Cerebrospinal Fluid Rhinorrhea Associated with Untreated Prolactinoma

—Case Report—

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Abstract

An 80-year-old female presented with non-traumatic cerebrospinal fluid (CSF) rhinorrhea due to untreated prolactinoma, with simultaneous development of bilateral leg pains and gait disturbance due to lumbar canal stenosis. Neuroimaging showed an intrasellar mass extending into the sphenoid sinus, right cavernous sinus, and suprasellar cistern. Computed tomography cisternography clearly showed the CSF pathway through the tumor. Subtotal removal of the tumor and reconstruction of the sellar floor via a transsphenoidal approach resulted in resolution of the CSF rhinorrhea. Both the invasive features and/or spontaneous shrinkage of the tumor might have created the abnormal CSF pathway. The clinical manifestation of lumbar canal stenosis might be triggered by such profound CSF leakage.

Key words: cerebrospinal fluid rhinorrhea, pituitary adenoma, presentation, prolactinoma, lumbar canal stenosis

Introduction

Cerebrospinal fluid (CSF) rhinorrhea is a well-known sequela of transsphenoidal surgery,⁹⁾ radiation therapy,^{12,16,24,26)} and bromocriptine treatment for pituitary adenomas.^{1,11,14,17,21,27)} However, CSF rhinorrhea as the first manifestation of untreated pituitary adenomas is exceptional.²³⁾

We describe an elderly patient with prolactinoma who presented with CSF rhinorrhea.

Case Report

An 80-year-old female suffered sudden onset of CSF rhinorrhea and subsequent bilateral leg pains 3 months before hospitalization. Gait disturbance began due to the intolerable pains. Her medical history included treatment for hypertension. She denied any history of head injury or meningitis.

Physical examination found that watery-clear fluid drained continuously from her right nostril

and the flow increased when she leaned forward. Neurological examination found hyporeflexia of the lower extremities. Endocrinological examination revealed elevated serum prolactin level (2440 ng/ml) and decreased serum gonadotropin level. Sagittal skull tomography showed extensive destruction of the sellar floor, dorsum sellae, and upper clivus (Fig. 1). Magnetic resonance (MR) imaging revealed an enhanced intrasellar mass extending into the sphenoid sinus, right cavernous sinus, and suprasellar cistern along the pituitary stalk (Fig. 2). No displacement of the optic apparatus or ventricular dilation was detected. The location of the normal pituitary gland was not clearly discernible. Computed tomography cisternography with Isovist (Schering AG, Berlin, Germany) injection localized the CSF pathway from the suprasellar cistern into the sphenoid sinus through a crevice of the tumor (Fig. 3).

One week after admission, she underwent transsphenoidal surgery following spinal drainage inser-

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Fig. 1 Lateral skull tomogram showing ballooning of the sella turcica and extensive destruction of the sellar floor, dorsum sellae, and upper clivus.

Fig. 2 T₁-weighted magnetic resonance images with contrast medium (upper left: axial image, upper right: sagittal image, lower row: coronal images) revealing an almost homogeneously enhanced intrasellar mass, extending into the sphenoid sinus (upper right), right cavernous sinus (upper left, lower row), and suprasellar cistern along the pituitary stalk (lower right). Displacement of the optic apparatus is not present (upper right, lower left).

Fig. 3 Coronal computed tomography cisternograms localizing the cerebrospinal fluid pathway from the suprasellar cistern to the sphenoid sinus through a crevice of the tumor (arrows). Bone defect of the sellar floor is present (right). The suprasellar cistern contains a few air bubbles (right).

Fig. 4 T₂-weighted magnetic resonance images of the lumbar spine (left: sagittal view, right: axial view) showing compression of the dural theca, most significantly at the L3-4 intervertebral level.

tion. The anterior wall of the sphenoid sinus was intact, but a soft grayish tumor with CSF filled most of the sphenoid sinus. Destruction of the sellar floor was present. Gross total removal of the intrasphenoidal and intrasellar tumor exposed the diaphragma sellae without identifiable perforation herniating into the sella. The rectus fascia, abdominal fat tissue, osseous nasal septum, and fibrin glue were used for packing of the tumor cavity and reconstruction of the sellar floor. The spinal drainage was left in place for 9 days. CSF cytology

findings were negative.

Histological examination of the surgical specimen revealed chromophobe adenoma without mitoses, nuclear atypia, or cytological pleomorphism. The tumor cells showed immunoreactivity for prolactin with the characteristic pattern of prolactinoma ("Nebenkern" pattern or perinuclear Golgi pattern). The MIB-1 proliferative index (Cat. No. 0607; Immunotech, Westbrook, Me., U.S.A.) was less than 0.5%.

She had an uneventful postoperative course. MR imaging of the lumbar spine disclosed a degenerative narrow canal without disseminated disease (Fig. 4). Her leg pains gradually resolved. Postoperative MR imaging showed a residual tumor and the serum prolactin level remained considerably elevated (909 ng/ml), but no further treatment was given. She showed no evidence of CSF rhinorrhea during the 14-month follow-up period. She is now able to walk with a cane.

Discussion

"Non-traumatic" CSF leakage caused by tumors can be divided into *direct* and *indirect* types,²⁵⁾ depending on whether the fistula is created directly by the tumor eroding the meninges and bone²⁵⁾ or indirectly via high intracranial pressure causing erosion of anatomically fragile areas.⁵⁾ *Direct* type CSF leakage may be caused by pituitary adenomas, meningiomas,^{11,16)} osteomas,^{11,16)} nasopharyngeal fibromas,¹⁶⁾ chordomas,¹¹⁾ and nasopharyngeal adenocarcinomas.²⁵⁾ The present case is the *direct* type. Intracranial hypertension caused by tumors could be relieved by CSF leakage through an anatomically fragile area in the skull base (*indirect* type).^{24,25)} The cribriform plate, sellar floor, and clivus are such vulnerable areas.^{5,10,25)} Furthermore, coincidental lesions or congenital anomalies such as empty sella,²⁵⁾ nasal encephalocele,²⁵⁾ cranial dysplasias in neurofibromatosis,⁴⁾ and osteomyelitic erosion²⁵⁾ may be associated with *indirect* type CSF leakage.

Untreated pituitary adenomas manifesting as CSF rhinorrhea are extremely rare.^{23,25)} Only one case occurred in over 1700 transsphenoidal resections of pituitary adenomas.²³⁾ At least 32 cases of untreated pituitary adenoma manifesting as CSF rhinorrhea have been reported. However, the histological diagnosis or endocrinological profiles were not well-documented in some cases.^{2,7,11,16,19,25)} Table 1 summarizes 12 cases of histologically and endocrinologically verified pituitary adenomas associated with CSF rhinorrhea.^{3,6,8,11,13,22,23,30)} The patients were seven males and five females aged from 23 to

80 years (mean 41.7 years). The pretreatment duration of CSF rhinorrhea ranged from 6 weeks to 10 years (mean 19 months). Four of 12 patients had meningitis preoperatively, and one had hydrocephalus causing increased intracranial pressure.¹¹⁾ The functional classification of the tumors was prolactinoma in six cases, non-functioning adenoma in four, adrenocorticotrophic hormone (ACTH)-producing adenoma in one, and prolactin- and ACTH-producing adenoma in one. Skull radiography identified erosion or destruction of the sellar floor in 11 cases. Based on the radiological or intraoperative findings, the adenomas extended into the sphenoid sinus in 11 cases, ethmoid sinus in four, and suprasellar region in six. Surgical treatment including eight transsphenoidal operations were performed in all patients and resulted in resolution of the CSF rhinorrhea. Postoperative adjuvant therapy was used in six patients.

Patients harboring sellar or parasellar tumors suffer CSF flow from the subarachnoid space into the nasal cavity only under three conditions: Connection between the subarachnoid space and cavum sellae, communication between the sella and paranasal sinuses, and presence of a CSF pathway within the tumor.²³⁾ Direction and degree of the tumor extension are associated with connection between the tumor and the subarachnoid space or nasal cavity. Pituitary adenomas are generally recognized as one of the most benign tumors, but frequently behave aggressively with infiltrative growth.^{20,28,29)} Diffuse invasion of the skull base by macroprolactinomas is common.¹⁸⁾ Hyperprolactinemia in older patients is clinically more covert than in younger patients, so the tumor tends to be larger at diagnosis. The vast majority of reported cases had sphenoidal extension, which must allow communication between the cavum sellae and the sphenoid sinus. Connection between the subarachnoid space and the cavum sellae also occurs by direct extension of the tumor through the diaphragma sellae. Approximately half of the reported cases showed suprasellar extension. In addition, anatomical variants of the sphenoid bone may be related to the development of CSF leakage. Twenty-seven bony defects were found in 138 adult sphenoid bones,¹⁵⁾ which could provide potential sites for the CSF fistula. Fourteen defects were located at the site of the superior opening of the transient lateral craniopharyngeal canal, and 13 along the pathway of the internal carotid artery. Coexistence of such a bony defect and tumor extension into the cavernous sinus may allow an alternative CSF pathway. In contrast, the tumor must not block CSF flow.^{7,12)} For instance, spontaneous occlusion of

Table 1 Summary of 12 cases of untreated pituitary adenomas manifesting as cerebrospinal fluid (CSF) rhinorrhea

Author (Year)	Age/ Sex	Tumor classifi- cation	Duration of CSF rhinorrhea	Meningi- tis	Erosion of the sellar floor	Tumor extension			Other prominent radiological findings	Surgery	Adjuvant treatment	Postoperative follow-up period
						Sphenoid sinus	Ethmoid sinus	Suprasellar region				
Giovanelli and Perria (1967) ^{1,3)}	40/F	NF	8 mos	+	+	+	+	-	ND	craniotomy	-	6 mos
Cole and Keene (1980) ^{1,1)}	41/M	PRL	6 mos	-	+	+	-	+	ND	TS	RT	12 mos
	28/F	PRL	3 mos	-	+	+	ND	-	ND	craniotomy followed by TS	RT	ND
	38/M	NF	17 mos	+	+	+	ND	ND	hydro- cephalus	TS	RT	ND
Nutkiewicz et al. (1980) ²²⁾	45/F	PRL, ACTH	3 yrs	-	+	+	ND	-	ND	craniotomy	-	22 mos
Rothrock et al. (1982) ³⁰⁾	24/M	NF	10 yrs	+	+	+	ND	-	ND	craniotomy followed by dural repair	-	18 mos
Bilo et al. (1984) ⁹⁾	42/M	PRL	2 yrs	+	+	-	-	ND	none	TS	-	ND
Obana et al. (1990) ²³⁾	63/M	PRL	1 yr	-	+	+	+	+	hemorrhagic foci	transethmoidal	RT, BRC	6 mos
	36/F	PRL	2 mos	-	+	+	+	+	none	TS	RT, BRC	7 yrs
Carroll et al. (1991) ⁹⁾	23/M	ACTH	8 wks	-	+	+	ND	+	displacement of the optic apparatus	TS	-	ND
Bell (1991) ⁹⁾	40/M	NF	6 wks	-	ND	+	+	+	none	TS	RT	12 mos
Present case	80/F	PRL	3 mos	-	+	+	-	+	crevice of the tumor	TS	-	14 mos

ACTH: adrenocorticotrophic hormone-producing adenoma, BRC: bromocriptine treatment, ND: not described, NF: non-functioning adenoma, PRL: prolactinoma, RT: radiation therapy, TS: transsphenoidal surgery.

the intratumoral vessels may occur as a possible cause of tumor shrinkage, which can create a crevice within the tumor as a CSF pathway. Furthermore, spontaneous regression of the tumor might occur as a result of decreased serum estrogen level after the menopause.

The histological or endocrinological subtype was prolactinoma in half of the reported cases. Invasive pituitary tumors usually exhibit significantly higher growth fractions or higher incidence of TP 53 mutations than noninvasive tumors.^{32,33} In the present case, the neuroimaging findings and very high serum prolactin level indicated invasive adenoma, but the tumor showed a low proliferative activity based on MIB-1 immunostaining. Invasive features of pituitary adenomas are not always correlated with the immunohistochemical classification.³¹ CSF rhinorrhea may be associated with any subtype of pituitary adenoma.

The abnormal CSF pathway in the present case may have resulted from the invasive features and/or spontaneous shrinkage of the tumor. The causative mechanisms of CSF rhinorrhea associated with pituitary tumors are complex and multifactorial. Neuroimaging should be carefully evaluated to assess the tumor extension, adjacent bone erosion, anatomical variants, and coincidental lesions before treatment.

Clinical manifestation of the lumbar canal stenosis occurred almost simultaneously with the CSF rhinorrhea in the present case. Such lumbar canal stenosis might be triggered by the profound CSF leakage. Continuous CSF rhinorrhea could result in reduction of the subarachnoid space and increased compression of the dural theca. Postoperative bed rest and resolution of the CSF rhinorrhea might lead to improvement of the symptoms.

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