TITLE: Stenosis Before Thrombosis – Intracranial Hypertension from Jugular Foramen Stenosis Secondary to Renal Osteodystrophy

AUTHORS:
Darian R. Esfahani, MD[1]; Ali Alaraj, MD[1]; Daniel M. Birk, MD[1]; Keith R. Thulborn, MD, PhD[2]; Fady T. Charbel, MD[1]

AFFILIATIONS
[1] Department of Neurosurgery, University of Illinois at Chicago, Chicago, IL, USA.
[2] Center for Magnetic Resonance Research, University of Illinois at Chicago, Chicago, IL, USA

CORRESPONDING AUTHOR
Fady T. Charbel, MD
Department of Neurosurgery (MC 799)
912 South Wood Street, 451-N NPI
Chicago, Illinois 60612
Phone (312) 996-4842
Fax (312) 996-9018

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ABBREVIATIONS
CSF: Cerebrospinal Fluid
CT: Computerized Tomography
CVST: Cerebral Venous Sinus Thrombosis
EVD: External Ventricular Drain
IIH: Idiopathic Intracranial Hypertension
MRI: Magnetic Resonance Imaging
MRV: Magnetic Resonance Venography
ONS: Optic Nerve Sheath
ROD: Renal Osteodystrophy

PREVIOUS PRESENTATIONS
None

Abstract

Background

Venous outflow obstructions are rare anatomic findings that can present with symptoms of elevated intracranial pressure, including headache and vision loss, and can be mistaken for more common diagnoses, such as idiopathic intracranial hypertension (IIH) or cerebral venous sinus thrombosis (CVST). While venous outflow obstructions have been reported in rare bone dysplasias and congenital abnormalities, to date they have not been reported in renal osteodystrophy (ROD), a relatively common disorder seen in patients with chronic kidney disease.

Case Description

In this case, the authors describe a patient with marked intracranial hypertension from jugular foramen stenosis secondary to ROD. After diagnosis by CT and magnetic resonance venography (MRV), catheter venography confirmed an osseus band around the left jugular bulb, and a 40mmHg pressure gradient across the stenotic foramen. The patient subsequently underwent ventriculoperitoneal shunting and optic nerve sheath (ONS) fenestration with symptom improvement. The postoperative course was significant for development of CVST, necessitating treatment.

Conclusions

This report reviews the presentation, pathology, and neurosurgical treatment of patients with ROD and venous outflow obstructions, and explores the differential diagnosis between outflow obstructions, IIH, and CVST. This is the first report of intracranial hypertension from jugular foramen stenosis secondary to renal osteodystrophy.

Keywords: Cerebral Venous Sinus Thrombosis, Idiopathic Intracranial Hypertension, Jugular Vein, Jugular Foramen, Pseudotumor Cerebri, Renal Osteodystrophy

Introduction

Intracranial hypertension is common in neurosurgery, and can result from a number of causes ranging from local mass effect to cerebrospinal fluid (CSF) outflow obstruction. In accordance with the Monro-Kellie doctrine, the fixed volume of the cranial vault dictates that an increase in parenchymal, CSF, or blood volume requires a compensatory decrease in another, otherwise intracranial pressure will rise[1]. The relationship between pressures of the CSF and venous space are closely coupled, with an increase in intravenous pressure associated with a greater CSF-venous transmural pressure gradient, decreasing CSF absorption and precipitating intracranial hypertension[2]. Venous pressures can be elevated in a number of conditions, including idiopathic intracranial hypertension (IIH), or pseudotumor cerebri[3], cerebral venous sinus thrombosis (CVST)[4], or, less commonly, focal sinus stenosis[5] or structural obstructions at the skull base.

Skull base venous outflow obstructions are fairly uncommon, and are reported almost exclusively as congenital cases in the pediatric literature[6-10]. Congenital stenosis of the jugular foramen has been demonstrated, for example, in anatomic studies of craniosynostosis[7], as well as achondroplasia[9], where smaller jugular foramen cross-sectional areas were measured versus controls. While congenital obstructions make up most reports, obstructions acquired over time are uncommon, and are confined to rare tumors[11] or pediatric bony dysplasias, such as osteopetrosis[8].

In this report we review the pathology, diagnosis, and neurosurgical treatment of an adult patient with renal osteodystrophy (ROD), a bone disorder from chronic kidney disease, presenting with stenosis of the jugular foramen and progressive visual loss. We review cases of ROD and venous outflow obstructions in the neurosurgical literature, and explore the differential diagnosis between outflow obstructions, IIH, CVST, and similar disorders. To date, this is the first case report of intracranial hypertension from jugular foramen stenosis secondary to ROD.

Case Report

History and Presentation

A 25-year-old man with longstanding hypertension and idiopathic end stage renal disease on dialysis presented with a two month history of worsening blurry vision and episodic vision loss. The patient was otherwise asymptomatic, denying headache, nausea, dizziness, and focal neurologic symptoms. To evaluate his complaints, he was referred to an ophthalmologist who noted marked papilledema and

diminished visual acuity at 20/200 bilaterally. The patient's remaining neurologic examination, including visual fields, was within normal limits.

Imaging Findings

The patient was sent to the emergency room where a CT of the head was performed, which revealed significant thickening of the calvarium, loss of differentiation between the inner and outer table, and granular deossification giving a "salt and pepper" appearance characteristic of renal osteodystrophy. Marked stenosis of the jugular foramen was noted bilaterally (Figure 1), as well as calcification of the falx and tentorium. An MRI was next obtained with magnetic resonance venography (MRV) (Figure 2a). Imaging demonstrated tight stenosis at the jugular foramen bilaterally, with loss of signal between the sigmoid sinus and internal jugular vein. Significant collateral flow, suggestive of longstanding, gradual stenosis was also present, without evidence of sinus thrombosis. A high volume lumbar puncture was performed which revealed an opening pressure of 55cm of water, with temporary improvement in symptoms after drainage of 25mL of cerebrospinal fluid (CSF). To evaluate for impaired venous drainage, quantitative MR angiography and venography was obtained which revealed decreased venous outflow relative to arterial influx. An initial cerebral angiogram and venogram (Figure 2b) was then performed which was negative for thrombosis but illustrated an osseous band across the left jugular bulb, limited contrast transit to the sigmoid and transverse sinuses, and a 40mmHg pressure gradient across the area of stenosis. Venous sinus stenting was considered, but not performed, because imaging exhibited circumferential bony stenosis that a stent could not dilate effectively.

Operations and Postoperative Course

The patient underwent ventriculoperitoneal shunting with image guidance and a programmable valve. Intraoperatively the calvarium was noted to be very vascular, soft, friable, and thick, with a depth of almost 2cm from inner to outer table, consistent with renal osteodystrophy. When the patient's visual symptoms persisted, the valve was gradually opened over several days without substantive improvement. The patient was subsequently referred to ophthalmology and underwent optic nerve sheath fenestration. On awakening from anesthesia after the fenestration, the patient had a seizure, a contralateral external ventricular drain (EVD) was placed, and an intracranial pressure of 30cm of water was recorded. Emergent CTV imaging revealed an "empty delta sign" suggestive of superior sagittal sinus thrombosis (Figure 3), for which the patient was started on a heparin drip.

A very small EVD tract hematoma developed after the heparin drip was started, but this did not expand and anticoagulation was continued. The heparin drip was transiently held for later removal of the

contralateral external ventricular drain and ultimate tracheostomy and gastrostomy tube placement before transition to warfarin. The remainder of the hospital course was otherwise unremarkable; the patient was discharged after an inpatient stay of forty days with an intact neurologic exam. On outpatient followup three months after discharge, the patient was found to have marked improvement of his vision to 20/40 bilaterally, with decreased papilledema. A second angiogram at that time revealed resolution of the venous sinus thrombosis and continued jugular foramen stenosis.

Discussion

This case represents a patient with intracranial hypertension from a venous outflow obstruction, jugular foramen stenosis, with subsequent development of cerebral venous sinus thrombosis. To date, it is the first report of intracranial hypertension from jugular foramen stenosis secondary to ROD. Although outflow obstructions are rare, their presentation can be similar to more common neurologic disorders, including IIH, CVST, and others. Consideration of medical conditions, like ROD, and maintaining a broad differential is essential in the evaluation and management of patients presenting with symptoms of intracranial hypertension.

Renal Osteodystrophy

Renal osteodystrophy (ROD) is an alteration of bone morphology seen in patients with chronic kidney disease[12]. ROD is characterized by varying levels of bone turnover, mineralization, and hyperostosis and is the result of hyperparathyroidism secondary to hypocalcemia and hyperphosphatemia from renal disease. Radiologically, patients with renal osteodystrophy exhibit osteomalacia, osteopenia, and exhibit areas of alternating osteolytic and sclerotic bone, with frequent calcification of the falx or tentorium. The calvarium in patients with ROD appears thick but friable, with loss of differentiation between the inner and outer tables of the skull, giving a ground-glass appearance called the “salt and pepper sign” (Figure 1)[13]. Intraoperatively, both cortical and trabecular bone in ROD can be thick, soft, and vascular, often requiring liberal use of bone wax and another methods of hemostasis. Bone changes in ROD are fairly hetereogenous between patients, ranging from focal sclerosis to substantial hypertrophy of the bones of the skull and face, referred to as uremic leontiasis ossea, or “lion face” syndrome[14]. Neurologic symptoms in ROD are very rare, however, with only sparse case reports noting vision loss from optic canal stenosis[15]. In this report, the patient developed symptoms of intracranial hypertension from progressive jugular foramen stenosis causing an obstruction of venous outflow. As the patient reported gradual worsening of his vision over several months, it is likely that hyperostosis from ROD had just approached a critical threshold at which the jugular stenosis became flow-limiting. To date this is the first report of

ROD causing symptomatic jugular foramen stenosis.

Several bone syndromes similar to ROD, however, have been associated with neurologic symptoms. Osteopetrosis[16] and fibrous dysplasia[17], for example, have both been associated with optic nerve compression, while hydrocephalus has been demonstrated in Paget's disease secondary to crowding of the posterior fossa and compression of CSF outflow pathways[18]. Although rare in adults, venous outflow obstructions have been described in pediatric anatomic studies, including congenitally smaller cross-sectional areas of the jugular foramen in craniosynostosis[7] and achrondroplasia[9] versus controls. A single pediatric case report has also reported jugular foramen stenosis, elevated intracranial pressure, and vision loss in a patient with osteopetrosis[8].

Differential Diagnosis: IIH and CVST

Idiopathic intracranial hypertension (IIH), also known as pseudotumor cerebrii, is a disorder most common in obese women of childbearing age that consists of elevated intracranial pressure presenting as headache, tinnitus, diploplia, and vision loss, including transient visual obscurations[3]. IIH is typically treated with an initial trial of acetazolamide, a carbonic anhydrase inhibitor, which reduces CSF production and lowers intracranial pressure. In patients with refractory symptoms, optic nerve sheath fenestration can be performed for worsening visual loss, and ventriculoperitoneal shunting for either intractable headache or visual symptoms[3]. Cerebral venous sinus stenting is a relatively recent option for patients who exhibit stenosis of the venous sinuses, typically the transverse or sigmoid. Although the long-term efficacy for this technique is still under study, it has been found effective in some patients, particularly those who demonstrate a significant pressure gradient across the stenotic area[19,20]. In this case, venous sinus stenting was considered, but not pursued, because the patient exhibited rigid, circumferential bony stenosis that an intravenous stent cannot dilate effectively.

Cerebral venous sinus thrombosis (CVST) shares some similarities with IIH and venous outflow obstructions in presentation. CVST is most common in women of childbearing age, and is associated with prothrombotic genetic disorders, pregnancy, use of oral contraceptives, cancer, and dehydration[4]. CVST can be diagnosed by either catheter, MR, or CT venography, the latter two which may demonstrate an "empty delta sign" (Figure 3). Patients with CVST typically present with headache, seizures, focal neurologic deficits, lethargy, and have a high rate of morbidity and mortality if not treated promptly. CVST is treated with systemic anticoagulation with careful monitoring for intracranial hemorrhage, which is common in this disease because of a high risk for venous infarction. In patients with concomitant hemorrhage, refractory thrombosis, or rapid clinical deterioration, local intravenous thrombolytics or

mechanical thrombectomy are effective second-line options. Once stabilized, patients with CVST are transitioned to oral anticoagulants for at least 3 months[4]. In this report, the patient likely developed CVST secondary to venous stasis from the outflow obstruction, with thrombosis exacerbated by the patients' multiple surgeries or prolonged hospital stay. Immediately after surgery, carbon dioxide retention may have further contributed to a transient ICP elevation, decreased venous drainage, and higher risk for CVST development.

Strategies for Venous Outflow Obstructions

Although rare, patients with venous outflow obstructions present with many similar symptoms as IIH and CVST. Symptoms of elevated intracranial pressure, including headache, decreased visual acuity, or episodic vision loss, as was the case in this patient, are common, and often present in a progressive manner. When presented with these symptoms, the neurosurgeon should start with a thorough clinical history and review risk factors, including bone disorders or longstanding renal failure, followed by a detailed neurologic examination, including funduscopic exam to assess for papilledema. CT imaging, often completed before consultation, can provide useful information about bone morphology. On reviewing CT images, careful attention should be devoted to the skull base and jugular foramenae (Figure 1), particularly if a bone disorder is suspected.

CT or magnetic resonance venography (Figure 2a) is the initial imaging modality of choice in the diagnosis of a venous outflow obstruction, and is necessary to rule out CVST or focal areas of intracranial sinus stenosis. Turbulent flow at the jugular foramen, however, can make MRV imaging at the skull base difficult to interpret. In such cases, quantitative flow measurements or a conventional cerebral angiogram (Figure 2b) are helpful. Of note, a high suspicion for development of CVST (Figure 3) must be maintained during workup and treatment of these patients, as outflow obstructions place patients at risk of venous stasis and development of thrombosis, as was the instance in this case.

Once diagnosed, a lumbar puncture may be performed to confirm elevated intracranial pressures, after which either ventriculoperitoneal shunting or optic nerve sheath fenestration are reasonable surgical options for control of symptoms. Cerebral venous sinus stenting will not be effective if the outflow obstruction is secondary to rigid bony stenosis, but warrants consideration. If patient symptoms persist despite both of these interventions, surgical decompression of the jugular foramen remains an option, however this procedure carries risk and should be reserved as an intervention of last resort.

Conclusions

This case is the first report of intracranial hypertension secondary to jugular foramen stenosis from renal osteodystrophy. Although outflow obstructions are rare, their presentation can be similar to more common neurologic disorders, including idiopathic intracranial hypertension and cerebral venous sinus thrombosis. In patients presenting with symptoms of intracranial hypertension, the neurosurgeon should maintain a broad differential and consider medical conditions, including osteodystrophies. If suspected, careful evaluation of the skull base should be performed to assess for outflow obstructions.

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295 260.

296 **Figure Legends**
297
298 **Figure 1**. CT images of the skull show marked jugular foramen stenosis (arrows) in this renal
299 osteodystrophy patient on both axial (**A**) and sagittal (**B**) views compared to a healthy control (**C** and **D**).
300 Left side shown in all images. Loss of differentiation of the inner and outer tables, the "salt and pepper"
301 appearance, and calcification of the cerebellar tentorium are also visible in the renal osteodystrophy
302 patient (**B**, arrowheads).
303
304 **Figure 2.** MR venography revealed an area of tight stenosis at the jugular foramen, with a loss of signal
305 between the sigmoid sinus and internal jugular vein (**A**, arrow). Significant collateral venous flow (**A**,
306 arrowhead) is suggestive of longstanding stenosis. Catheter venography redemonstrated this area of
307 jugular foramen stenosis, with limited contrast transit to the sigmoid and transverse sinuses (**B**, arrow).
308 Left side shown in both images.
309
310 **Figure 3.** Later CT venography demonstrated a thrombus in the superior sagittal sinus (**A**, arrow), the
311 "empty delta sign". This thrombus is also apparent on sagittal view (**B**, arrow), along with calcification of
312 the falx (arrowhead).