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Spontaneous “pneumo-apoplexy” as a presentation of pituitary adenoma

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ABSTRACT

Cases of spontaneous CSF leak associated with pituitary tumor apoplexy are uncommon in the literature with pneumocephalus or pneumosella being rare, especially spontaneous occurrence of pneumocephalus being extremely rare. We present a case of pituitary macroadenoma apoplexy resulting in spontaneous CSF leak and a large volume of intra-tumoral gas. A 65-year-old female presented with severe headache, profuse rhinorrhea and acute vision loss and was found to have a large sellar and suprasellar lesion with air and hemorrhage with mild peripheral enhancement. The patient underwent trans-sphenoidal tumor resection and repair of skull base for CSF leak with nasoseptal flap placement. Pathology demonstrated a pituitary adenoma exhibiting immunoreactivity for ACTH. To our best knowledge, our case is the first report of features of pituitary tumor apoplexy with hemorrhage and pneumosella, which could be summarized by the term “pneumo-apoplexy”.

1. Introduction

We present a case of pituitary macroadenoma apoplexy resulting in spontaneous cerebrospinal fluid (CSF) leak and a large volume of intra-tumoral gas. Cases of spontaneous CSF leak associated with pituitary tumor apoplexy are uncommon in the literature with pneumocephalus or pneumosella being very rare. To our best knowledge, our case is the first report of features of a pituitary tumor presenting with apoplexy and pneumosella, which could be summarized by the term “pneumo-apoplexy”.

2. Case report

2.1. History

A 65-year-old female presented to neurosurgery clinic with a 3 week history of abrupt severe headache, initially associated with several days of profuse rhinorrhea and subsequently acute vision loss. In the days preceding the clinic visit, rhinorrhea had gradually improved and vision loss was improving.

2.2. Examination and workup

The patient's physical exam findings were unremarkable except for vision 20/40 on the right and 20/70 on the left, corrected. The initial laboratory workup was notable for an elevated Adrenocorticotropic hormone (ACTH) level.

Magnetic resonance imaging (MRI) of the brain demonstrated a large sellar lesion extending from the floor of the sphenoid sinus to the optic chiasm, containing a central cystic region with an air-fluid level (Fig. 1A, B, arrows). T1-weighted imaging demonstrated the fluid level to be of hyperintense signal indicating hemorrhage/blood products (Fig. 1C, arrow). Following the administration of intravenous contrast, there was mild enhancement of the periphery/rim of the lesion (Fig. 1D, arrow). A noncontrast computed tomogram (CT) of the head was subsequently performed which demonstrated marked expansion of the sella with osseous remodeling and erosion and a large central collection of air/gas within the sella and suprasellar cistern causing compression on the optic pathways (Fig. 2A, B, arrows).

2.3. Management

The patient was taken to the operating room for endoscopic trans-sphenoidal exploration. Intraoperatively, a large necrotic mass was identified extending into the sphenoid sinus with associated erosions of the dura mater, bone, and sphenoid sinus mucosa. Superiorly also, some of the tumor capsule was noted to be necrotic. The patient underwent uncomplicated tumor resection and repair of skull base for CSF leak with nasoseptal flap placement.

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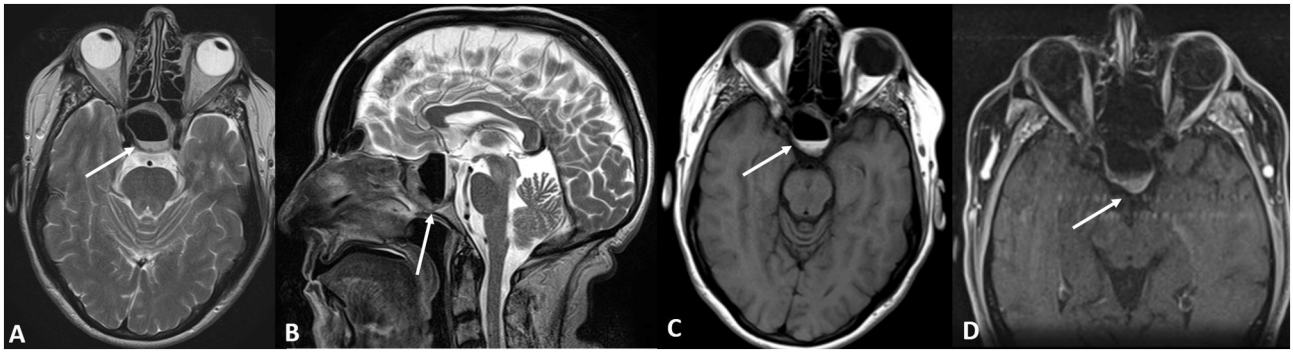

Fig. 1. (A) Axial T2-weighted image demonstrates a large sellar lesion containing central cystic region with an air-fluid level. (B) Sagittal T2-weighted image shows the lesion extending from the floor of the sphenoid sinus to the optic chiasm. (C) Axial T1-weighted image demonstrates the fluid level to be of hyperintense signal indicating hemorrhage/blood products. (D) Following the administration of intravenous contrast, an axial T1-weighted, fat-saturated image revealed enhancement of the periphery/rim of the lesion.

2.4. Pathological findings and postoperative course

Pathology demonstrated a pituitary adenoma exhibiting immunoreactivity for ACTH. Post-operatively, the patient's vision was better with 20/30 right, 20/40 left at 6 weeks and 20/20 right, 20/25 left corrected at 3 months. On subsequent follow-up, there was no evidence of tumor recurrence or CSF leak upto 3 years.

3. Discussion

Pituitary tumor apoplexy is a constellation of findings characterized by a relatively acute onset of severe headache, vision field deficit, ophthalmoplegia, and endocrine dysfunction due to hemorrhage or infarction of a pituitary tumor. The rapid increase in ischemic/hemorrhagic tumor volume results in compression of adjacent neurovascular structures, including the optic chiasm and cavernous sinuses. The sudden increased intracranial pressure and stretching of the adjacent dura result in severe headache. In addition, leakage of blood products and necrotic tissue into the adjacent subarachnoid space results in meningeal irritation, nausea, vomiting, headache, and potentially vasospasm [1–3]. This phenomenon occurs in approximately 0.5–10% of adenomas [2]. Importantly, *pituitary tumor apoplexy* should be distinguished from the term *pituitary apoplexy*, which refers to ischemia of normal pituitary tissue, and is a much rarer event.

The imaging features of pituitary tumor apoplexy are dependent on the age of the infarction, and on whether or not hemorrhage is also present. During the first few hours following an apoplectic event, intratumoral hemorrhage can be detected as hyperdensity within the sella on a non-contrasted CT exam. However, this finding of hyperdensity is non-specific and could be due to calcification from a Rathke's cleft cyst, craniopharyngioma, or adjacent vascular structures. Proteinaceous contents in Rathke's cleft cyst or craniopharyngioma can also mimic hemorrhage. MRI is the preferred method for characterizing adenomas and to evaluate features of tumor apoplexy. Furthermore, MRI can accurately characterize cases of apoplexy due to bland infarction versus hemorrhagic infarction [4]. Non-hemorrhagic pituitary tumor apoplexy is typically identified as tumoral tissue demonstrating T2 hyperintensity, and central hypointensity with peripheral enhancement on post-contrast T1-weighted images. Diffusion-weighted imaging is also helpful in identifying infarcted tumor tissue [5]. Intra-tumoral hemorrhage present for 3 days (early subacute), or up to several weeks old (late subacute), can be identified as hyperintense material on T1-weighted MR images. During this same time frame, blood products are initially hypointense on T2-weighted images and gradually increase in intensity over time [2,6]. The T1 hyperintense/T2 hyperintense fluid within the central tumor cavity in our case indicates subacute hemorrhage.

Our patient developed acute onset of copious clear rhinorrhea, that had a close temporal relationship with headache and visual deficits. The surgical, clinical and radiologic findings support the presence of a transient CSF leak and CSF rhinorrhea. The development of a spontaneous, pre-surgical CSF leak is a rarely reported event in patients with pituitary adenoma. In the majority of non-surgical cases, the leak develops after starting medical therapy (bromocriptine, for example) or post radiation [7]. In a retrospective review of patients with macroprolactinomas and non-functioning pituitary adenomas between 1985 and 2004, Suliman et al. identified non-surgical CSF rhinorrhea in 8.7% of 112 patients with macroprolactinomas, out of which only 2.6% had spontaneous rhinorrhea without preceding medical therapy whereas no nonsurgical rhinorrhea was found in non-functioning adenomas cases [8]. One recent literature review identified 52 cases of non-surgical CSF leak reported between 1980 and 2011, and the leak was non-iatrogenic in only 14 (27%) patients [9]. A skull base defect adjacent to the adenoma was identified in majority of non-surgical CSF leak cases, as it was in our case. Eighty one percent of the associated tumors were found to be prolactinomas, whereas only 1 patient (2%) out of 52 had an ACTH producing tumor [9,10]. The proposed mechanisms behind development of CSF rhinorrhea are based on the premise that invasive adenomas cause skull base defects and where the arachnoid is also breached, a CSF fistula can develop. Tumors generally occlude the opening by acting as a “plug” preventing a CSF leak. If the tumor shrinks, such as with medical therapy with dopamine agonists for prolactin-secreting tumors, a CSF leak manifests. The causes of non-iatrogenic CSF rhinorrhea are postulated to be tumor shrinkage from infarction or hemorrhage or continuing invasion through the arachnoid/skull base, with or without elevated intracranial pressure causing a CSF fistula [9].

Although skull base defects, dural invasion, and CSF leak/rhinorrhea have been reported with invasive macroadenoma, pneumocephalus has been only occasionally described in the literature in cases of pituitary adenoma, out of which gas confined to the sella is rare [11–15]. Gas confined to the sella has been variably described with different terms such as pneumosella, sellar pneumocele, pneumatocele, pneumocyst, or aerocoele, with the term pneumosella used here for discussion purposes. Most commonly, pneumosella has been described in association with post surgical states with an underlying skull base defect [16] or invagination of the sphenoid mucosa years after surgery [11] or as a manifestation of relatively recent tumor resection [12–14,17] or rarely as a sequel of radiation [18]. Isolated spontaneous pneumosella in the absence of prior medical or surgical therapy as the presenting feature of pituitary tumor has been reported exceedingly rarely in the literature, only once previously to our best knowledge [19]. The previously reported pneumosella patient reported in the pre-CT or MRI era by Sage et al., had recurrent headaches for 3 years and

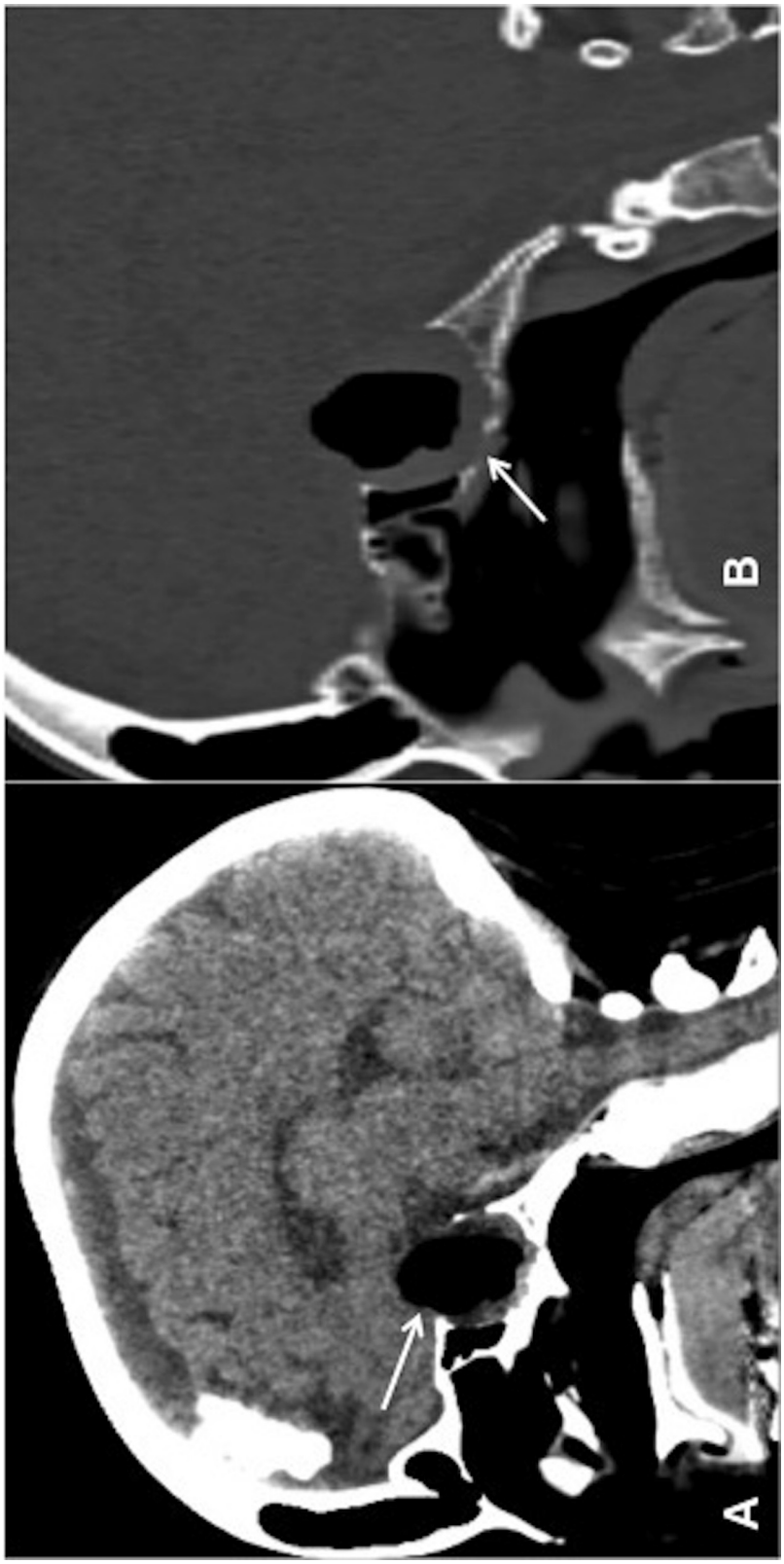

Fig. 2. Midline sagittal non-contrast CT image of the head in soft tissue window (A) and slightly off-midline sagittal image in bone window (B) demonstrate marked expansion of the sella, and a large central collection of air/gas within the sella and suprasellar cistern causing compression on the optic pathways (A, arrow) and erosion of the sellar floor (B, arrow).

progressive visual loss for 2 months and was found to have a chromophobe adenoma [19]. Another case has been reported in the literature with spontaneous pneumocephalus with a pituitary adenoma by Wein et al., however the pneumocephalus was found between the suprasellar mass (non-functioning null cell adenoma) and medial temporal lobe. This patient developed a 3 day history of severe supraorbital pain and blurred vision after a sneeze [20]. In contrast, our patient presented with a 3-week history of sudden onset headache with rhinorrhea and vision loss and features of apoplexy on imaging. The pathology was found to be a pituitary adenoma exhibiting immunoreactivity for ACTH. To our best knowledge, our case is the first report of features of pituitary tumor apoplexy with hemorrhage and pneumosella, therefore summarized by the term “pneumo-apoplexy”.

The conspicuous bony defect in the sellar floor, and the dural and sinus mucosal erosion identified intraoperatively, permitted communication between the necrotic tumor and the sphenoid sinus. This defect was the likely source of the large amount of intra-tumoral gas seen in this case. Mechanisms described in literature to explain development of pneumocephalus include the one-way or ball-valve mechanism and the “inverted bottle theory”. The ball- valve mechanism refers to the entry of air through a skull defect following CSF leakage mechanism, with positive pressure events, such as coughing, sneezing, and Valsalva maneuvers without the ability to escape out. The inverted bottle theory refers to entry of air into the intracranial spaces to account for the negative pressure created by CSF leakage [12,20]. The gas in this case, likely accumulated following tumor ischemia and hemorrhage and as the friable inferior tumor margin broke down, it allowed a communication between the necrotic tumor core and the sphenoid sinus via the pre-existing sellar bony defect. As a corollary to the mechanism proposed previously, due to the necrosis, the tumor stopped acting as a “plug” over the bony defect. The reason behind the lack of spread of this gas to the remaining subarachnoid spaces, despite the preceding clinical symptom of rhinorrhea is unclear. We hypothesize that once the gas entered and filled the necrotic tumor cavity, any remaining solid tissue got pushed to the periphery again “plugging” any CSF fistula defect, or potentially it could be limited superiorly by arachnoid adhesions or simply by lack of a pressure gradient into the intracranial compartment [19], hence preventing escape of the air from the sellar tumor cavity. This could also explain clinical improvement of patient's rhinorrhea in the days prior to presentation.

4. Conclusion

In summary, while CSF rhinorrhea has been reported in cases of pituitary macroadenoma, whether associated with medical or surgical therapy or spontaneously, pneumocephalus associated with cases of pituitary macroadenoma is rare with spontaneous development being further extremely rare and here we present such a case in conjunction with findings of tumor apoplexy.

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