Cerebrospinal Fluid Rhinorrhea and the Empty Sella

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Cerebrospinal fluid rhinorrhea is associated infrequently with abnormalities of the pituitary fossa or sphenoid sinus. It has almost always been described in reference to tumor, cyst, infection, head injury, nasal or cranial operation, yttrium or x-ray therapy. The occurrence of cerebrospinal fluid rhinorrhea in the absence of the above and in the presence of an "empty sella" had not been reported in the English literature prior to June, 1968. At that time Ommaya, et al., reviewed 18 cases of nontraumatic rhinorrhea including two patients with "empty sellas." One was a 57-year-old man with seizures and mild hypopituitarism, in whom pneumoencephalography and surgery showed that the anterior portion of the sella was empty. A second patient, mentioned only briefly, had an arachnoidal hernia through a hole in the floor of the sella. Both patients were operated on successfully for arrest of the rhinorrhea.

The "empty sella" syndrome usually refers to a rare late complication of radiotherapy for pituitary adenomas. Years after receiving radiation, these patients characteristically develop vision impairment, probably due to involvement of the optic nerve and chiasm by dense scar tissue or radiation degeneration, without evidence of tumor recurrence.

In our four new patients cerebrospinal fluid rhinorrhea was associated with leakage through an "empty sella" as verified at operation. None had received radiotherapy and in none was there any evidence of tumor.

Case Reports

Case 1. A 53-year-old woman had had intermittent cerebrospinal fluid rhinorrhea since May, 1965, and one episode of meningitis in January, 1966. In August, 1966, she was admitted to the Neurological Institute because of recurrent cerebrospinal fluid rhinorrhea. There was no history of head trauma or previous surgery. The patient had had six pregnancies, and a normal menopause had begun 2 years prior to admission.

Examination. Physical examination was normal except for moderate obesity and right-sided cerebrospinal fluid rhinorrhea. Neurological examination was normal. There was no visual defect. Endocrine evaluation revealed no abnormality. Skull x-ray films showed a fluid level in the right sphenoid sinus. Coronal and sagittal tomograms of the sella turcica revealed erosion of the floor of the sella, slightly more on the right side. Bilateral carotid arteriography was normal.

Operation. Operation performed through a right frontal craniotomy showed the sella to be markedly enlarged. There was space on each side of the pituitary gland. The diaphragma sellae was widely patent, and no tumor or opening into the sphenoid sinus was seen. The sella turcica was then packed with muscle.

Postoperative course. The postoperative course was uneventful, and the patient has had no more rhinorrhea.

Case 2. A 52-year-old woman had had cerebrospinal fluid rhinorrhea since September, 1966, and an episode of meningitis in December, 1966. Because of persistent cerebrospinal fluid rhinorrhea she was admitted to the Neurological Institute in January, 1966. There was no past history of trauma or head surgery. A hysterectomy had been performed in 1955 for fibroids, but the ovaries had not been removed.

Examination. Physical examination was normal except for moderate obesity and right-sided cerebrospinal fluid rhinorrhea. Neurological examination was normal. There

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was no visual field defect. Endocrine evaluation was normal. X-ray films revealed a sella turcica which was larger than normal.

**Operation.** A right frontal craniotomy showed that the sella turcica was enlarged and filled with arachnoid trabeculae. There was no sign of tumor. The stalk of the pituitary was resting on the dorsum of the sella. Neither pituitary tissue nor diaphragma sellae could be found. The empty sella was then packed with muscle.

**Postoperative course.** Postoperatively the patient did well and had no subsequent rhinorrhea.

**Case 3.** A 57-year-old woman had had persistent cerebrospinal fluid rhinorrhea since February, 1962. She was admitted to the Neurological Institute in November, 1964, for evaluation and treatment. There was no history of trauma or head surgery. The patient’s sister had been successfully operated on at another hospital for cerebrospinal fluid rhinorrhea. In 1942, the patient had undergone hysterectomy for fibroids. She had been on thyroid replacement therapy for several years.

**Examination.** Physical examination was normal except for obesity and left sided rhinorrhea on bending forward. Neurological examination was normal. There was no visual field defect. Endocrine evaluation was normal. X-ray films of multiple skull positions revealed a fluid level in the left sphenoid sinus with enlargement of the right side of the floor of the sella turcica.

**Operation.** Through a left frontal craniotomy it was revealed that the left side of the sella turcica was empty. The pituitary gland occupied only the right side of the sella, and the chiasm was prefixed. Although no opening into the sphenoid sinus could be seen, muscle was packed into the left side of the sella, the presumed location of the leak.

**Postoperative course.** Postoperatively the patient did well with no recurrent cerebrospinal fluid rhinorrhea.

**Case 4.** A 45-year-old woman had had intermittent left-sided cerebrospinal fluid rhinorrhea since February, 1967, following an upper respiratory infection. She was admitted to the Neurological Institute in August, 1967, for evaluation and treatment of persistent rhinorrhea. There was no history of trauma or previous surgery. The patient was pre-menopausal. Six years prior to admission she had a severe bifrontal headache lasting 8 days.

**Examination.** Physical examination was normal except for moderate obesity. Neurological examination was normal. There was no visual field defect. Endocrine evaluation revealed no abnormality. Laminograms (5 mm cuts) showed an area which was at first interpreted as being a large defect in the sella floor; polytomograms (2 mm cuts) revealed this area to be the intrasphenoid septum. The polytomograms further showed an opacified left sphenoid sinus (Fig. 1 left) with a defect in the antero-lateral aspect of the sella in proximity with the anteriorly placed sphenoid sinus (Fig. 1 right). Radio-iodinated human serum albumin (RISA, 2 cc) was injected into the lumbar subarachnoid space. Serial brain scans and radioactive counts from cotton pledgets in both nostrils revealed a definite left-sided cerebrospinal fluid leak and increased uptake of radioactive material in the area of the sella (Fig. 2).

**Operation.** A left-fronto-temporal crani-
otomy revealed a large empty space within the sella turcica (Fig. 3). Neither pituitary tissue nor an opening into the sphenoid sinus could be seen. The pituitary fossa was then packed with stamps of temporal muscle.

Postoperative course. The patient's immediate postoperative course was uneventful. One month later, however, she again developed left-sided rhinorrhea, which was intermittent. Ten months later she was hospitalized again for re-evaluation. Another RISA study revealed a bolus of radioactive uptake in the region of the sella turcica and an increase in radioactivity in the cotton pledgets inserted in the left nostril. The patient was reoperated through a left frontal craniotomy. Many dense adhesions were encountered. The sella was packed again with muscle. The patient, now 2 months after the operation, has no rhinorrhea.

Discussion

Cerebrospinal fluid rhinorrhea is usually associated with leakage through the cribiform plate of the anterior cranial fossa, but may occur through an opening into the sphenoid sinus in the middle fossa. Rhinorrhea may also result from cerebrospinal fluid leakage through the middle ear and Eustachian tube from either the middle or posterior fossae. Trauma is the most common cause for rhinorrhea from all three fossae. Traumatic rhinorrhea occurs in approximately 2% of unselected head injuries. A dural tear over the sphenoid sinus was found in 13% of 84 cases of cerebrospinal fluid rhinorrhea after closed head injury, and was the only tear in relation to the paranasal sinuses in 5 (6%). Most of these patients had profuse rhinorrhea and air in the chiasmatic cistern; therefore, they were subject to a high risk of infection which necessitated operative repair of the leak.

Non-traumatic rhinorrhea is a rare condition. Only 82 cases were found in a recent review of the literature. Of these, 37 were associated with tumors, 18 involving the sella turcica. In only two of these was the actual site of cerebrospinal fluid leakage demonstrated through a fistula in the floor of the sella. Most of the pituitary tumor cases were associated with internal hydrocephalus. Increased intracranial pressure precipitated the escape of cerebrospinal fluid in these and other cases through an accessible outflow pathway, usually the cribiform plate.

Infection is an infrequent primary cause of cerebrospinal fluid rhinorrhea. Som and Kramer reported a case of rhinorrhea due to acute osteomyelitis of the posterior wall of the sphenoid sinus secondary to a submucosal abscess. A defect in the dura was
noted on the cranial surface of the clivus. Bateman mentions a case of rhinorrhea secondary to a pituitary abscess.

A more common cause of rhinorrhea from the pituitary fossa and sphenoid sinus is transsphenoidal hypophysectomy. This may be controlled by placing a muscle graft in the pituitary fossa and packing the sphenoid sinus for 7 days with an antibiotic impregnated gauze.

Other patients have developed rhinorrhea after implantation of yttrium 90 into the pituitary gland or a tumor thereof. A report of seven cases emphasizes the unlikely occurrence of spontaneous recovery; it was recommended that surgical correction with a muscle graft be delayed at least 10 weeks after insertion of the irradiated material.

Pituitary cysts and primary arachnoid cysts of the sella are rare, and have very seldom been associated with cerebrospinal fluid rhinorrhea. One case having rhinorrhea was found at operation to have an associated pituitary cyst and tumor. Another patient who died of meningitis after the onset of rhinorrhea was found at postmortem examination to have a cyst encompassing the pituitary stalk and compressing the gland. The reason for the rhinorrhea was not clear.

The non-traumatic form of rhinorrhea has a characteristic clinical profile which differs in many respects from the traumatic type. Non-traumatic rhinorrhea is often intermittent but usually persists for years if untreated. The leakage is often minimal at first, but later may become profuse. Spontaneous arrest occurs in about one-third of the cases. Laterality is variable and often bears no relation to the side of the fistula. Aerocle is uncommon and sense of smell is usually preserved. Headache and elevated intracranial pressure are common and are characteristically relieved by the onset of flow. Patients are almost always adults, and females predominate by at least a 2:1 ratio.

Our four patients with rhinorrhea and an "empty sella" had a somewhat different but clinically distinctive syndrome. All were moderately obese white women between 45 and 57 years of age. Three were post-menopausal. Pituitary, thyroid, and adrenal function were normal in all patients as determined by exhaustive endocrine evaluation. Only two had meningitis. In none was there an aerocele. Rhinorrhea was right-sided in two and left-sided in two. The side of the leak proved helpful in localizing the side of the fistula in the three cases in which this was possible. In the fourth patient a left-sided leak was associated with a bilaterally empty sella, and there was no x-ray or surgical evidence of lateralization of the fistula. None of these patients had elevated intracranial pressure or headache.

Modification of this profile is provided by Ommaya's case of a 57-year-old man with a partially empty sella, mild hypopituitarism, seizures, and non-traumatic rhinorrhea.

There are several possible explanations for rhinorrhea associated with an "empty sella." Engles has demonstrated the existence of a hypophyseal subarachnoid space by pneumoencephalography and histologic section. The foramen of the diaphragma sellae is often very large, allowing the subarachnoid space to come into contact with the hypophysis and perihypophyseal tissues with the aperture of the diaphragma.

A possible explanation for a defect in the sella floor is that a pituitary tumor may have caused erosion through the bone. Subsequent infarction of the tumor may explain the empty sella and the failure to demonstrate tumor tissue. The presence of a large sella in two of our cases and laminographic evidence of erosion of the sella floor in three are consistent with a tumor. It is quite rare for pituitary tumors to cause a fistulous opening through the floor of the sella into the sphenoid sinus. In a review of 339 cases of pituitary tumors, nasopharyngeal extensions were found to have developed in only 2.4%, and none of these patients had cerebrospinal fluid rhinorrhea. In patients with rhinorrhea and gross tumor involvement of the sella, it is rare for the tumor to establish the leakage directly by boney erosion. This has been reported by Boyd in a case of a malignant pituitary adenoma causing a fistula through the maxillary antrum, and by Norsa in a case of chromophobe adenoma causing a fistula through the sella floor into the sphenoid sinus.

Another possibility is the opening up of a potential embryologic channel with or without elevated intracranial pressure. Transiently elevated pressure due to hard work, exercise, coughing, sneezing, or straining at
stool may be sufficient. The craniopharyngeal canal may provide the appropriate communication between the cerebrospinal fluid and oral-nasal cavity in the present cases of rhinorrhea and empty sella. One of the two hypophyseal primordia is Rathke's pocket or craniopharyngeal duct. This ectodermally-lined space is an extension of the oral cavity and grows in the midline toward the infundibular process of the diencephalic floor between the fourth and sixth week of gestation. The path of ingrowth of the craniopharyngeal duct extends from the oral pharynx through the sphenoid bone into the sella turcica. The possibility of cerebrospinal fluid escaping through the nose via the cranial pharyngeal duct has been suggested by Loftus and Johnston. The latter describes a patient with pituitary disease operated on by Cushing. The patient subsequently developed rhinorrhea and on the ninth postoperative day, had a severe sneezing spell, developed meningitis, and died on the 13th day. At autopsy a persistent craniopharyngeal canal was found which had been opened at the time of operation. The anterolateral defect in the sella as seen in our Case 4 is not thought to represent such a canal which is a more posterior and midline structure.

The theory of focal atrophy as advanced by Ommaya, et al. is plausible and relevant. He suggests that atrophy may develop either in the area of the sella or cribriform plate. The empty space is filled with cerebrospinal fluid in an extension of the subarachnoid space. The normal cerebrospinal fluid pressure pulse may exert an erosive effect in the surrounding bone.

An intriguing feature in the cases of cerebrospinal fluid rhinorrhea with grossly "empty sellas" is the presence of normal pituitary function. It is possible that adequate pituitary tissue actually remained in the sella but was not visible at the time of surgery. The relative paucity of pituitary tissue may have been caused by partial pituitary infarction or a more physiological involution (menopausal in three of the four patients). Another possible explanation is that pituitary tissue existed in an ectopic location, along the path of ingrowth of the craniopharyngeal duct. This may have caused the patency of such a duct enabling it to be the route for the cerebrospinal fluid fistula.

Several diagnostic features are helpful in locating the site of the cerebrospinal fluid fistula. Skull x-rays may show an air-fluid level as occurred in two of our four cases. Polytomograms of the sella turcica may show boney defects or sinus opacification. Intrathecal RISA may give evidence of location of the cerebrospinal fluid leak, as noted in Case 4 where the radioactivity accumulated in the area of the sella.

Treatment in each case was by frontal craniotomy and an intradural approach so that the sella could be packed with muscle. This procedure was successful in preventing a recurrence of the rhinorrhea in three of the four cases. Re-operation was necessary and presumed to be successful in the fourth.

Summary

A syndrome has been described in which cerebrospinal fluid rhinorrhea through the sella turcica and sphenoid sinus was associated with a grossly empty sella in the absence of known trauma, pituitary tumor, radiation therapy, or neurological symptoms. This condition occurred in four obese women between 45 and 57 years of age with pituitary function and visual fields intact. The diagnostic aids of sphenoid sinus x-ray films, sella polytographs, and intrathecal RISA have been described. Packing of the empty sella with muscle has been recommended.

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References


7. Hughes, J., Brisman, R., Mount, L., and Holub, D. Endocrine evaluation of the empty sella. (Unpublished data.)


