

Case Report

Management of cerebrospinal fluid leakage in combination with craniofacial fibrous dysplasia

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Abstract: Fibrous dysplasia is a benign bone disorder that most commonly affects craniofacial bones; one or multiple adjacent bones can be involved which can severely deform the skull base. Cerebrospinal fluid leakage in combination with extensive craniofacial fibrous dysplasia is an extremely rare condition that leads to complicated skull base deformation and possible neurovascular structure impingement. We described four cerebrospinal fluid leakage cases with extensive craniofacial fibrous dysplasia, highlighting the surgical complexity and individualized treatment strategy according to the different surgical indications. These cases exemplified the diverse repair options and demonstrated that individualized treatment strategy could achieve successful outcomes with minimizing complications.

Keywords: CSF leak, craniofacial, fibrous dysplasia, surgical treatment

Introduction

Fibrous dysplasia (FD) is a progressive, fibro-osseous disease in which normal bone is replaced by abnormal fibro-osseous tissue [1]. It is caused by somatic activating mutations in a subunit of the stimulatory G protein encoded by the gene *GNAS* [2], and accounts for 2.5% of all bone tumors and 7% of benign bone tumors [3]. FD has three patterns: monostotic FD (single bone involved), polyostotic FD (multiple bones involved), and McCune Albright syndrome (MAS) characterized by the following triad of PFD, café-au-lait spots, and hyperfunctioning endocrinopathies. The craniofacial regions are the most commonly involved sites; one or multiple continuous bones can be involved, but which does not necessarily meet the precise criteria for MFD or PFD [4, 5].

Cerebrospinal fluid (CSF) leaks are common when there is disruption in the arachnoid and dura mater, coupled with an osseous defect due to accidental trauma or iatrogenic, tumors, congenital, or spontaneous reasons. If untreated, CSF leakage can lead to life-threatening meningitis and other complications [6]. CSF

leakage in combination with extensive craniofacial FD is an extremely rare condition and repair is challenging in patients with complicated skull base deformation who also have neurovascular structure impingement.

The present study described four patients with CSF leaks along with extensive craniofacial FD. We reviewed the literatures and discussed surgical indication and treatment, highlighting the surgical complexity and individualized strategies according to different surgical indications.

Case reports

Case 1

A 31-year-old male patient was admitted for right nasal discharge and progressively worsening headache after a sneezing episode 3 weeks earlier. He denied any history of trauma to the skull or iatrogenic injuries. He had no other complaints. Physical examination revealed facial asymmetry associated with bulging of the left frontal-orbital region, but neurologic and other clinical findings were normal. A plain chest X-ray demonstrated multiple bone lesions

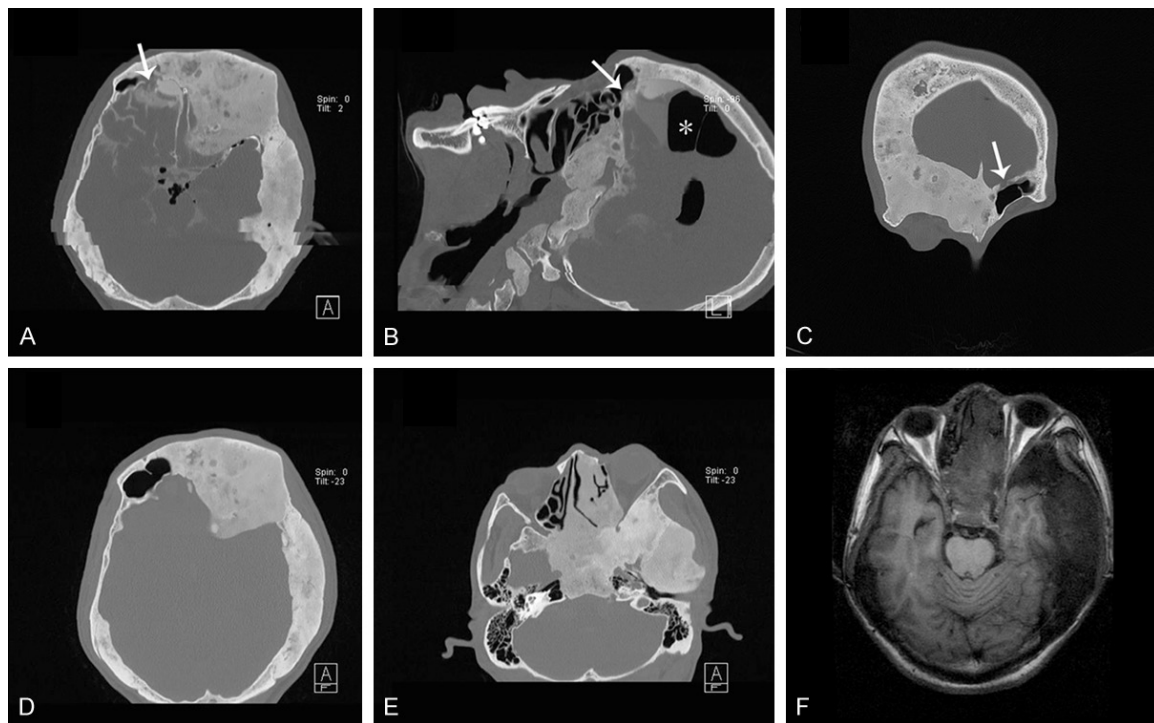


Figure 1. Case 1. Cranial CT axial, sagittal and coronal sections (A-C) showed typical bone lesions as FD of the skull. The cisternography CT scan also showed contrast material flowing through a dehiscence in the posterior wall of the right frontal sinus and into the sinus (indicated by arrow). There was also obvious tension pneumocephalus (*). (D) Axial temporal bone CT scan images showed the thinning of the right temporal bone and the over pneumatized frontal sinus. (E) Axial CT scan images showed the over-pneumatized mastoid processes. (F) MRI showed the optic nerve sheath tortuosity.

on the ribs consistent with FD. Computed tomography (CT) scans showed typical a “ground-glass” appearance with a thin cortex and cystic degenerations of the left frontal-temporal, and sphenoid and clivus bones. The cisternography CT scan also showed contrast material flowing through a dehiscence in the posterior wall of the right frontal sinus and into the sinus. Obvious tension pneumocephalus was noted (**Figure 1A-F**).

The patient underwent a standard bifrontal craniotomy. Following a bicoronal incision and subgaleal dissection, the pericranial flap was harvested. The left frontotemporal lesions were contoured with a high-speed burr to ensure appropriate skull capacity. The frontal sinus was cranialized in a standard fashion. The mucosal surfaces, inflammatory substance, and herniated parts were totally removed to avoid mucocoele formation and infection. Afterward, the pericranial flap was placed along the anterior floor of the skull and sutured micro-surgically to the dura for a watertight seal. The

postoperative course was uneventful. There was no evidence of postoperative CSF leak recurrence during a 4-year follow-up.

Case 2

A 26-year-old man experienced accident trauma at the age of 24 from which he sustained a multiple skull base fracture and left nasal discharge, which laboratory examination later identified as CSF. He was hospitalized with conservative treatment for several weeks and made an uneventful recovery. Six months later, the CSF leak relapsed and was exacerbated by bending or straining. As a result of this relapse the patient experienced severe headaches with high fever, neck stiffness, and seizures, which prompted hospitalization. Upon CSF examination, the patient was diagnosed with meningitis and prescribed an appropriate antibiotics.

Physical examination showed facial defects, contour deformities, and bilateral anosmia. Cranial CT scans revealed findings consistent

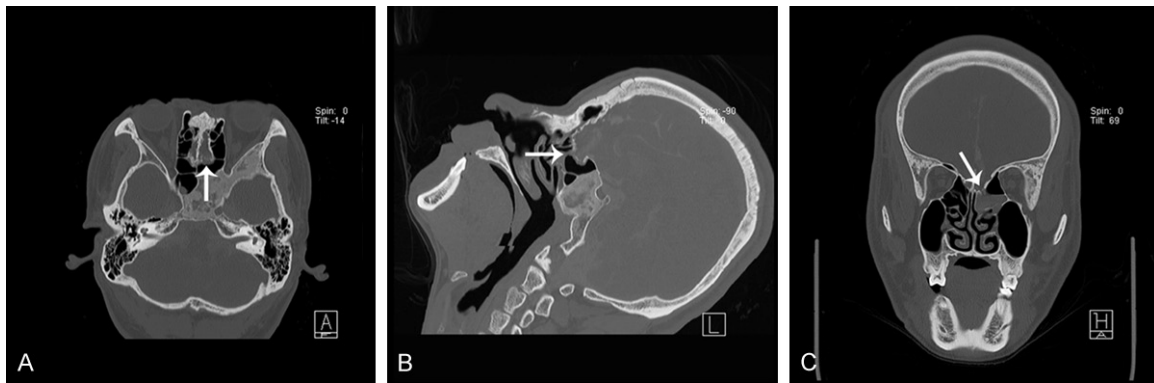


Figure 2. Case 2. Cranial CT axial, sagittal and coronal sections (A-C) showed typical bone lesions as FD of the skull in axial, sagittal and coronal sections (A-C). The cisternography CT scan also showed a bone defect in the left ethmoidal roof. Cisternography CT revealed contrast material flowing through the bone defect of the left ethmoidal roof and into the posterior ethmoidal air cells (indicated by arrow).

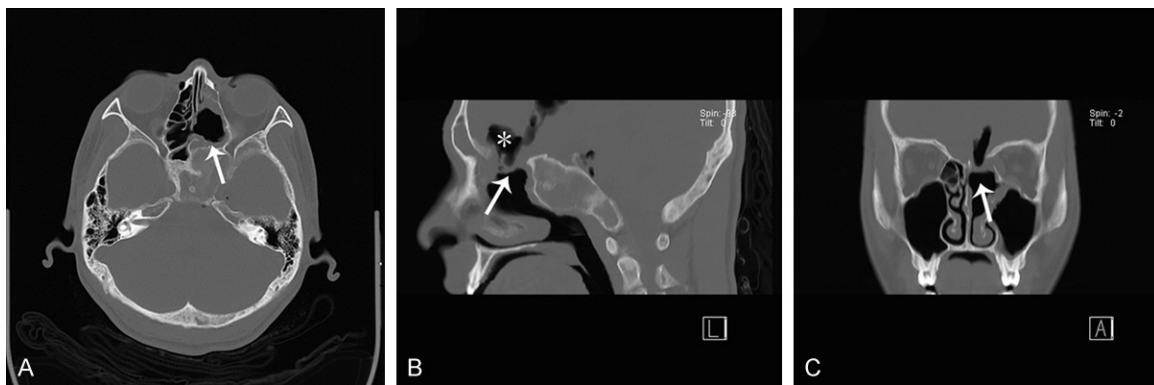


Figure 3. Case 3. Cranial CT axial, sagittal and coronal sections (A-C) revealed clivus lesions and a bone defect in the anterior cranial base (indicated by arrow) and there was significant pneumocephalus (*).

with FD of the frontal-temporal bone, anterior cranial fossa, and clivus. There was also a bone defect in the left ethmoidal roof. Cisternography CT revealed contrast material flowing through the bone defect of the left ethmoidal roof and into the posterior ethmoidal air cells (**Figure 2A-C**). Endoscopic endonasal repair was performed through the left sinonasal tract with a rod-lens endoscope. A partial left middle turbinectomy and a wide unilateral ethmoidectomy were performed. A small bone defect on ethmoid roof was found, and the mucoperiosteum around the bone defect was completely resected. A multilayer reconstruction was performed using the free nonvascularized autologous fat and fascia lata. The reconstruction area was further stabilized with Gelfoam. The nasal cavity was then packed with iodoform gauze for support, and the gauze was removed 2 week

postoperatively. The patient's postoperative recovery was uneventful. He remains stable without CSF leak recurrence and FD progression.

Case 3

A 19-year-old male patient was admitted for bilateral nasal discharge after undergoing an endoscopic endonasal operation 2 months earlier to remove a cranial base lesion from nasal congestion at another hospital. Cranial CT scans taken on admission revealed anterior cranial base and clivus lesions presenting as an enlarging mass with typical "ground-glass" appearance with a bone defect in the anterior cranial base from the previous operation. There was also obvious pneumocephalus (**Figure 3A-C**).

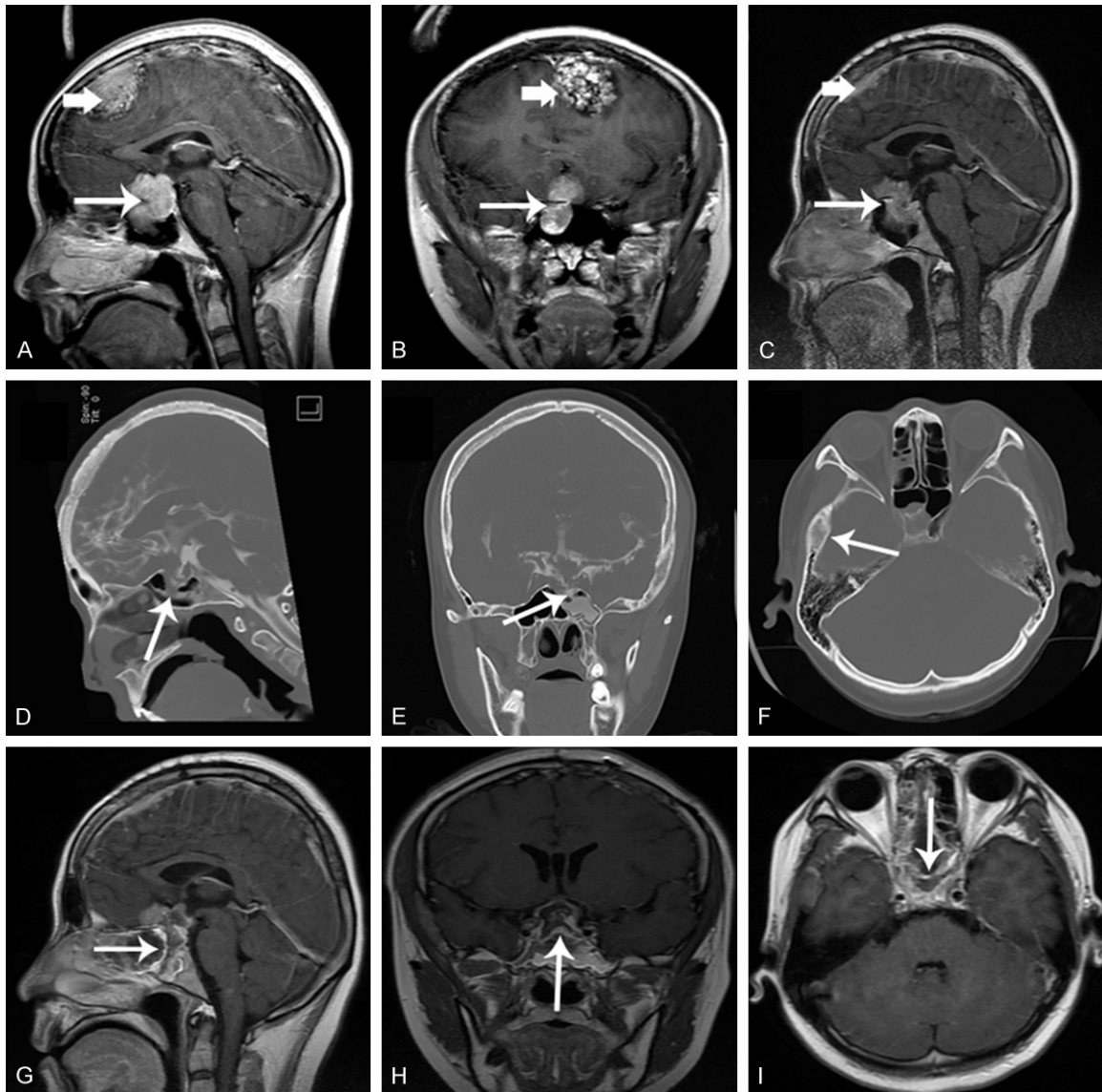


Figure 4. Case 4. Contrast MRI sagittal and coronal sections (A, B) showed a clear border mass lesion with irregular enhancement signal located in the left frontal parasagittal sinus (indicated by thick arrow). A homogenous enhancement of mass lesion was also found intrasellarly and suprasellarly; the intrasellar area was significantly enlarged, with involvement and invagination of the sellar base (indicated by thin arrow). (C) Postoperative MRI showed no significant meningioma recurrence after 5 years, and the sellar area lesion was significantly reduced after oral bromocryptine was taken. (D, E) Cisternography CT revealed contrast material flowing through the bone defect on the right sellar base into the sphenoid sinus. (F) Cranial CT showed enlarging mass with typical “ground glass” appearance on right temporal bone. (G-I) Postoperative cranial MRI showed the tumor was removed subtotally and the CSF leak was repaired. The repair material can be seen on the sellar base (indicated by arrow).

Endoscopic endonasal repair was performed and a large bone defect (nearly 2 cm) of anterior cranial base was found. There was no pedicle nasal septum mucosal flap to harvest due to the previous nasal operation. We used free autologous fat and fascia lata to repair the defect followed by Gelfoam. Finally, the nasal cavity was packed with iodoform gauze for sup-

port and the gauze was removed after 2 weeks. Eight months post-operation, the CSF leak relapsed; the patient experienced high fever and was admitted to our hospital a second time. After he was in a stable condition, we performed a bifrontal craniotomy to repair the CSF leak. The pericranial flap was placed along the anterior floor of the skull and sutured micros-

Cerebrospinal fluid leak complicated with craniofacial fibrous dysplasia

Table 1. Patient's data

No.	Age	Gender	CSF leaks Etiology	CSF duration	CSF Complications	FD Intracranial location	FD other part location	FD related sign and symptoms	Surgical approach	Repair material	Repair method	FD resection degree
1	31	Male	Spontaneous	3 weeks	Tension pneumocephalus	Left fronto-temporo-parietal, right frontal, ethmoid, sphenoid, occipital	Plain x-ray of chest: multiple bone lesions of ribs	Facial deformity and asymmetry	Bifrontal craniotomy	Pericranial flap	Turnover suture	Partial resection
2	26	Male	Traumatic	2 years	Seizures; meningitis	Sphenoid body, left greater wing of sphenoid bone	No	No	Endoscopic endonasal	Free autologous fat and fascia lata	Multilayer reconstruction	Partial resection
3	19	Male	Iatrogenic	2 months	Tension pneumocephalus	Petrous bone: greater wing of sphenoid bone, left	Plain x-ray of chest: multiple bone lesions of left ribs	Nasal congestion	1st Op: endoscopic endonasal; 2nd Op: bifrontal craniotomy	1st Op: free autologous fat and fascia lata; 2nd Op: pericranial flap	1st Op: multilayer reconstruction; 2nd Op: turnover suture	Partial resection
4	25	Female	Medically induced tumor reduction	40 days	Meningitis	Right temporal bone	No	No	Endoscopic endonasal	Free autologous fat and fascia lata	Multilayer reconstruction	No

gically to the dura for a watertight seal. The patient's postoperative recovery was uneventful and the CSF leak has not recurred.

Case 4

A 25-year-old female patient was admitted for a 3-year-old menstrual disorder accompanied with headaches and progressive vision deterioration. On admission, MRI showed mass lesions in the sellar area and left frontal lobe (**Figure 4A, 4B**); blood examination showed high level of serum prolactin (1913 ng/ml). We performed a craniotomy to remove the tumor in the left frontal lobe and pathological examination reported meningioma. The patient's postoperative recovery was uneventful and oral bromocriptine was taken regularly. 5 years later, patient was admitted to our hospital again due to a CSF leak (**Figure 4C-E**). This was accompanied with high fever which prompted hospitalization. Later, an appropriate dosage of antibiotics was prescribed.

Endoscopic endonasal repair was performed to repair the CSF leak. Intraoperatively, a bone defect on right sellar base was confirmed. The tumor was extended from intrasellar area to the sphenoid sinus with dural invasiveness. After dural opening, the tumor appeared to be red grayish, soft in characteristic with rich blood supply. Most of the tumor was located intrasellarly and had invaded the anterior cranial base. The tumor was removed subtotally, a multilayer reconstruction was performed using the free nonvascularized autologous fat and fascia lata. The reconstruction area was further stabilized with Gelfoam (**Figure 4G-I**). The patient's postoperative course was uneventful. She remains stable without CSF leak recurrence and the serum prolactin level was reduced to 118 ng/ml.

Discussion

FD was first described by Lichtenstein in 1938. However, the natural history of the disease and a standard treatment protocol remain undefined [7, 8]. There are still some controversies on optimal treatment timing and strategy [9-13]. There are several reasons for this. Firstly, FD is relatively rare, and clinical manifestations vary, so multiple specialties could be involved. Thus, previous publications were mostly case reports or single institution reports. Secondly, none of the studies included subjects

that experienced thorough skeletal and/or endocrine screening, thus, accurate epidemiological data was lacking [7]. The craniofacial bones are the most common locations of FD [4], and the anterior cranial base is involved in over 95% of PFD and MAS cases [13]. Neurovascular impingement and serious bone deformity can occur when multiple continuous bones of the anterior cranial base are involved. Thus, the treatment of craniofacial FD is very challenging and should be carried out on a case-by-case basis. The four patients were all post-pubertal and asymptomatic (**Table 1**). Since there was a possibility that the lesions would remain stable, we did not perform an aggressive resection. Rather, we performed partial resections to repair the defects and confirm the diagnosis and continued with closed follow-up. It is vital to have an in-depth understanding of both the etiology and pathophysiology of each CSF leak when one is determining the most appropriate treatment. Even though all three CSF leaks were located on the anterior cranial base, it is important to note that the etiology and pathogenesis of each case was unique; particularly for the patient with serious skull deformity due to FD. This underscores the need to select a treatment approach based on an individual circumstances.

There is a correlation between spontaneous CSF leaks and idiopathic intracranial hypertension [14]. Patients with spontaneous CSF leaks generally present typical clinical and radiographic signs that show increased intracranial pressure [15]. At the same time, expansive pneumatization of the nasal sinuses is another important cause of spontaneous CSF leak. All these characteristics were noted in the first case. In that patient, serious deformation and thickening of skull bone decreased the cranial volume, which could have exacerbated ICP and made the skull base dura weak and vulnerable to tears due to intracranial pulsation. Accordingly, three steps were performed to reduce ICP (increased intracranial pressure). First, extensive drilling was performed to reduce thickness of the deformed skull bone. Secondly, a partial bone flap was removed by craniotomy. Thirdly, the skull dura was reduced sutured with artificial material. Postoperatively, the patient's ICP was within a normal range on lumbar puncture and the CSF leak did not recur. Close follow-up is needed to assess for recurring and new leaks.

Traumatic CSF leak contributes to 80%-90% of CSF fistulas [16]. Although the majority of cases can be treated conservatively, when this approach fails, surgical repair raises the risk of meningitis or pneumocephalus [17, 18]. The posterior ethmoid skull base is a common CSF leak location because of the thin fragile dura and its firm adherence to the skull base [19]. Endoscopic repair without vascularized multi-layer reconstruction is a practical option for this type of small or low-volume CSF fistula, as in the second case [20]. During the operation, preparation of the leak site is crucial. The mucosa around the fistula should be removed, bony edges should fully exposed, and bony deformations and protrusions should be carefully drilled out to prepare an ideal site for positioning reconstructive materials.

The most common cause of iatrogenic CSF leak is functional endoscopic sinus surgery, which has become popular in the past 30 years [21]. The third patient was initially operated on in another hospital where he was misdiagnosed with common nasal congestion. The lesion was relatively limited to the sphenoid bone, where a biopsy was obtained to confirm the diagnosis. Normally, biopsies are unnecessary when the lesion is quiescent or asymptomatic or in the cranial base; it is usually sufficient to establish a diagnosis based on history, clinical examination and the classic radiographic presentation [7]. The patient underwent two reparation surgeries. We determined that the first endonasal endoscopic reparation failed because the bone and dura defects were large and accompanied with high-flow leaks. Additionally, it was impossible to harvest the pedicle nasal septum mucosal flap for skull base construction because it had been used in a previous surgery [22, 23]. The leak was successfully repaired in the second attempt using a transcranial approach.

The clinical history of the patient in case 4 is relatively complex. This patient had fibrous dysplasia of the temporal bone accompanied with pituitary adenoma and hyperprolactinemia; these symptoms meet the criteria for McCune-Albright syndrome (MAS) [24, 25]. Interestingly, this patient also had a meningioma in the frontal lobe. However, there is no definite relationship between meningioma and MAS. Medically induced CSF leaks associated with pituitary adenomas are one type of special spontaneous

CSF leak [26]. While this type of leak is uncommon, if found, it is usually a result of dopamine agonist therapy, prescribed to combat functional pituitary adenomas. The mechanism is as follows: the pituitary adenoma expands into and ruptures the surrounding dural and skull base structure, especially for larger and more invasive tumors. Then, reduction in tumor size from the medicine results in CSF leaks [27, 28]. Surgical treatment, preferentially an endonasal endoscopic approach, is the recommended initial treatment for definitive repair of the CSF leak and achievement of maximal tumor resection [29]. In our study, the patient underwent this procedure and the leak was successfully repaired. The patient's postoperative recovery was uneventful followed by significant decrease of the blood serum PRL.

CSF leakage in combination with extensive FD of the skull base is an extremely rare condition. Surgical treatment of these patients is challenging, particularly given the possibility of neurovascular impingement. Individualized treatment strategies should be selected based on patient's unique surgical indications to achieve successful outcomes with minimal complications.

Disclosure of conflict of interest

None.

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