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CASE REPORT

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Gorham-Stout Disease of the Cranial Bone Causing Recurrent Cerebrospinal Fluid Rhinorrhea and Bacterial Meningitis

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Gorham-Stout disease (GSD) is a rare disorder characterized by the proliferation of vascular tissue in the bones and the progressive destruction of bones. We report the case of a 25-year-old man with GSD involving the cranial bone, who presented with recurrent cerebrospinal fluid (CSF) rhinorrhea and bacterial meningitis. Because of the rarity of this disease, arriving at the diagnosis of GSD was challenging. After excluding other etiologies, the clinical and radiological findings helped us to make a diagnosis of GSD. Serial computerized tomography scans and brain magnetic resonance imaging findings over a long period of time were crucial in the diagnosis of GSD. The patient required surgical repair of the CSF leak using a septal flap. Recently, the efficacy of sirolimus has been shown in several studies. Therefore, our patient was referred to a specialist in this disease, and sirolimus was started.

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Gorham-Stout disease (GSD) is a rare bone disorder, otherwise called vanishing, disappearing, or phantom bone disease.[1] It is characterized by idiopathic, progressive, and extensive osteolysis with localized proliferation of vascular tissue.[2] A recent review of the literature noted approximately 200 cases of GSD, of which only 3% had skull base involvement.[3] Few cases with cerebrospinal fluid (CSF) leakage and recurrent meningitis secondary to GSD with skull involvement have been reported. Only three cases of CSF rhinorrhea and recurrent meningitis related to GSD have been reported.[4-6] To our knowledge, ours is the first case of GSD in Korea to present with recurrent CSF rhinorrhea and bacterial meningitis.

Here we present the case of our patient with recurrent CSF rhinorrhea and bacterial meningitis related to an approximately 10-year period of erosion of the cranial bone. We describe the clinical features, diagnostic process, and treatment of GSD involving the cranial bone and causing recurrent CSF leakage and bacterial meningitis.

CASE REPORT

A 25-year-old man visited our emergency department in July 2018, presenting with headache, nausea, and vomiting for a 1-day period. His headache worsened when he stood up and was accompanied by fever and chills. He also presented with rhinorrhea from the right nostril that had been present for months. He had developed CSF rhinorrhea in 2006. He first noticed watery discharge from his left nostril in 2006, which was finally diagnosed as CSF rhinorrhea in 2011. At that time, the CSF leakage point was localized to the left lateral wall of the sphenoid sinus by intrathecal fluorescein injection through a lumbar drain. This was treated by covering it with a septal flap. There had been no CSF leakage until recently. He had a history of bacterial meningitis in 2007, which had improved with antibiot-

ic treatment without any sequelae. He had a history of falling off a bicycle when he was 6 years old.

His neurologic examination findings were normal except for neck stiffness. Lumbar puncture revealed a normal opening pressure of 5 cm H_2O, 882 leukocytes (94% polymorphonuclear leukocytes, 4% lymphocytes, 2% other cells), glucose 45 mg/dL with a blood glucose of 94 mg/dL, and protein 159 mg/dL. No organisms were detected on Gram staining or isolated in the culture. Polymerase chain reaction results of CSF samples for virus and tuberculosis were all negative. No fungal antigen was detected in either the serum or CSF specimens. Cytology studies showed no malignant cells. At presentation, a computerized tomography (CT) scan of the head showed skull destruction with osteolytic changes in the right frontal bone, right temporal bone and body, and lesser wing and pterygoid plate of the right sphenoid bone (Fig. 1C-F). There had been no abnormality in the skull on a CT scan performed when he had fallen in 2001 (Fig. 1A). However, when he was admitted for treatment of bacterial meningitis in 2007, his CT scan showed mild cortical thinning and erosion of the right frontal, temporal, and sphenoid bone (Fig. 1B). The cortical thinning had progressed, and marked osteolytic bone destruction was identified on a CT scan performed in 2018 (Fig. 1C, D). Brain magnetic resonance imaging (MRI) demonstrated right-sided lytic bony lesions and revealed multifocal T2 hyperintense lesions of the right frontal, parietal, and sphenoid bones and left temporal bone with heterogeneous enhancement on T1-weighted contrast-enhanced imaging. These were matched with lytic lesions on his CT

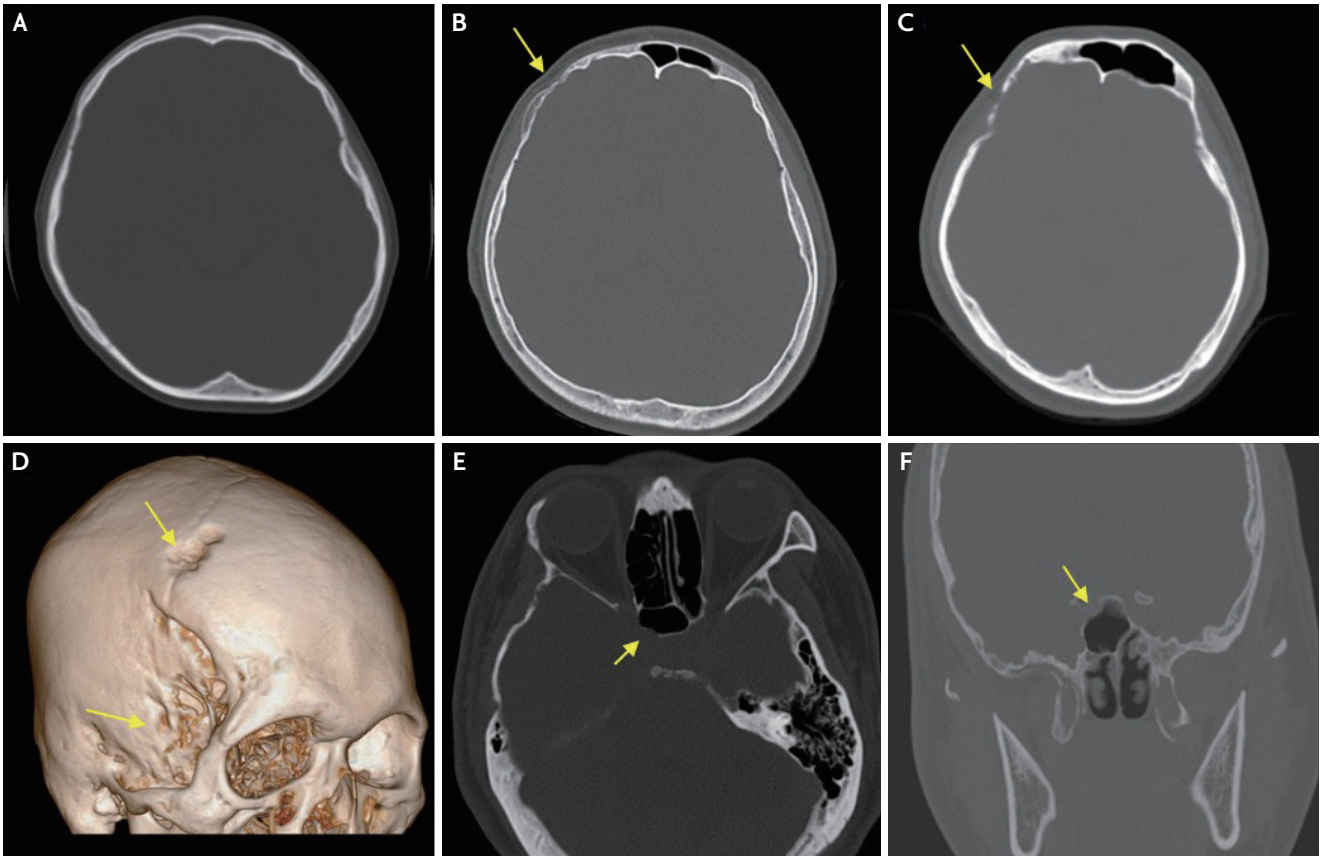

Fig. 1. Serial brain CT scan, 3D reconstruction, and OMU CT scan. Serial brain CT scans over a period of more than 10 years revealed progressive cortical thinning of the skull, especially the right frontal bone, right temporal bone and body, and lesser wing and pterygoid plate of the right sphenoid bone. Brain CT performed in 2001 (A) when he fell showed no evidence of cortical thinning, but his CT scan performed in 2007 (B) when he was admitted for bacterial meningitis showed mild erosion of the right frontal bone (yellow arrow). In 2018, the bony destruction had progressed, and extensive cortical thinning (yellow arrow) was identified on a CT scan (C) and the 3D reconstruction of it (D). He underwent an OMU CT for his rhinorrhea, which showed a bony defect (yellow arrow) on the posterior wall of the sphenoid sinus both on axial (E) and coronal reconstruction (F) images. CT; computed tomography, OMU; ostiomeatal unit.

scan (Fig. 2A-D). The pathomechanism of the lesions was obscure, but presence of several linear shaped lesions with heterogeneous enhancement suggested the possibility of a vascular abnormality.

Brain MRI also showed dural thickening of the bilateral convexity and interhemispheric fissure with enhancement on fluid attenuated inversion recovery imaging, which was more severe on the right side (Fig. 2E), and venous distension signs on T1-weighted contrast-enhanced imaging (Fig. 2F), both of which suggested intracranial hypotension. He underwent a sinus endoscopy and ostiomeatal unit CT scan for his rhinorrhea, both of which showed a bony defect on the posterior wall of the sphenoid sinus (Fig. 1E, F). By fluorescein dye injection via the lumbar drain, the CSF leakage point was identified, and a CSF leakage repair was performed with a septal flap again. A whole body bone scan performed to exclude malignancy showed no abnormal findings.

A diagnosis of bacterial meningitis secondary to CSF leak was made, and the patient was treated with empirical antibiotics of ampicillin (2 g given intravenously every 4 hours), ceftriaxone (2 g given intravenously every 12 hours), and vancomycin (1 g given intravenously every 12 hours) for two weeks. Within two days, his headache showed remarkable improvement. A follow-up lumbar puncture at the end of three weeks showed a normal opening pressure of 9 cm H_2O, eight leukocytes (six

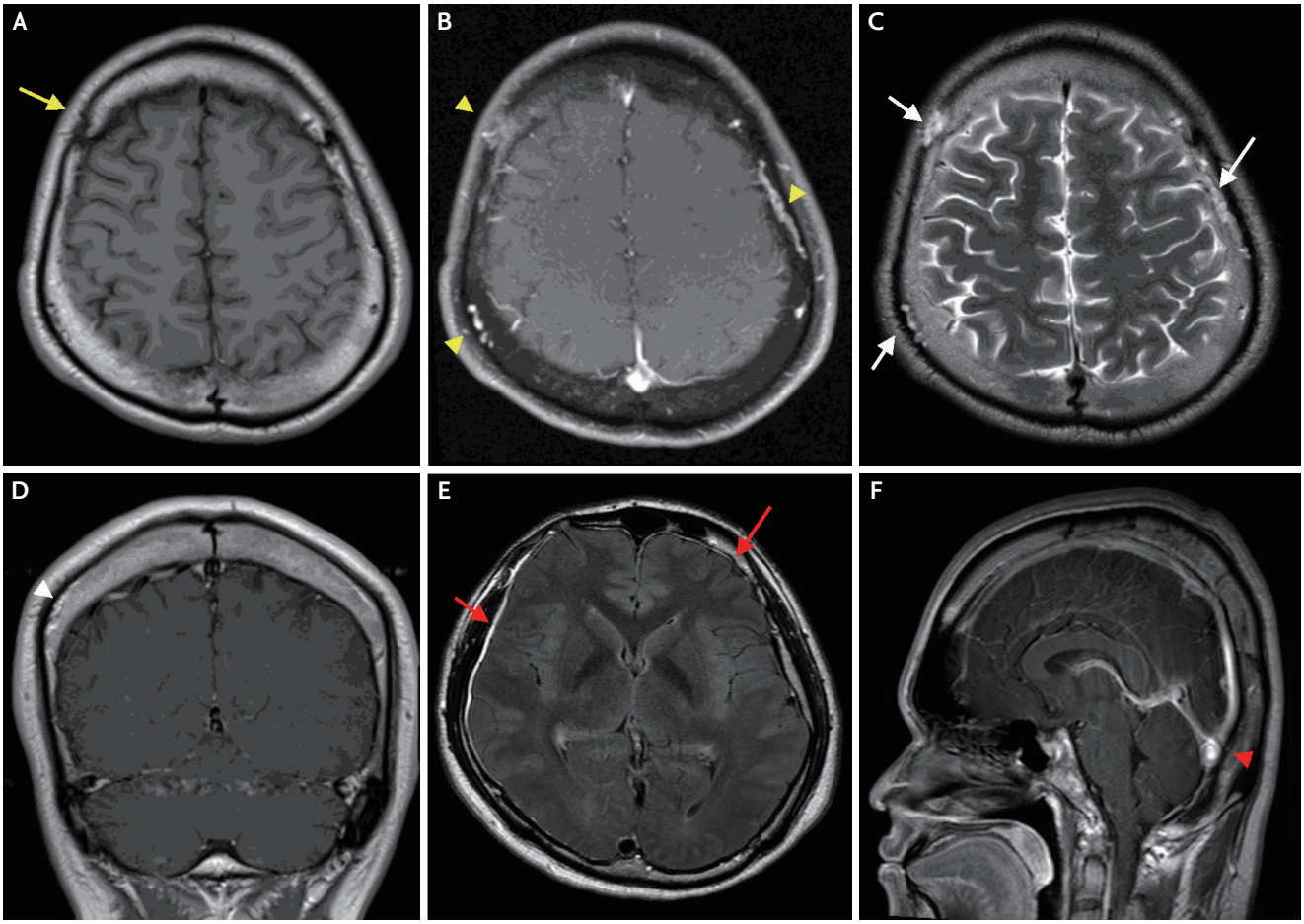

Fig. 2. Brain MRI findings. The patient's brain MRI demonstrated right-sided lytic bony lesions and showed T2 hyperintense lesions of the right frontal and parietal and left temporal bones (white arrows) (C). These lesions showed heterogeneous enhancement on T1-weighted contrast-enhanced axial (yellow arrowheads) (B) and coronal images (white arrowhead) (D) compared to pre-contrast T1-weighted images (yellow arrow) (A). Brain MRI showed dural thickening of bilateral convexity with enhancement on fluid attenuated inversion recovery images, which was more severe on right side (red arrows) (E), and venous distension sign on T1-weighted contrast-enhanced imaging (red arrowhead) (F), both of which suggested intracranial hypotension. MRI; magnetic resonance imaging.

lymphocytes, two other cells) and glucose 91 mg/dL with a blood glucose of 107 mg/dL and protein of 59 mg/dL. Subsequently, he was referred to a specialist in bone diseases, and sirolimus was started at an initial dose of 4 mg twice a day. After checking the serum level and side effects of sirolimus, his dose was adjusted, and his maintenance dose was 2 mg twice a day. During the four months of treatment, he had neither serious drug side effects nor complications of GSD. Currently, the specialist is considering dose reduction.

DISCUSSION

GSD is a rare disease of unknown etiology characterized by proliferation of endothelial-lined vessels in bone leading to progressive and massive osteolysis.[1,2] Our case shows the challenges of arriving at a diagnosis of GSD. The initial differential diagnosis for the bone destruction included inflammation, infection, trauma, and malignancy. However, his serial CT scans showed that the bone destruction had started at least 10 years previously and had progressed slowly, leading to recurrent CSF rhinorrhea and bacterial meningitis. The indolent, spontaneous, and progressive bone destruction was not consistent with infection, trauma, or malignancy. Additionally, his routine laboratory tests, microbiological studies, chest and abdomen CT scans, and whole body scan findings showed no evidence of systemic disease or malignancy. His brain MRI showed multifocal T2 hyperintense lesions at the right frontal, parietal, and sphenoid bone and left temporal bone with heterogeneous enhancement, which could suggest vascular malformation. Therefore, after exclusion of other causes of bone destruction, the clinical and radiological findings were concluded to be consistent with a diagnosis of GSD. With histological examination, the diagnosis of GSD would have been more confirmative. In this case, however, the diagnosis of GSD was reached based on clinical and radiological findings. His long period of serial CT scans and brain MRI findings had a crucial role in diagnosing GSD.

Several therapeutic strategies for GSD are used, which include surgery, radiotherapy, and medical treatment. This is another reason that timely diagnosis is important. Recent reports showed that sirolimus (Rapamune), an inhibitor of mammalian target of rapamycin, is effective in stabilizing or reducing signs and symptoms of disease in patients with GSD by regulating numerous cellular processes.[7] In our patient, sirolimus was started to protect from further invasion of vascular proliferation.

An accurate and timely diagnosis of GSD is critical because patients with GSD can experience severe complications depending on the body part affected. Patients with thoracic involvement can experience chylothorax,[8] and involvement of the vertebrae can cause severe neurologic defects, deformity, and death.[9] Therefore, if a previously healthy patient has a recurrent CSF leak and meningitis due to unexplainable cranial bone destruction, as in our case, GSD should be considered as one of the differential diagnoses. An evidence-based reliable diagnosis of GSD can allow early medical treatment such as treatment with sirolimus.

Conflicts of Interest

No potential conflicts of interest relevant to this article was reported.

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