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Case report

Cerebrospinal fluid leakage and Chiari I malformation with Gorham's disease of the skull base: A case report

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ABSTRACT

Background: Gorham's syndrome is a rare bone disorder characterized by massive osteolysis of unknown etiology. There are no reports of comorbidity involving cerebrospinal fluid (CSF) leakage and Chiari I malformation with Gorham's syndrome. Here, we report an unusual case of an acute presyrinx state complicated by bacterial meningitis due to CSF leakage and Chiari I malformation associated with Gorham's disease of the skull base.

Case presentation: A 25-year-old woman with Chiari I malformation associated with Gorham's syndrome presented with aggressive paresthesia following bacterial meningitis. Axial magnetic resonance imaging (MRI) and computed tomography (CT) cisternography revealed CSF leakage in the right petrous apex. A presyrinx state was diagnosed based on the clinical symptoms and MRI findings. With resolution of the bacterial meningitis, the spinal edema and tonsillar ectopia also improved. Surgical repair of the CSF leakage was performed by an endoscopic endonasal transsphenoidal approach to prevent recurrence of meningitis. The postoperative course was uneventful.

Conclusion: Skull base osteolysis in Gorham's syndrome may induce Chiari I malformation and CSF leakage. We should pay attention to acute progression of clinical symptoms because Gorham's syndrome may predispose to development of Chiari I malformation and may be complicated by CSF leakage.

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1. Introduction

Gorham's syndrome is a rare bone disorder characterized by massive osteolysis and lymphangiomatosis of unknown etiology. Approximately 200 cases have been reported to date.

Only 3% of cases with Gorham's syndrome have had skull base involvement [1]. Chiari I malformations associated with Gorham's syndrome are extremely rare and have been reported in only 7 cases to date [1–3]. In addition, cerebrospinal fluid (CSF) leakage and recurrent meningitis has been described in only 5 cases [4–7]. Most importantly, there are

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no reports of combined cases of CSF leakage and Chiari I malformation with Gorham's syndrome. Here, we report an unusual case of an acute presyrinx state complicated by bacterial meningitis due to CSF leakage and Chiari malformation associated with Gorham's syndrome involving the skull base.

2. Case presentation

A 25-year-old woman had been treated for meningitis 5 years earlier in another hospital. Computed tomography (CT) revealed a lytic lesion of the right petrous apex, craniocervical junction, and right occipital bone. Biopsy of the osteolytic lesion in the right occipital bone was performed. The histopathological diagnosis was Gorham's syndrome (Fig. 1a, b). A fistula of the dura mater in the right petrous bone was expected due to a past history of meningitis. However, there was no pneumocephalus and no obvious CSF leakage. Therefore, the patient was treated with intravenous antibiotics for 1 month and discharged without any neurologic complications.

The patient was followed up subsequently for 5 years and showed no symptoms. She was then transferred to our hospital due to relocation. The patient was followed up as an outpatient, until she developed a headache with high fever for 3 days. The headache became progressively worse, and she developed impaired consciousness with a Glasgow Coma Scale score of 14 (E3 M5 V6). Physical examination revealed a stiff neck and Kernig's sign was positive. No CSF rhinorrhea was evident. There was low-tone hearing loss in the right ear. Laboratory tests revealed a leukocyte count of 17,700 cells/ μ l with 98% polymorphonuclear cells, and C-reactive protein (CRP) of 0.09 mg/dl. Lumbar puncture revealed a normal opening pressure of 10 cm H₂O (normal: 5–15 cm H₂O). CSF cytology demonstrated increased white blood cells up to 7160 white cells/ μ l (98% were polymorphonuclear cells), elevated levels of protein (658 mg/dl; reference range: 15–45), and low glucose concentration (<1 mg/dl; reference range: 40–70 mg/dl). These findings suggested bacterial meningitis. CT revealed a lytic lesion of the right petrous apex and craniocervical junction (Fig. 2a, b). CT cisternography showed leakage of contrast medium in the right petrous apex and occipital condyle (Fig. 2c, d). Axial magnetic resonance imaging (MRI)

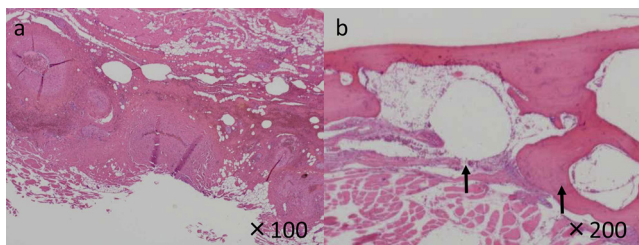


Fig. 1 – Biopsy of osteolytic bone showing fibrosis, vascular and lymphatic channels. Hematoxylin and eosin, $\times 100$ (a). Biopsy of osteolytic bone showing proliferation of thin walled vascular channels (arrow) and osteolytic bone. Hematoxylin and eosin, $\times 200$ (b).

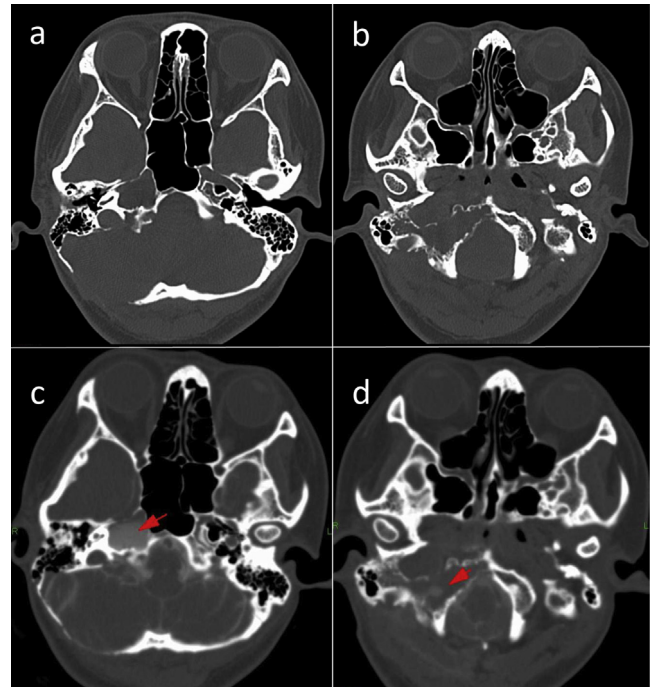


Fig. 2 – CT and CT cisternography on admission. Noncontrast axial CT. Thinner skull base and partially lytic lesion in the right petrous apex and occipital bone (a, b). CT cisternography (3 h after intrathecal injection of iotrolan) revealing asymmetric CSF leakage (red arrow) at the right petrous apex (c) and occipital condyle (d). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

revealed CSF leakage in the right petrous apex (Fig. 3a). Development of mild tonsillar ectopia was evident on sagittal fluid-attenuated inversion recovery MRI, with the tip of the cerebellar tonsils protruding 7 mm below the foramen magnum with a C2-5 mild high-intensity area (Fig. 3b). The patient has hospitalized with bacterial meningitis. Ceftriaxone 12 g/day and vancomycin 1.25 g/day were started.

On hospital day 3, the patient developed paresthesia. Sagittal MRI revealed upper spinal edema with syringomyelia, with the tip of the cerebellar tonsils protruding 20 mm below the foramen magnum on midline sagittal images (Fig. 4a, b). MRI of the cervical spine revealed swelling of the cervical cord at the C2-T4 level, with an intramedullary hyperintensity on T2-weighted images (T2WI) and hypointensity on T1 weighted images (T1WI). The diagnosis was a presyrinx state due to exacerbation of tonsillar ectopia associated with intracranial hypertension due to bacterial meningitis or bacterial myelitis. A CSF culture yielded *Streptococcus agalactiae*. We started penicillin G 12 g/day and concentrated glycerin 400 ml/day. We decided to follow up by continuing the antibiotic and concentrated glycerin. We scheduled foramen magnum decompression in case the symptoms did not improve. The meningitis and other symptoms were treated conservatively.

On hospital day 15, MRI revealed improvement of the swelling of the cervical cord and tonsillar ectopia (Fig. 4c, d).

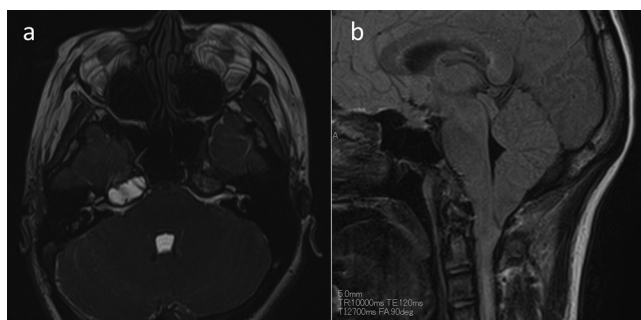


Fig. 3 – MRI on admission. T2WI MRI (a) showing fluid accumulated in the right petrous apex, suggesting a CSF leak. Sagittal fluid-attenuated inversion recovery MRI (b) demonstrating the tonsillar ectopia with the tip of the cerebellar tonsils protruding 7 mm below the foramen with a C2-5 mild high intensity area.

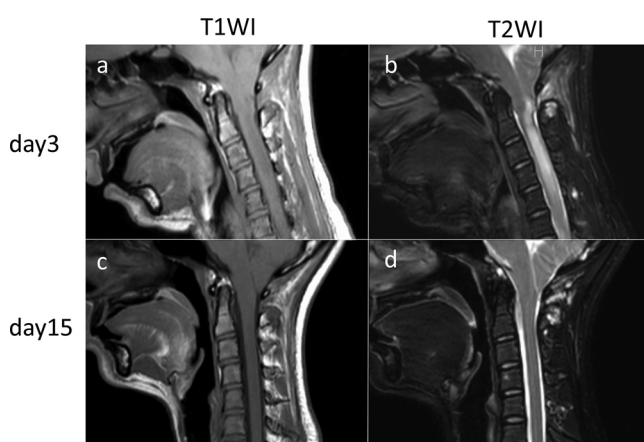


Fig. 4 – Sagittal MRI on hospital day 3 and day 15. Sagittal T1WI (a) and T2WI (b) on hospital day 3 (when the paresthesia appeared) demonstrate tonsillar ectopia progression with new enlargement and marked T2 hyperintensity at the spinal cord. Follow-up sagittal T1WI (c) and T2WI (d) on hospital day 15 (when the paresthesia improved) demonstrate the disappearance of the T2 high signal intensity and the tonsillar ectopia improved.

Lumbar puncture revealed a normal opening pressure of 10 cm H₂O (normal: 5–15 cm H₂O). There was no growth on CSF culture, and cytology showed only a few lymphoid cells. We decided to follow up by continuing antibiotic prescription for 42 days.

On hospital day 57, repair of the CSF leakage at the right petrous apex was performed using an endoscopic endonasal transsphenoidal approach. When exploring the petrous apex, a clear fluid came out from the petrous apex. These defects were covered with a superficial abdominal fat pad and nasoseptal flap, and were sealed with fibrin glue. The postoperative course was uneventful. The spinal drain was removed 3 days after surgery. Postoperative CT cisternography showed no CSF leakage in the right petrous apex and occipital

condyle. The patient was discharged 18 days after surgery. MRI performed 3 months after surgery demonstrated reappearance of a T2-high lesion at the right petrous apex suggesting recurrence of the fistula. As there was no clinical evidence of CSF leakage, the patient is now being followed up closely on an outpatient basis.

3. Discussion

In our case, this patient may have developed Chiari malformation due to bone resorption and then experienced neurological deterioration after continuous CSF leakage. We made a diagnosis of the acute presyrinx state due to exacerbation of tonsillar ectopia associated with intracranial hypertension from meningitis, or the pressure difference between cranial and spinal subarachnoid space by diagnostic lumbar puncture. The findings that neurological symptoms and the high-signal intensity lesions on T2WI improved with the improvement of meningitis and tonsil ectopia were suspected to be the presyrinx state. Gorham's syndrome may be potentially associated with Chiari I malformation, and CSF leakage may complicate the condition leading to a presyrinx state. Therefore, we require attention for acute progression of symptom when these comorbid conditions occur.

3.1. Gorham's syndrome

Gorham's syndrome is a rare disease of unknown etiology characterized by proliferation of endothelial-lined vessels in the bone and the progressive destruction of bone [8]. Approximately 200 cases have been reported to date. Gorham's syndrome appears to occur sporadically in childhood or young adulthood. It may affect any bone, and patients may present with innumerable symptoms in an affected region. The diagnosis is made on the basis of clinical, radiological, and histopathological evidence [9]. CT reveals osteolysis of the diseased bone. MRI shows that affected bones may be examined using a low signal intensity on T1WI and high signal intensity on T2WI. Enhancement of the lesions may be observed following intravenous administration of gadolinium. Histopathological examination reveals a non-malignant proliferation of the vascular channels of lymphatic origin in bone, which appears as progressive osteolysis. There is no standard therapy available due to the rarity of the disease. The treatment options include surgery, radiotherapy, etidronate therapy, and the use of interferon α -2b [10]. Surgical treatment is effective but does not always prevent progression. The natural history is variable and usually dependent on the affected sites, but in general the prognosis is typically favorable.

3.2. Association with Chiari I malformation

Chiari I malformation is a craniocervical junction disorder associated with deformity and elongation of the cerebellar tonsils [11]. Changes in the CSF flow in the foramen magnum frequently lead to development of syringomyelia. Gorham's syndrome can predispose the onset of Chiari I malformation due to a process of skull base softening, remodeling, and

settling, particularly in the occipitocervical region [1,2]. Only 3% of Gorham's syndrome cases have had skull base involvement. Of these, Chiari I malformations have been observed extremely rare. Seven cases of Chiari I malformation associated with Gorham's syndrome have been previously reported (Table 1) [1-3]. Five of the 7 patients with Chiari I malformation had occipital bone erosion around the foramen magnum.

In our case, Chiari I malformation is likely because the patient has a pointed tonsillar tip, but it cannot be determined without sagittal MRI before the admission. Many patients acquired Chiari I malformation also have mild tonsillar displacement before the onset of symptom. The intracranial hypertension associated with meningitis might cause acute tonsillar displacement, or the diagnostic lumbar puncture might contribute the symptom onset and tonsillar displacement. The pressure difference between cranial and spinal subarachnoid space may cause tonsillar displacement. Importantly, Chiari I malformation should be included in the differential diagnosis of Gorham's syndrome located in skull base, specifically in the occipital bone. Furthermore lumbar puncture should be performed carefully in that case.

Surgical treatment may be appropriate in cases of Chiari I malformation associated with Gorham's syndrome. Of the 7 previously reported cases of Chiari I malformation associated

with Gorham's syndrome, 2 patients were managed conservatively, 1 patient's treatment was unknown, and 4 patients underwent foramen magnum decompression [1]. In the 4 operated cases, there was no recurrence. However, it is possible that surgical treatment may exacerbate osteolysis [1]. We succeeded with conservative management; the patient had no neurological deficits. Because foramen magnum decompression can lead to exacerbate osteolysis and collapse of craniocervical junction already weakened by the pathological process, it is necessary to decide on surgical adaptation carefully. Acute exacerbation of Chiari I malformation might be reversed by stopping CSF leakage.

3.3. Association with cerebrospinal fluid leakage

Meningitis secondary to CSF leakage is a potentially fatal complications of Gorham's syndrome. Of the 5 previously reported cases of Gorham's syndrome with CSF leakage (Table 2) [4-7], 2 patients had meningitis. Three of 5 patients had CSF leakage from the petrous bone, but the patients did not present with apparent rhinorrhea [4,5]. Therefore, CT findings are useful to detect the extent of bone destruction, and T2WI MRI can reveal abnormal CSF. In addition, CT or MR cisternography and radioisotope (RI) were useful to diagnose CSF leakage. Importantly, we should be careful with CSF

Table 1 – List of the literature on case with Chiari malformation associated with Gorham's syndrome.

Year	Author	Age (years)	Sex	Skull base involvement of osteolysis	FMD
2003	Jea et al.	4	F	Yes	Yes
2006	Agrawal et al.	25	F	Unknown	Unknown
2006	Girn et al.	2	F	Yes	No
2006	Puertas et al.	17	M	Yes	Yes
2007	Pavenello et al.	4	M	Yes	No
2010	Hughes et al.	4	M	No	Yes
2014	Coulter et al.	37	F	Yes	Yes
2016	Present case	25	F	Yes	No

FMD, foramen magnum decompression.

Table 2 – List of the literatures on case with cerebrospinal fluid leakage associated with Gorham's syndrome.

Year	Author	Age (years)	Sex	Rhinorrhea	Meningitis	Other symptoms	Osteolytic lesion of skull base	Repair of CSF leakage
1990	Evans et al.	4	F	None	Yes	Facial swelling	Left temporal bone (petrous bone)	Combined transmastoid/middle fossa approach
1990	Nazarian et al.	19	F	None	Yes	Ear effusion, facial swelling	Left temporal bone (petrous bone)	Transmastoid approach
2010	Cushing et al.	12	M	None	None	Hearing loss	Right temporal bone (petrous apex), mandibular condyle	Transmastoid approach
2011	Hernandez et al.	2	M	Otorrhea	Yes	Ear infection	Right temporal bone (petrous bone)	Transmastoid approach
2013	Morimoto et al.	11	F	None	None	Hearing loss	Right temporal bone (petrous apex)	Extradural middle fossa approach
2016	Present case	25	F	None	Yes	None	Right temporal bone (petrous apex) occipital bone	Endonasal endoscopic approach

CFS, cerebrospinal fluid.

leakage in Gorham's syndrome with skull base osteolysis, specifically in the petrous bone. An extradural middle fossa approach and trans-mastoid approach with a temporal fascia flap were performed in two previous cases [5]. Endoscopic endonasal CSF repair can be a treatment option, as in our case.

3.4. Presyrinx state

A presyrinx state has been described as the reversible change of an intramedullary high signal intensity on T2WI MRI as a result of abnormal CSF flow dynamics at the craniocervical junction; examples include Chiari malformations, cervical stenosis, and basilar meningitis [12]. There is no contrast enhancement, and the signal abnormality is attributed to interstitial cord edema of controversial etiology. In fact, it is difficult to differentiate presyrinx state from bacterial myelitis by radiologic findings alone, because of similar imaging characteristics. Commonly, *Mycoplasma pneumoniae* and infectious granulomatous disease (*Tuberculosis*, *Syphilis*, and *Brucellosis*) occur as a bacterial myelitis. In addition, the other bacterial myelitis occurs as a result of compression or ischemia associated with accumulation of purulent exudate in subarachnoid space and immune reaction [13,14].

4. Conclusion

Skull base osteolysis in Gorham's syndrome may cause Chiari I malformation and CSF leakage. CT and MRI, including upper cervical studies, may be helpful to detect asymptomatic Chiari malformation and CSF leakage with Gorham's syndrome. In addition, we should pay attention to acute progress of clinical symptoms because the Gorham's syndrome has a potential of Chiari I malformation and may be complicated with meningitis from CSF leakage.

Consent

Written informed consent for publication of this case report and accompanying images was obtained from the patient's mother. A copy of the written consent is available for review by the editor of this journal.

Authors' contribution

HN wrote the entire manuscript. KM carried out the literature search and revised the manuscript. KM and YY were the patients' attending doctors and assisted in the operation. MT performed the patient's operation, helped draft the manuscript, and revised the manuscript. EK revised and helped draft the manuscript. All authors read and approved the final manuscript.

Conflict of interest

None declared.

Acknowledgement and financial support

None declared.

Ethics

The work described in this article was conducted in accordance with the World Medical Association (Declaration of Helsinki) Ethical Principles for Medical Research Involving Human Subjects and uniform requirements for manuscripts submitted to Biomedical Journals.

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