prolonged or multi course medical therapy is frequently necessary.

REFERENCES


Disorders of the brain and spine are complex. But finding the right doctor is simple. As the Philadelphia area’s only hospital dedicated to neuroscience, Jefferson Hospital for Neuroscience combines world-class specialists, compassionate caring, advanced treatment technologies and leading-edge research to devise aggressive treatment plans for patients with everything from aneurysms to epilepsy. And when our neurologists, neurosurgeons, radiation oncologists and radiologists put their heads together, you’re connected to the best care anywhere.

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- The PROTECT Trial – for traumatic brain injury
- The BOOST Trial – for traumatic brain injury
- The SHINE Trial – for patients following stroke
- The CLEAR Trial – for patients following stroke
- The NACTN Registry – for patients following spinal cord injury
- The POINT Trial – for patients following stroke

Our Department’s research spans the breadth of clinical neurosurgery, covering vascular and endovascular neurosurgery, functional neurosurgery, spine and peripheral nerve surgery, oncological neurosurgery, neuro-intensive care, and trauma. The Department’s Clinical Research Unit is the only clinical research unit in the region with 24/7 staffing to conduct and support ongoing neurosurgical research projects. This unit also supports vascular neurology research stroke trials. The Department also collaborates with multiple Jefferson Hospital for Neuroscience laboratories to study behavioral and systems cognitive neuroscience, the neurobiology of disease, cellular and molecular neuroscience, and translational and clinical neuroscience. Furthermore, our state of the art telemedicine program supports our research initiatives across the region.

A listing of recently published, peer-reviewed articles authored by Jefferson neurosurgery faculty is provided below.

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• Developed in collaboration with the American Academy of Neurology Society for Vascular Medicine, and Society for Vascular Surgery. for Cardiovascular Angiography and Interventions, Society of Atherosclerosis Imaging and Prevention, Society of Neuroradiology, Congress of Neurological Surgeons, American College of Radiology, American Association of Neuroscience Nurses, American Association of•

- Interparticle interactions: energy poten-

during Spinal Cord Stimulation.

- In-stent stenosis after

- Flow diversion versus traditional aneurysm embolization strate-

- Flow diversion and Traditional Embolization Strategies.


- Intraoperative Ultrasound Guidance

- Flow diversion versus traditional aneurysm embolization strategi-

- Flow diversion and Traditional Embolization Strategies.

- Flow Diversion and Traditional Embolization Strategies.


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- Flow diversion and Traditional Embolization Strategies.


- S1053-8119(13)00758-1.10.1016/j.neuroimage.2013.07.006. [Epub ahead of print]


Support Groups

Brain Aneurysm and AVM Support Group at Jefferson

The Brain Aneurysm and AVM (arteriovenous malformation) Support Group provides support for individuals, family members and friends who have been affected by cerebral aneurysms, subarachnoid hemorrhage and AVMs. The purpose of the group is to gain and share knowledge and understanding of these vascular anomalies and the consequences of these disease processes. The group provides mutual support to its members by creating an atmosphere that engenders active listening and sincere and thoughtful speech within a caring environment.

**When** Third Wednesday of every month (September through June)
**Time** 6:30-8:30 p.m.
**Place** 909 Walnut Street, 3rd Floor, Conference Room Philadelphia, PA 19107
**Moderators** Mariana Evanitsky, RN and Cynthia Labelle, RN
**Secretary** JD Galvan
**Parking** Complimentary parking is provided in the parking garage located in the JHN Building (Jefferson Hospital for Neuroscience) on 9th Street (between Locust & Walnut)

**Information** For additional information please call: 215-503-1714

The Delaware Valley Brain Tumor Support Group at Jefferson

The Delaware Valley Brain Tumor Support Group at Jefferson provides an opportunity for patients and their families to gain support in obtaining their optimal level of well being while coping with, and adjusting to the diagnosis of brain tumor. Members are encouraged to share their support strategies so members can confront the challenges that this disease process has imposed on their lives. The strength gained from group can be a source of comfort and hope for whatever lies ahead.

**When** Second Thursday of every month (except July and August)
**Time** 7:30 p.m.
**Place** Jefferson Hospital for Neuroscience, 3rd floor conference room 900 Walnut Street Philadelphia, PA 19107
**Facilitator** Alisha Amendt, CRNP 215-955-4429
Light refreshments and snacks will be served. Free parking is available at the Jefferson Hospital for Neuroscience parking lot.

**Neurosurgical Emergency Hotline**

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Overall Goals & Objectives

- Evaluate current controversies in neurosurgery
- Discuss routine occurrences in neurosurgical practice and evaluate them in terms of outcome and alternative methods of management
- Review recent advances and current therapeutic options in the treatment of various neurosurgical disorders.

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For additional information and a schedule of speakers, please contact:
Janice Longo
215-503-7008
janice.longo@jefferson.edu

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As an integral part of Jefferson Hospital for Neuroscience, the region’s only dedicated hospital for neuroscience, the Department of Neurological Surgery is one of the busiest academic neurosurgical programs in the country, offering state-of-the-art treatment to patients with neurological diseases affecting the brain and spine, such as brain tumors, spinal disease, vascular brain diseases, epilepsy, pain, Parkinson’s disease and many other neurological disorders (http://www.jefferson.edu/jmc/departments/neurosurgery.html).

As part of a larger educational initiative from the Jefferson Department of Neurological Surgery, the Jefferson Office of Continuing Medical Education is offering the following continuing professional educational opportunities for 2013-2014:

• 3rd Annual Brain Tumor Symposium: Current Innovations in Brain Tumor Treatments
  November 1, 2013
  The Ritz-Carlton, Philadelphia

• 25th Annual Pan Philadelphia Neurosurgery Conference
  December 6, 2013
  The Union League of Philadelphia

• 3rd Annual Neurocritical Care Symposium: A Case-Based Approach
  January 24, 2014
  The College of Physicians of Philadelphia

• 13th Annual Cerebrovascular Update
  March 20-21, 2014
  Hyatt at the Bellevue, Philadelphia

• 5th Annual Navigating Spinal Care Symposium
  May 2014
  Philadelphia (Location TBD)

For additional information regarding these and other Jefferson CME programs, please visit our website at http://jeffline.jefferson.edu/jeffcme/ or call the Office of CME at 888-JEFF-CME (888-533-3263).
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