

## Increased Intracranial Pressure in a Boy with Gorham-Stout Disease

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### Key Words

Gorham-Stout disease · Intracranial hypertension · Headache · Migraine

### Abstract

Gorham-Stout disease (GSD), also known as vanishing bone disease, is a rare disorder, which most commonly presents in children and young adults and is characterized by an excessive proliferation of lymphangiomatous tissue within the bones. This lymphangiomatous proliferation often affects the cranium and, due to the proximate location to the dura surrounding cerebrospinal fluid (CSF) spaces, can result in CSF leaks manifesting as intracranial hypotension with clinical symptoms to include orthostatic headache, nausea, and vertigo. We present the case of a boy with GSD and a known history of migraine headaches who presented with persistent headaches due to increased intracranial pressure. Although migraine had initially been suspected, he was eventually diagnosed with intracranial hypertension after developing ophthalmoplegia and papilledema. We describe the first known instance of successful medical treatment of increased intracranial pressure in a patient with GSD.

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### Introduction

Gorham-Stout disease (GSD), also known as vanishing bone disease, is a rare disorder, which most commonly presents in children and young adults and is characterized by an excessive proliferation of lymphangiomatous tissue within the bones [1]. This lymphangiomatous proliferation most frequently affects the cranium and axial skeletal bones [2] and, due to the proximate location to the dura surrounding cerebrospinal fluid (CSF) spaces, can also

result in CSF leaks manifesting as intracranial hypotension with clinical symptoms to include orthostatic headache, nausea, and vertigo [3–6]. We are presenting the case of a boy with GSD who presented with headaches due to increased intracranial pressure.

### Case Presentation

An 8-year-old boy with a known diagnosis of GSD presented with a worsening, nearly continuous headache. The patient's diagnosis of GSD was made at the age of 5 after an episode of left jaw swelling, for which imaging revealed lytic lesions of the skull base, clivus, left mandible, and first cervical vertebra (fig. 1). These lesions had remained stable with interval imaging.

The patient's prior headache history was that of episodic migraine headaches occurring every several months, for which he was on cyproheptadine 4 mg twice daily for prophylaxis. This most recent headache was similar to his prior headaches but had now lasted over 1 week. It was described as frontal in location, severe, throbbing, and squeezing, and with associated nausea and vomiting, photophobia, and phonophobia. A consistent positional worsening while lying supine was not reported.

He was initially evaluated in the emergency department (ED) after the first week of headaches and had a head computed tomography (CT) scan and lumbar puncture (LP) performed due to his additional symptoms of fatigue and vomiting. The head CT was without abnormalities of the brain, and the CSF profile was normal, but an opening pressure was not measured. The patient experienced some relief in the ED after receiving intravenous fluids (acetaminophen) and after the LP. The patient was taking no other chronic medications, had a normal BMI and blood pressure, and had a normal laboratory workup.

One week later, due to continued and worsening headaches, he was admitted for further headache management. His neurological examination was nonfocal, although a fundoscopic examination was difficult due to his severe photophobia. Magnetic resonance imaging (MRI) of the brain and MR angiography and venogram of the brain were normal, with the patient's known bony lesions remaining stable in appearance. The patient was initially treated in the hospital with intravenous ketorolac without improvement and then intravenous dihydroergotamine with mild improvement. The patient seemed to be feeling somewhat better, although still with a mild headache, and was discharged home.

One week later, the patient returned to the ED with a new symptom of horizontal diplopia, along with his headache that had continued to persist. On examination, he presented with right eye esotropia with horizontal diplopia in primary gaze and with limited abduction of the right eye with right lateral gaze (fig. 2), which produced a worsening of the horizontal diplopia. Formal ophthalmological examination also revealed bilateral papilledema.

The patient was readmitted, and a repeat brain MRI was performed without new abnormalities noted. LP was performed, and his opening pressure in the lateral decubitus position and his legs relaxed was 53 cm H<sub>2</sub>O. The LP was completed with a final closing pressure of 28 cm H<sub>2</sub>O, as he had reported that his headache was completely resolved at the conclusion of the LP. Analysis of his CSF revealed a normal profile to include no pleocytosis. The patient was started on oral acetazolamide, titrating up to 500 mg twice daily.

The patient's ophthalmoplegia resolved completely within 3 weeks and has not returned since then in 2 years of follow-up. His headaches have recurred intermittently but have responded readily to increasing doses of acetazolamide and the addition of low-dose topiramate. Formal visual fields have not revealed any visual field deficits.

## Discussion

Intracranial hypertension describes the clinical and physiological occurrence of increased intracranial pressure. The term idiopathic intracranial hypertension is often used when there is an absence of a space-occupying lesion, ventriculomegaly, or CSF inflammation, but the delineation between idiopathic and secondary intracranial hypertension is not always so clear. The underlying pathogenesis has not been clearly defined, but current theories highlight the link between the lymphatic system and CSF reabsorption. Due to the wide range of possible underlying risk factors that predispose to intracranial hypertension, it is likely that differing mechanisms are involved with the varying etiologies. Some of these risk factors that can predispose to intracranial hypertension include systemic conditions, infections, endocrine abnormalities, and certain medications (specifically antibiotics, isotretinoin, and endocrine hormonal therapies) [7].

Headache is the most common presentation of intracranial hypertension in children; however, the headache characteristics can be variable [8]. Some features that are more suggestive of headache due to intracranial hypertension include worsening when supine, worsening with valsalva maneuvers, nocturnal or early-morning headaches, and visual disturbances [8]. However, headaches due to intracranial hypertension can often resemble, and be difficult to differentiate from, migraine headaches, with photophobia, phonophobia, and nausea possibly presenting with both headache types [9].

The examination finding most suggestive of intracranial hypertension is papilledema, a reflection of bilateral optic disk swelling. Abducens (cranial nerve VI) palsies may occur due to stretching of the VI nerve over the petrous tip due to downward displacement of the brainstem from the increased intracranial pressure. Patients with abducens nerve palsies will often complain of horizontal diplopia, often worsening with ipsilateral gaze. Other examination findings that can be present are visual field abnormalities, to include enlargement of the physiological blind spot or constriction of the visual fields.

Measurement of the opening pressure and exclusion of meningeal inflammation with LP is required to accurately diagnose intracranial hypertension. However, neuroimaging should be obtained first to evaluate for structural abnormalities. When no contributing abnormalities such as intracranial masses are found on neuroimaging, the term idiopathic intracranial hypertension is often used. Some MRI features that are nonspecific but have been associated with idiopathic intracranial hypertension include an empty or partially empty sella, flattening of the posterior globe of the eyes, and optic nerve sheath enlargement [10]. LP should be obtained for opening pressure with the patient in the lateral decubitus and leg-relaxed position. Many consider an elevation of opening pressure over 28 cm H<sub>2</sub>O to represent an abnormality signifying intracranial hypertension [7], but the opening pressure is one part of the data that should be used in the context of clinical judgement. For example, the relief of headache after lowering the intracranial pressure with adequate CSF removal (resulting in a lower closing pressure upon completion of the LP) is supportive of a diagnosis of intracranial hypertension.

The treatment of intracranial hypertension is aimed at not only decreasing headaches but, more importantly, preserving vision. Carbonic anhydrase inhibitors such as acetazolamide are often used, but other diuretics such as furosemide as well as other carbonic anhydrase inhibitors such as topiramate can be used as alternatives or as supplemental therapy. When medical therapy fails, however, surgical management to preserve vision can include optic nerve sheath fenestrations and ventriculoperitoneal or lumboperitoneal shunt placement.

Our patient presented initially with what was thought to be his typical migraine headaches with vascular features. However, due to its persistence and, finally, the presentation of his abducens palsy with diplopia, a LP that was both diagnostic and therapeutic was performed. Unfortunately, due to his severe photophobia, a good funduscopic examination had not been possible until he presented with his abducens palsy and formal ophthalmological examination was utilized at that time due to the high clinical suspicion of intracranial hypertension.

Of particular interest is our patient's diagnosis of GSD. GSD, also known as vanishing bone disease, is a rare disorder that most commonly presents in children and young adults and is characterized by an excessive proliferation of lymphangiomatous tissue within the bones [1]. This lymphangiomatous proliferation can affect any bone in the body but most frequently affects the cranium and axial skeletal bones [2], with resulting progressive osteolysis and bone destruction. Visceral involvement can occur, inducing complications such as chylothorax with pleural effusions [2]. Bony lesions proximate to the dura and surrounding CSF spaces can also result in CSF leaks, manifesting as otorrhea and concomitant meningitis [11]. In addition, there have been several cases in the literature reporting patients with GSD and CSF leaks with subsequent intracranial hypotension requiring surgical repair [3–6], with clinical symptoms to include orthostatic headache, nausea, and vertigo. In 1 of these cases, the authors reported a patient with GSD in whom it was felt that intracranial hypertension was the cause of the patient's subsequent CSF leak [12].

It is not clear whether there is an association between increased intracranial hypertension and GSD, but a possible mechanism could be that the abnormal lymphangiomatous tissue found in patients with GSD leads to a rise in the resistance to CSF reabsorption that could explain the increased intracranial pressure. However, it seems clearer based upon case reports that patients with GSD are at risk for intracranial hypotension due to CSF leaks into proximate bony lesions. Thus, any risk for CSF leakage should be diagnosed and addressed as early as possible to include the occurrence of intracranial hypertension.

## Conclusion

Primary headaches such as migraine headaches occur commonly in children, but alternative headache etiologies should be suspected when pediatric patients either do not respond to treatments, develop new neurological signs or symptoms, or when there is a known underlying pathology. Measurement of opening pressure with LP should be pursued following neuroimaging in those patients suspected of possibly having intracranial hypertension.

We describe the first known instance of successful medical treatment of increased intracranial pressure in a patient with GSD. We believe early diagnosis and treatment could represent a mechanism for preventing spontaneous CSF leaks in patients with GSD, bringing up a possible theory to stimulate further research.

## Statement of Ethics

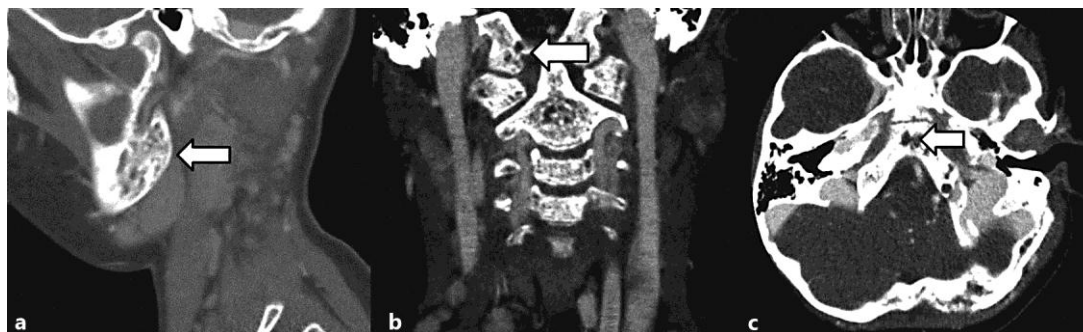
Verbal assent from the patient and written consent from the patient's mother was obtained.

## Disclosure Statement

The authors declare that there is no conflict of interest regarding the publication of this paper. The view(s) expressed herein are those of the author(s) and do not reflect the official policy or position of the San Antonio Military Medical Center, the U.S. Army Medical Department, the U.S. Army Office of the Surgeon General, the Department of the Army, the Department of the Air Force and Department of Defense or the U.S. Government.

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**Fig. 1.** CT of the skull and cervical spine reveals multiple bony lytic lesions (arrows): **a** sagittal, left mandible, **b** coronal, cervical vertebra and occipital condyles, and **c** axial, clivus.



**Fig. 2.** The patient presented with limited abduction of the right eye with right lateral gaze (**a**), causing a worsening horizontal diplopia and a right esotropia in primary gaze (**b**). No diplopia was induced with left lateral gaze (**c**).