

Pituitary stone resulting in visual dysfunction and spontaneous rhinorrhea in nonfunctioning pituitary adenoma: illustrative case

Takuya Kanemitsu, MD, PhD,¹ Naokado Ikeda, MD, PhD,¹ Masao Fukumura, MD, PhD,¹ Satoshi Sakai, MD, PhD,² Hidehiro Oku, MD, PhD,³ Motomasa Furuse, MD, PhD,¹ Naosuke Nonoguchi, MD, PhD,¹ Ryo Hiramatsu, MD, PhD,¹ Shinji Kawabata, MD, PhD,¹ Akihisa Imagawa, MD, PhD,² Tsunehiko Ikeda, MD, PhD,³ and Masahiko Wanibuchi, MD, PhD¹

Departments of ¹Neurosurgery, ²Internal Medicine (I), and ³Ophthalmology, Osaka Medical College, Takatsuki, Osaka, Japan

BACKGROUND Calcifications in pituitary adenomas are rare, being found in only 5.4%–25% of reported cases. These are divided into eggshell-like calcifications around the tumor and nodular calcifications at the center of the tumor, the latter of which are called “pituitary stones” (PSs).

OBSERVATIONS The authors report the case of a 60-year-old male with a nonfunctional pituitary adenoma with PSs and asymptomatic ventricular dilatation who presented with spontaneous cerebrospinal fluid (CSF) rhinorrhea and rapid visual aggravation without an increase in tumor size over the course of 4 years. After endoscopic transnasal surgery, his visual acuity immediately improved temporarily. It was believed that the increased intracranial pressure due to secondary hydrocephalus resulted in visual aggravation; thus, a ventriculoperitoneal (VP) shunt was created. After creation of the VP shunt, the patient’s visual acuity improved gradually and completely. Histological findings showed that adenoma cells were observed among the lamellar bone trabeculae. To the best of the authors’ knowledge, this is the first report of osteoid metaplasia–type PSs in nonfunctioning pituitary adenoma.

LESSONS PSs formed near the sellar floor and caused spontaneous CSF rhinorrhea due to direct mechanical stress on the dura mater and optic nerves, which may have caused meningitis and secondary hydrocephalus that resulted in visual impairment independent of tumor size.

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KEYWORDS pituitary; stone; nonfunctioning; adenoma

According to previous reports, pituitary adenomas with calcifications are radiographically observed in 0.2–14% of cases and histologically in 5.4–25% of cases.^{1–5} Furthermore, spontaneous cerebrospinal fluid (CSF) rhinorrhea in patients with untreated pituitary adenomas is extremely rare, with only 16 cases having been reported in the English-language literature.⁶ We report a unique symptomatic nonfunctioning pituitary adenoma that exhibited these 2 rare conditions, and we review the relevant literature.

Illustrative Case

A 60-year-old male patient had been experiencing rhinorrhea and severe headaches for about 8 months. Four years before being admitted to our institute, an intrasuprasellar mass was pointed out incidentally by magnetic resonance imaging (MRI). MRI showed an

isointense suprasellar lesion on T1-weighted imaging and was homogeneously enhanced after gadolinium administration (Fig. 1A and B). Because no symptoms related to the lesion were observed, the patient was seen in follow-up in the meantime. Four months before being admitted to our institute, he was diagnosed with memory disturbances and disorientation secondary to hyponatremia (127 mEq/L). His symptoms improved with conservative treatment, and compared with 4 years prior, the suprasellar lesion had not increased in size. Thus, the patient was advised to undergo follow-up. However, 3 months later, he complained of visual disturbances and was admitted to our institute. Upon admission, the patient presented with disorientation, with a Glasgow Coma Scale score of 14/15, a Mini Mental State Examination score of 26/30, and an ophthalmological examination that revealed that the left visual acuity was reduced to a log minimum angle

ABBREVIATIONS ACTH = adrenocorticotropic hormone; CSF = cerebrospinal fluid; CT = computed tomography; ETNS = endoscopic transnasal surgery; GH = growth hormone; logMAR = logarithm of the minimum angle of resolution; MRI = magnetic resonance imaging; POD = postoperative day; PRL = prolactin; PS = pituitary stone; VP = ventriculoperitoneal.

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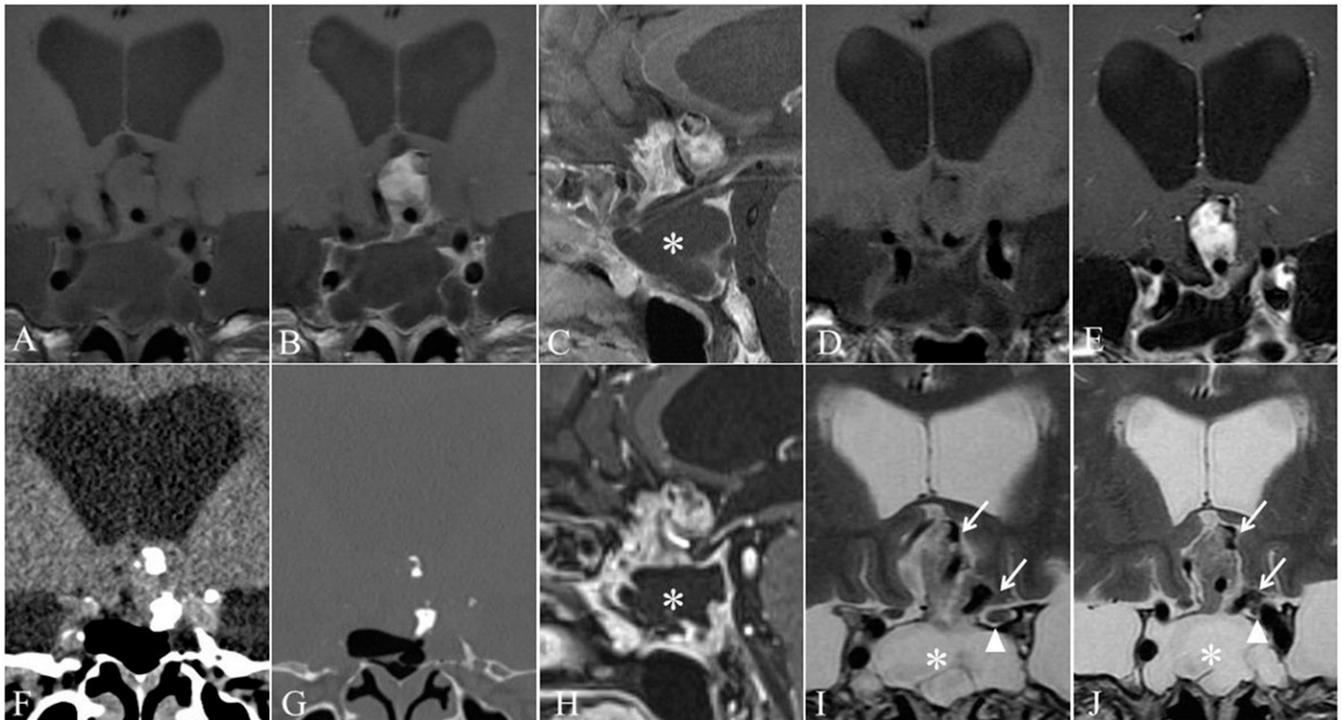


FIG. 1. MRI 4 years before ETNS showing supra- and intrasellar tumor isointensity in coronal T1-weighted MRI (A) and homogeneously enhanced after gadolinium administration (B). Sagittal T1-weighted MRI after gadolinium administration shows disruption of the sella turcica (C). MRI just before ETNS demonstrates that the tumor size was similar to that of 4 years ago, but ventricle size was enlarged (D, coronal T1-weighted MRI; E and H, coronal and sagittal T1-weighted MRI, respectively, with gadolinium administration). CT (F, soft tissue window; G, bone window) just before ETNS demonstrates that a calcified lesion was in the tumor and the sellar floor was eroded. T2-weighted MRI just before ETNS (I and J) demonstrates that the optic chiasma and optic nerves were deviated caudally with the tumor and the calcified lesion (arrows) was located just above the left optic nerve (arrowheads). The sphenoid sinus was filled with fluid that was of the same intensity as CSF (asterisks in C and H–J).

of resolution (logMAR) of 2. The visual field test confirmed bilateral hemianopia. Hematological and biochemical parameters and the hormone profile, including a hormone loading test with luteinizing hormone–releasing hormone, growth hormone (GH)–releasing peptide 2, corticotropin-releasing hormone, and glucagon, were all within normal limits, indicating hypothalamopituitary function despite a slight increase in prolactin (PRL) levels (Table 1). Computed tomography (CT) showed solid, calcified lesions in an isodense intrasuprasellar lesion and bone erosion of the sella turcica and anterior wall of the sphenoid sinus (Fig. 1F and G). MRI showed an isointense suprasellar

TABLE 1. Hormone level of the present patient

Hormone	Test Value	Reference Range
Cortisol	10.03 µg/dL	6.24–18.00 µg/dL
Growth hormone	0.63 ng/mL	0–2.47 ng/mL
Free thyroxine	1.10 ng/dL	0.90–1.70 ng/dL
Thyroid-stimulating hormone	2.69 µIU/mL	0.500–5.000 µIU/mL
Luteinizing hormone	2.72 mIU/mL	0.8–5.7 mIU/mL
Follicle-stimulating hormone	3.8 mIU/mL	2.0–8.3 mIU/mL
Prolactin	14.3 ng/mL	4.29–13.69 ng/mL
Adrenocorticotrophic hormone	27.0 pg/mL	7.2–63.3 pg/mL

lesion on both T1- and T2-weighted imaging and was homogeneously enhanced after gadolinium administration. The size of the lesion was 22 mm, similar to that of 4 years ago, but the ventricle size was observed to be enlarged. The optic chiasma was deviated caudally with the lesion, and the calcified lesion was observed to be located just above the left optic nerve (Fig. 1D, E, I, and J).

The observed rapid visual aggravation despite no increase in suprasellar lesions was considered to be due to the spread of inflammation to the optic nerve secondary to meningitis or mass effects caused by the lesions and subsequent ventricular dilatation. Endoscopic transnasal surgery (ETNS) was performed for the purpose of histological diagnosis of the lesions and decompression for the optic nerves. Intraoperatively, the pulsating mucosa of the sphenoid sinus was confirmed after the anterior wall of the sphenoid sinus was removed. The mucosa was partially deflected, and the arachnoid membrane was exposed directly. The CSF was drained out from this position (Fig. 2A). After incision of the mucosa on the posterior wall of the sphenoid sinus and partial removal of the tumor, the calcified lesion located directly above the left optic nerve was removed (Fig. 2B). This resulted in the release of pressure on the left optic nerve and grossly improved flexion of the chiasma and the left optic nerve (Fig. 2C). The intraoperative pathological diagnosis was pituitary adenoma, and in order to avoid exacerbation of CSF leakage and damage to the anterior cerebral artery, the surgical procedure was terminated by partial removal. The patient's subjective visual acuity improved 1 day after the

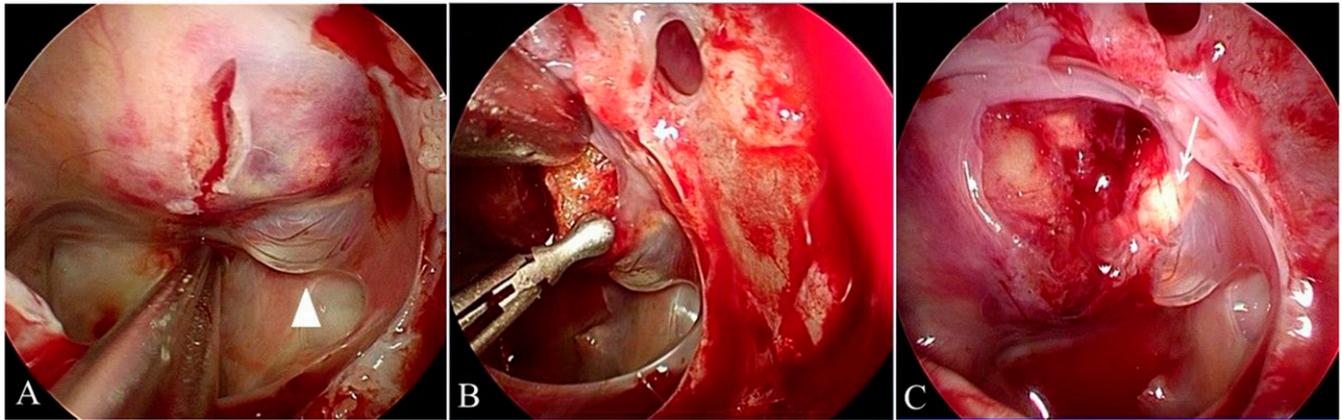


FIG. 2. Intraoperative photographs. (A) The sellar floor was eroded and covered by mucosa of the sphenoid sinus. The mucosa had a partial defect, and the arachnoid membrane was exposed directly (arrowhead). CSF leakage from here was observed. (B) After the intrasellar tumor was partially removed, the calcified lesion (asterisk) just above the left optic nerve was removed gently. (C) After the calcified lesion was removed, the caudal shift of the left optic nerve was improved (arrow).

operation, and his visual acuity on postoperative day (POD) 7 showed a remarkable improvement in the left visual acuity with a logMAR of 0.3. The visual field defect was also improved; however, the visual acuity test on POD 26 revealed that the left visual acuity was a logMAR of 1.2, which was exacerbated. Therefore, it was considered that the physical compression of the tumor to the optic nerve was aggravated by increased intracranial pressure due to hydrocephalus. On POD 40, a ventriculoperitoneal (VP) shunt was created (with CERTAS plus programmable valve, Integra LifeScience Corporation). Seven days after creation of the VP shunt, the patient's visual acuity was improved to a logMAR of 0.5 in the left eye and a logMAR of -0.1 in the right eye. Although the left visual acuity gradually declined, adjusting the shunt valve pressure from 7 to 5 (238 to 178 cm H₂O) improved it to a logMAR of 0.4 (Fig. 3). Histopathological findings showed that tumor cells with a rounded nucleus and an eosinophilic cytoplasm had proliferated and that the tumor cells were immunohistologically negative for PRL, GH, and adrenocorticotropic hormone (ACTH). Those of the calcified lesion

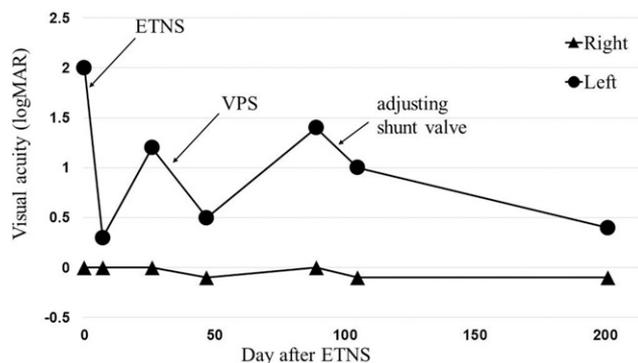


FIG. 3. Clinical course of visual acuity of the present patient. The left visual acuity 7 days after ETNS showed a remarkable improvement compared with that before the surgery. Although the visual acuity deteriorated temporarily through 26 days after ETNS, it improved again after the VPS and adjustment of the pressure of the shunt valve. VPS = ventriculoperitoneal shunt.

showed that most of the parenchyma was replaced by mature lamellar bone tissue. The tumor cells were observed among the lamellar bone trabeculae (Fig. 4).

Discussion

Observations

Calcifications of pituitary adenomas are commonly divided into eggshell-like calcifications around the tumor and nodular calcifications at the center of the tumor. The latter are also known as “pituitary stones” (PSs) and are relatively rare, with fewer than 20 reported cases. Furthermore, these types of tumors are histologically classified into 2 types, namely those with prominent calcification and those with osteoid metaplasia, but pathophysiological mechanisms have not yet been well elucidated for both types.^{4,7,8} Because 74–90% of pituitary adenomas with intratumoral calcification were prolactinomas, it had been thought that elevated PRL was the cause of PS formation.⁹ However, in a systematic review of PSs, prolactinoma was observed in only 4 (25%) of 16 cases among these cases, suggesting that hormone secretion may not be the main mechanism of PS formation.^{4,10–12} In previous reports, pituitary apoplexy, radiation therapy, and drug treatment as well as mass compression and the increased intrasellar pressure induced by tumor nodules were considered to be the cause of PSs.^{1,13–15} Although it is just speculation because complete histological confirmation was not performed for partial tumor removal, among them, pituitary apoplexy was the comfortable predicted cause of PS formation in the present case.

Among the PSs, because most of the prominent calcification was in the form of psammoma bodies scattered between adenoma cells or in the form of stratified calcospherites, they were considered to be merely an accumulation of psammoma bodies.¹¹ However, histological features of the osteoid metaplasia show extensive ossification with eosinophilic tumor cells distributed between mature lamellar bone trabeculae.⁹ The osteoid metaplasia of pituitary adenoma has been reported in 6 cases, only 2 of which had formed PSs, both of which were prolactinoma cases.⁴

In our patient, microscopic findings showed that the tumor cells with eosinophilic endoplasmic reticulum proliferated in an alveolar shape and were also found in the lamellar bone trabeculae, which suggested

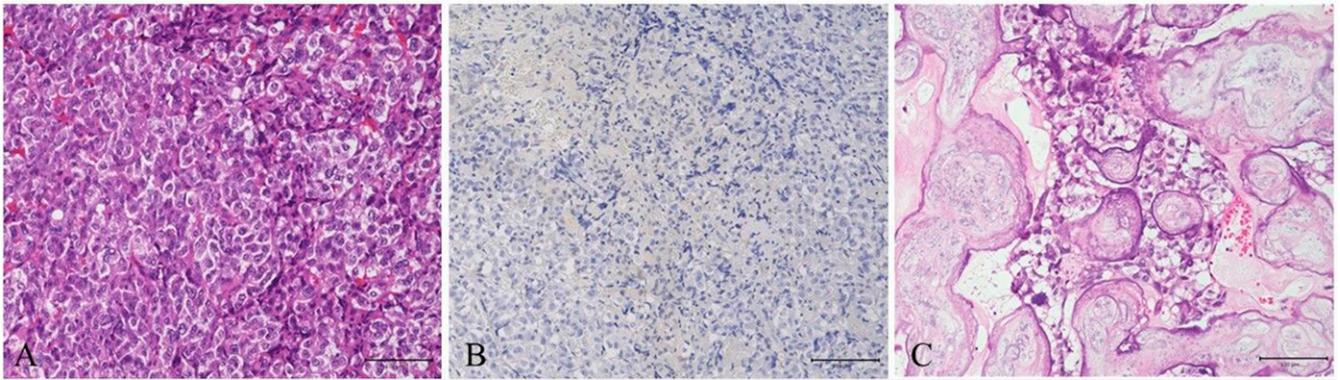


FIG. 4. Histopathological photomicrographs of the tumor and the calcified lesion. **(A)** Tumor cells with a rounded nucleus and an eosinophilic cytoplasm proliferated. Original magnification $\times 200$. **(B)** The tumor cells were immunohistologically negative for PRL. Original magnification $\times 200$. **(C)** A photomicrograph of the calcified lesion shows that most of the parenchyma was replaced by mature lamellar bone tissue. The tumor cells were observed among the lamellar bone trabeculae. Original magnification $\times 200$.

osteoid metaplasia (Fig. 4). The tumor cells were immunohistologically negative for PRL, GH, and ACTH. To the best of our knowledge, this is the first report of osteoid metaplasia–type PSs in nonfunctioning pituitary adenoma. Because hormone secretion including PRL was not observed and the tumor size was not large, the mechanism of osteoid metaplasia in our patient remained unknown.

There have been several episodes suggesting CSF rhinorrhea before the operations, and intraoperative findings also suggested CSF leakage near the floor of the sella turcica in the present case. Even though CSF rhinorrhea was not evident, because MRI revealed disruption of the sellar bony structure, PSs, and the CSF intense fluid collection in the sphenoid sinus 4 years before the patient was admitted to our institute, a dural tear of the sella turcica was already present. Approximately 80% of CSF leakage was associated with nonoperated pituitary adenoma in prolactinomas treated with dopamine agonists. Other causes, such as bone destruction due to pituitary apoplexy or tumor growth, have been reported.^{16–18} Spontaneous CSF rhinorrhea often occurs on the cribriform plate of the ethmoid bone, the posterior or lateral walls of the sphenoid sinus, and the subarachnoid tissue that penetrates into the sella turcica from a small fistula as a result of the destruction of dura and the sellar floor due to CSF pulsations, which causes serious CSF leakage.^{17,19,20} Chu et al. reported a case in which a small pituitary adenoma was accidentally found when repairing spontaneous CSF rhinorrhea.⁶ In the present patient, although the tumor was not as large as the one in the previously reported case, pituitary apoplexy that might involve PS formation, as described above, resulted in partial necrosis of the tumor cells and led to CSF collection into the sella turcica. Then, initial CSF leakage occurred through disruption of the dura, which had been thinned by the tumor mass. Additionally, enlargement of the dural tear and erosion of the sellar floor were due to the amplified mechanical stimulation by the PS near the sellar floor. Furthermore, it was considered that erosion of the sellar floor and CSF leakage were aggravated with hydrocephalus caused by secondary meningitis.

The cause of the decreased visual acuity despite the small size of the tumor in our patient was due not only to the direct compression on the left optic nerve by the PSs but also to the unusual traction on the optic nerve due to adhesion with the surrounding tissues caused by meningitis. Additionally, downward compression on the optic nerve by the increased intracranial pressure from hydrocephalus because the

visual acuity was improved after creation of the VP shunt. Thus, we suggest that the PS near the sellar floor, which was rare as a pituitary adenoma, was related to the specific pathology and the clinical course in the present case.

Lessons

PSs formed near the sellar floor cause spontaneous CSF rhinorrhea, which might cause meningitis and secondary hydrocephalus that result in loss of visual acuity independent of tumor size. Therefore, careful follow-up may be necessary in such cases, even if the tumor size is small.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Ikeda, Kanemitsu, Kawabata, Wanibuchi. Acquisition of data: Kanemitsu, Oku. Analysis and interpretation of data: Kanemitsu, Fukumura, Sakai, Hiramatsu. Drafting the article: Ikeda, Kanemitsu, Fukumura, Kawabata. Critically revising the article: Oku, Nonoguchi. Reviewed submitted version of manuscript: Oku, Furuse, Nonoguchi, Hiramatsu, Imagawa, Ikeda. Approved the final version of the manuscript on behalf of all authors: Ikeda. Study supervision: Kawabata, Wanibuchi.

Correspondence

Naokado Ikeda: Osaka Medical College, Takatsuki, Osaka, Japan. neu098@osaka-med.ac.jp.