

Spontaneous Cerebrospinal Fluid Rhinorrhea Associated With Chronic Renal Failure

—Case Report—

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Abstract

A 39-year-old woman was admitted with complaints of headache and nasal discharge on the left for 3 months which was later on proved to be cerebrospinal fluid (CSF). Neurological examination found no abnormalities except bilateral papilledema. Neuroimaging demonstrated enlargement of the lamina cribrosa foramina through which the olfactory nerves pass, as well as empty sella and cerebral cortical atrophy. Bone mineral densitometry showed osteopenia. CSF Ca^{++} and blood parathyroid hormone levels were elevated. CSF pressure was 280 mmH₂O. Bilateral frontal craniotomy was performed to expose the anterior fossa. Foraminal enlargement at the lamina cribrosa was confirmed, and islands of extraosseous calcifications on the arachnoid membrane were identified. The base of the anterior fossa was repaired intradurally with fascial graft and fibrin glue on both sides. No CSF leakage was noted at 1-year follow up. Spontaneous CSF leakage probably resulted from enlargement of the foramina at the lamina cribrosa due to Ca^{++} mobilization from bones and pseudotumor cerebri not to the extent of hydrocephalus caused by poor CSF absorption at the arachnoid granulations obliterated by extraosseous calcareous accumulation.

Key words: cerebrospinal fluid, chronic renal failure, empty sella, spontaneous rhinorrhea, pseudotumor cerebri

Introduction

Chronic renal failure (CRF) is associated with bone tissue changes, known as renal osteodystrophy, in approximately 5–30% of patients undergoing renal dialysis.¹²⁾ Renal osteodystrophy may be caused by diminished gastrointestinal absorption of Ca^{++} because of impaired vitamin D metabolism, phosphate retention, increased concentrations of parathyroid hormone, and aluminum toxicity.^{10,28)} Manifestations of renal osteodystrophy include osteitis fibrosa cystica and osteomalacia characterized by very fragile bone tissue,¹⁷⁾ and usually involve the terminal phalanges, long bones, distal ends of the clavicles, upper and lower margins of the vertebrae.^{18,21)} Enhanced cortical resorption and the development of areas of increased trabecular density may cause

granularity and mottled appearance (“salt and pepper” skull) in the cranium.¹⁸⁾ The radiographic appearance of the skull in patients with renal failure may occasionally resemble that of Paget’s disease or multiple myelomas, in which focal radiolucent areas of 1 to 3 cm in diameter may be seen.^{2,18)}

We treated a patient with CRF who suffered spontaneous cerebrospinal fluid (CSF) leakage arising from thinning of the anterior skull base associated with pseudotumor cerebri.

Case Report

A 39-year-old woman was admitted to our hospital with complaints of nasal discharge on the left, previously identified as an episode of allergic rhinitis and headache for the last 3 months. Her history included the diagnosis of CRF established 4 years ago and hemodialysis therapies three times a week for the last 18 months. On admission, the patient had

papilledema, but no other neurological abnormalities. Simultaneous glucose assays revealed the glucose level of the nasal discharge (33 mg/dl) was about half that of blood (79 mg/dl) which was consistent with CSF. The diagnosis was rhinorrhea. Laboratory investigations identified blood Ca^{++} level as 8.3 mg/dl (normal 8–11 mg/dl), parathyroid hormone 216 pg/ml (12–72 pg/ml), phosphorus 7.8 mg/dl (1–1.6 mg/dl), and alkaline phosphate 230 mg/dl (114–176 mg/dl). The CSF pressure was 280 mmH₂O (normal 50–180 mmH₂O) and CSF Ca^{++} level was 7 mg/dl (3 mg/dl).

Coronal computed tomography (CT) displayed enlargement of the bilateral holes in the lamina cribrosa through which the olfactory nerves pass (Fig. 1). CT demonstrated multiple extra-osseous calcifications at two different sites, on the right side near the temporal horn (Fig. 2 left), and at the level of craniovertebral junction, considered to be calcification of left vertebral artery (Fig. 2 right). Intrathecal CT with contrast medium could not be obtained because of the presence of CRF. Sagittal magnetic resonance imaging displayed cortical atrophy and the coexistence of empty sella sign (Fig. 3). Whole body bone mineral densitometry using dual energy x-ray absorptiometry revealed osteopenia at both femoral necks and the spine (Fig. 4).

The patient underwent bilateral anterior fossa exploration for repair of the CSF leakage through the lamina cribrosa. The foramina of the lamina cribrosa were found to be relatively large, particularly on the left side (Fig. 5). White extra-osseous calcified le-

sions were observed on the arachnoid membrane (Fig. 6 upper) and confirmed by histological examination (Fig. 6 lower). The lamina cribrosa was obliterated with muscle and fascial grafts on both sides without affecting the olfactory tracts. No CSF leakage was observed at the 1-year follow up.

Discussion

CSF leakage is of either spontaneous or traumatic origin. Spontaneous CSF leakage is rare and can be divided into normal pressure and high pressure types, also known as the direct and indirect types, respectively.²³⁾ The direct type is associated with bone defects at the skull base due to congenital or acquired factors. Congenital anomalies, such as basal

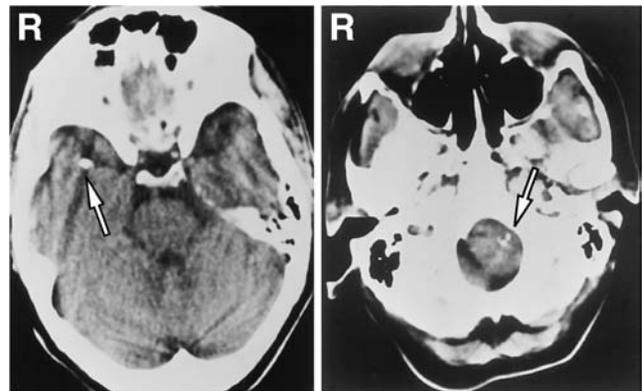


Fig. 2 Computed tomography scans showing extra-osseous intracranial calcification foci (arrow) near the right temporal horn (left) and at the level of craniovertebral junction (right).

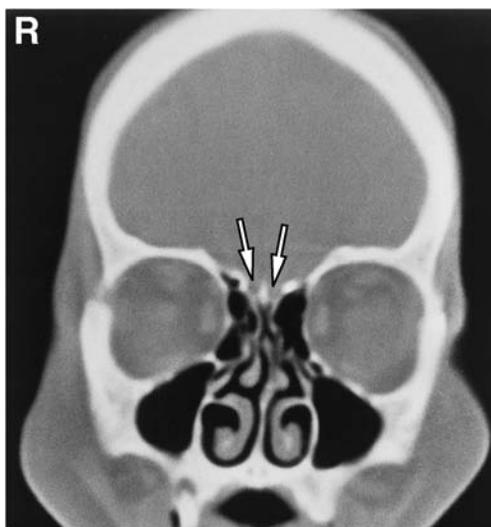


Fig. 1 Coronal computed tomography scan showing enlargement of the bilateral olfactory nerve grooves (arrows).

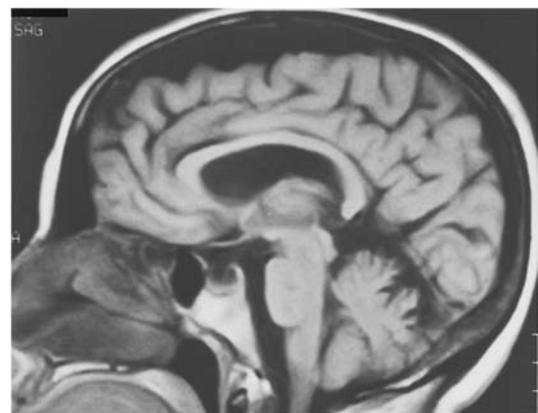


Fig. 3 T₁-weighted sagittal magnetic resonance image showing cerebral cortical atrophy and empty sella.

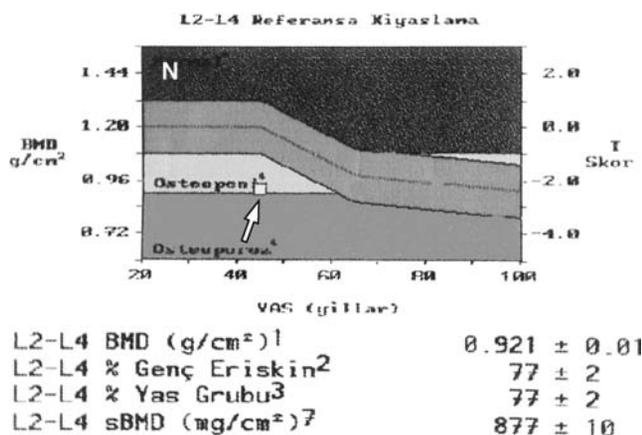


Fig. 4 Bone mineral densitometry diagram of the patient using dual energy x-ray absorptiometry showing osteopenia (arrow) at the spine. N: normal range.

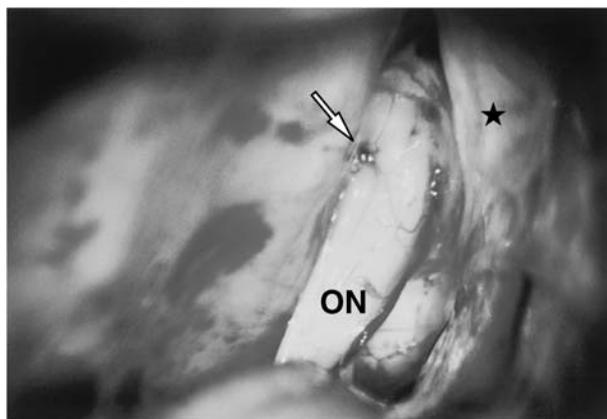


Fig. 5 Intraoperative photograph showing the left frontal lobe retracted posteriorly, and enlargement of the left olfactory nerve (ON) foramen (arrow) on the lamina cribrosa. star: Falx cerebri.

encephalocele or congenital defect of the lamina cribrosa, are the usual causes of the direct type of CSF leakage.^{1,3,9,24} Acquired pathologies, such as intracranial and extracranial tumors, cholesteatoma, or tuberculoma are also known to erode the bone directly.^{3,13,20,23} CRF may also result in acquired bone defect due to mobilization of Ca⁺⁺ from the skull base. However, such a defect tends to remain undetected as long as CSF leakage or meningitis does not occur. Subperiosteal resorption in hyperparathyroidism is responsible for the cortical bone erosion associated with CRF.¹⁸ Therefore, bone resorption is sometimes more prominent at the site of the cortical bones just underneath and all along

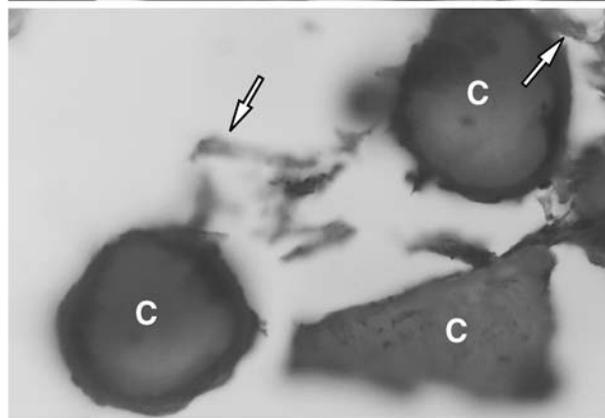
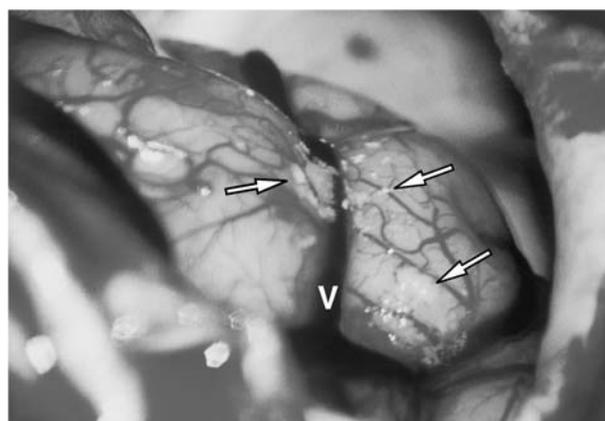


Fig. 6 (upper) Intraoperative photograph showing multiple extra-osseous arachnoid membrane calcifications (arrows) on the right frontal lobe, which almost covered the vein (V) coursing in the sulcus. (lower) Photomicrograph of the calcifications (C) on the arachnoid membrane (arrows) colored purple by HE staining. ×400.

the periosteum.^{6,11,14} Facial nerve stimulation by a cochlear implant was reported recently in a hemodialysis patient with bone of low mineral density.¹⁶ Although the bone mineral density of the patient's cochlear bone could not be measured, the pathologic mechanism was presumed to be cortical bone change caused by CRF and long-term hemodialysis.¹⁶ In the present case, diffuse osteopenia on bone mineral densitometry indicated the loss of volume and strength of cortical bone tissue, which was probably the cause of the enlargement of the foramina of the lamina cribrosa, as observed by preoperative neuroimaging and confirmed intraoperatively. The cortical bone erosion at this site may not be enough to cause CSF leakage per se, so a secondary supervening factor, pseudotumor cerebri, probably aggravated the pathology.

The indirect type of spontaneous CSF leakage is

related to the increased intracranial pressure associated with tumor, hydrocephalus, and pseudotumor cerebri.^{3,5,13,23} Increased CSF pressure may cause tearing of the fragile parts of the dura-arachnoid complex and/or may directly promote the erosion of bone tissue, thus facilitating spontaneous CSF leakage. Both the direct mechanism by erosion of the meninges and bone and the indirect mechanism via high intracranial pressure may be involved in our case as in intracranial tumor cases.²³ Fluid overload and increased cerebral blood flow may be involved in the elevation of intracranial pressure in patients with CRF.¹⁵ Dura and arachnoid membranes surround the olfactory nerve fibers and pass through the foramina of the lamina cribrosa.³⁰ Therefore, enlargement of the weakened lamina cribrosa associated with high intracranial pressure could lead to invagination of the arachnoid with nerve tissue, followed by CSF leakage.²⁶ High intracranial pressure pseudotumor cerebri is rare but known in patients with CRF.^{7,19,27} In our case, the presence of headache, papilledema, and high CSF pressure was consistent with the syndrome of pseudotumor cerebri. Increased CSF pressure associated with diaphragma sellae defects is considered to be the main pathogenic factor for empty sella, which occurs in 10% of patients with pseudotumor cerebri.^{25,29} The coexistence of pseudotumor cerebri and empty sella was believed to be incidental in our case. Increased intracranial pressure may promote CSF leakage in empty sella, through the sellar floor.²⁵ However, the absence of CSF leakage at the 1-year follow up in our case proved that the site of leakage was the lamina cribrosa, not the empty sella.

The mechanism of pseudotumor cerebri in patients with CRF is unclear.^{7,19,27} The endocrine disturbances resulting in abnormal Ca^{++} and phosphorus metabolism may be involved in the association of pseudotumor cerebri and CRF.²² Intracranial extra-osseous calcifications are encountered in hyperparathyroidism, which is a manifestation of changed mineral metabolism.^{8,18} Likewise the two separate hyperdense foci in our patient seemed to result from extra-osseous calcareous accumulation induced by CRF. The CSF Ca^{++} level was high and calcification islands were also present on the arachnoid membrane. Therefore, blockade of the arachnoid granulations due to Ca^{++} deposits may have caused the CSF pressure rise, ultimately leading to pseudotumor cerebri but not to the extent of hydrocephalus. Such a proposed blocking mechanism at the arachnoid granulations is similar to that of subarachnoid hemorrhage, but these two pathological entities differ in their acute and chronic courses and manifestations, since the latter causes

only frank hydrocephalus without pseudotumor cerebri. No previous study supports this hypothesis, but confirmation would be provided by autopsy of patients with CRF.

The onset of spontaneous CSF leakage is insidious and correct diagnosis requires detailed evaluation of clinical history. The presence of CSF leakage may be missed if not considered in the differential diagnosis and may well be mistaken for rhinitis as in our case. Any previous history of head injury, attacks of recurrent meningitis, and coexistence of intracranial mass should be investigated meticulously. The discharge is usually unilateral and may be postural. Testing with a glucose oxidase reagent diagnostic strip will confirm whether the fluid has a high concentration of glucose.^{4,23}

The present case shows that the changes in calcium metabolism associated with CRF may cause erosion of the skull base, resulting in spontaneous rhinorrhea requiring prompt surgical repair of the leakage site.

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