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Pituitary abscess presenting a very rapid progression: report of a fatal case

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Abstract

Pituitary abscess is a rare disease presenting with nonspecific clinical symptoms, and diagnosis is often difficult. This disease is potentially life-threatening, but the majority of cases have a chronic and indolent course. We report a case of a 60-year-old male with a pituitary abscess associated with pituitary adenoma who died 5 days after the onset of clinical symptoms without a definitive diagnosis. Postmortem computed tomography and autopsy findings revealed a sellar mass with cystic change and extension towards the optic chiasm. Histopathology of the lesion demonstrated an abscess with suppurative meningitis and encephalitis. The disturbance of the cardiac autonomic nervous system due to hypothalamus involvement was suggested as the cause of rapid progression and death. This case provides useful information for clinicians to avoid a lethal outcome.

Key words: Pituitary abscess; Pituitary adenoma; Rapid progression; Fatal case; Hypothalamic involvement; Histopathology
1. Introduction

Pituitary abscess is a rare entity of the purulent disease, which most often has an indolent course and can be in remission with appropriate therapies. This is also a potentially life-threatening condition, but rapid deterioration leading to death within several days is very rare (1-6).

Since Heslop described the first case in 1848 (7), around 250 cases of pituitary abscess have been reported in the medical literature. Although most of these reports are case presentations (6-19), recent reviews improved understanding of the clinical features of this entity (1-5). Based on these reports, pituitary abscess is characterized as follows: it represents less than 1% of all cases of pituitary disease referred to specialists; there is a slightly female predominance; the age of patients ranges from 12 to 76 years; 82% of cases are chronic; and the average time between the onset of symptoms and diagnosis is 8.3 months (ranging from 7 days to 36 months, with a median of 6 months).

Pituitary abscess can develop de novo in a normal pituitary gland (about 70%) or in preexisting pituitary pathology (about 30%) (3, 20). Of preexisting lesions, a pituitary adenoma is most common, followed by a Rathke’s cleft cyst, craniopharyngioma and lymphoma (2). A correct preoperative diagnosis is difficult for clinicians, because
symptoms such as chronic headache, visual impairment and abnormal pituitary function are not specific, and the radiological findings cannot distinguish it from other pituitary lesions (1-5). In addition, 70-80% of cases do not present with infectious manifestations like fever, leukocytosis, and meningismus (1, 4, 5), further complicating preoperative diagnosis. Pituitary abscess is diagnosed postoperatively or at necropsy in the majority of instances. The recommended therapies are transsphenoidal surgery, administration of antibiotics, and hormonal replacement (2, 11, 12).

We report a case of pituitary abscess associated with pituitary adenoma, which resulted in death 5 days after the onset of clinical symptoms without a definitive diagnosis. In addition, we describe the histological findings in detail, attempting to clarify the relationship between his clinical course and histopathological findings. A record of the clinicopathological correlation of this rare case is meaningful for both clinicians and forensic pathologists.
2. Case report

2.1 Case history

A 60-year-old male presented to a local hospital with complaints of headaches for 5 days associated with bleary eyes for the last 2 days. His cerebral images showed a large-size pituitary lesion suggesting a pituitary adenoma. Although there were no findings indicating a need for urgent treatment such as pituitary apoplexy, the medical physician referred him to a neurosurgeon as soon as practical because of his visual disturbance, and sent him back home. Several hours after returning home, he complained to his family of worsening headache and took a non-steroidal anti-inflammatory drug prescribed by the physician around midnight. His family found him dead in the lavatory early the next morning. He had a known history of hypertension, hyperlipidemia and hyperuricemia, but no recent history of infectious disease including upper respiratory infection.

2.2. Postmortem computed tomography (CT) findings

Postmortem CT scan was performed 6 hours after death. Sagittal section through brain showed a sellar mass measuring 3.0 cm with partial low-density areas (Fig 1). Extension towards the optic chiasm of a slightly high-density lesion was also detected in the
suprasellar region (Fig 1). The findings of other organs were unremarkable.

2.3 Autopsy findings

A complete post mortem examination was performed about 40 hours after death. His body was 168.0 cm tall and weighed 75.0 kg. He was neither cushingoid nor acromegalic. In the examination of intracranial contents, greyish-white edematous tissue was detected in the suprasellar region and appeared to push the optic chiasm upward. After opening the sella, a pituitary tumor with self-destruction was detected and yellowish-white creamy pus was oozed out of it (Fig. 2a). The formalin-fixed tumor, about 3.0 cm in diameter, was covered with tan to grey capsule-like tissue and exhibited cystic change with hemorrhage (Fig. 2b). The brain with slightly clouded pia mater weighed 1559 g and was swollen. Although sulcal narrowing and gyral flattening were observed, a hernia of the uncus or the cerebellar tonsils was not detected. The examination of other organs was unremarkable. Postmortem blood alcohol and drug tests were negative.

2.4 Histological findings

Histopathology of the intrasellar lesion revealed that a large portion of the cut surface
was occupied by an abscess with extensive neutrophilic aggregation and degenerative change surrounded by hemorrhage, and the remaining region was pituitary adenoma (Fig. 3a). The Gram stain of this abscess revealed Gram-negative cocci and phagocytosis by neutrophils (Fig. 3b, inset). The hemorrhagic area with fibrin accumulations circumscribed the abscess, and small granulation tissue was also observed in the abscess (Fig. 3c). In a part and adjacent area of the abscess, a pituitary adenoma composed of polyhedral cells with acidophilic and chromophobic cytoplasm arranged in diffuse and papillary patterns of growth was identified (Fig. 3d). In immunohistochemical studies, this adenoma was positive for synaptophysin, a neuroendocrine marker (Fig. 3d, inset), but immunonegative for the following anterior pituitary hormones: growth hormone, adrenocorticotropic hormone, thyroid stimulating hormone, luteinizing hormone, and follicle stimulating hormone (data not shown). In the capsule-like tissue covering this lesion, a non-neoplastic region of the anterior pituitary lobe with atrophic glands surrounded by fibrosis was identified (Fig. 3e). The suprasellar portion of the lesion located beneath the optic chiasm also consisted almost entirely of abscess and necrotic tissue without proliferation of fibroblasts (Fig. 4a). Consecutive infiltration of neutrophils into the subarachnoid cistern (Fig. 4a) and the brain parenchyma including the hypothalamic region was observed (Fig. 4b and c).
Examination of other organs did not show notable findings except for mild steatosis of the liver.
3. Discussion

This pituitary abscess progressed very rapidly and resulted in death 5 days after the onset of clinical symptoms without a definitive diagnosis. Previously reported cases reveal a mortality of 10% (2). However, a case presenting with rapid deterioration leading to death within several days is very rare (6). In an effort to achieve early diagnosis of this entity, it is meaningful to reveal the pathophysiology leading to his death through a detailed description of the histopathological findings compared with his clinical course.

The atrophic change with fibrosis of the non-neoplastic region of the pituitary gland in Fig. 3d indicates that the adenoma grew and expanded gradually over a prolonged period and compressed the region before the appearance of his headache. The negative immunohistochemical staining for anterior pituitary hormones also indicate a non-functioning adenoma without characteristic symptoms. Meanwhile, the synaptophysin immunopositivity as shown in Fig. 3d confirms that his tumor had a neuroendocrine differentiation consistent with pituitary adenoma. The clinical course in the last several days was composed of three steps: headache, visual disturbance, and rapid deterioration leading to death. His headache for several days before death was probably due to the formation of the abscess. As formation of granulation tissue
generally occurs several days after an injury, the localized granulation tissue in his abscess (Fig. 3c) also indicates that the abscess developed several days before his death. Next, his visual disturbance for the last 2 days before visiting the hospital suggested that the compression of the optic chiasm due to enlargement of the suprasellar portion of his adenoma occurred by that time. Histopathological findings of the abscess beneath the optic chiasm as shown in Fig. 4a also reveal that the abscess had spread there within a few days and consisted only of the aggregation of neutrophils and necrotic tissue in the absence of fibrous organization. Finally, he also had severe suppurative meningitis and encephalitis with hypothalamic involvement extending from the pituitary abscess as shown in Fig. 4b and c. A similar case of pituitary abscess with hypothalamic involvement was described by Whalley in 1952 (6). The 50-year-old male in the report also showed a very rapid progression and complained of severe headache followed by blindness and died within 4 days. The autopsy showed a suprasellar and intrasellar adenoma of the pituitary gland with abscess formation similar to our case, and the author diagnosed the disturbance of the cardiac autonomic nervous system following the suppurative inflammation of the hypothalamus by spread along the pituitary stalk as the cause of the death (6). Based on the similarity in the clinical presentation and autopsy findings between Whalley's case and ours, we infer that the cause of death was also
hypothalamic involvement of the pituitary abscess, which probably induced fatal arrhythmias by disturbance of the cardiac autonomic nervous system. However, our case is the first report to present the microscopic findings and detailed descriptions of the hypothalamic involvement from the pituitary abscess because those of Whalley's case were not shown in his report (6). It is unclear why the pituitary abscess of our case demonstrated such a rapid extension, unlike other chronic cases in previously published reports, although the extremely intense aggregation of neutrophils in this lesion suggests an exaggerated immune response to the infection.

The pituitary abscess of this case was associated with a pituitary adenoma (6, 8, 9, 11). Some authors suggested that the tumor vulnerability to infection probably depends on impaired circulation, areas of necrosis, and local immunological impairment (2, 3, 6). The infection is caused either by hematogenous seeding of the pituitary gland or by direct extension of an adjacent infection (3). The most common infectious agents are bacteria such as *Staphylococcus* sp, *Streptococcus* sp, *Neisseria* sp, *Mycobacterium* sp, *Micrococcus*, *Citrobacter*, *Escherichia coli*, *Brucella*, *Salmonella* and *Corynebacterium*; the second agents are fungi such as *Aspergillus* and *Candida* (1-5, 13). However, the positive rate for Gram staining or cultures ranged from 0 to 64%, and the diagnosis was based on other circumstantial evidence (1, 2, 4, 5). In our case, a lot
of Gram-negative cocci were detected in the tissue specimen from pituitary abscess as shown in Fig. 3a inset. Bacterial phagocytosis by neutrophils indicates that the bacteria have already grown in the pus before death. Because Neisseria sp is the only Gram-negative cocci among the above bacteria, this species is the most likely responsible microorganism of this case (2, 21) although there was no definitive positive culture result.

In conclusion, a pituitary abscess associated with adenoma rapidly spread via a suprasellar lesion to the hypothalamus and induced disturbances of visual perception and the cardiac autonomic nervous system. His death highlights the difficulty of diagnosing this disease and also reminds clinicians that pituitary abscess should be included in the differential diagnosis of sellar masses such as Rathke’s cleft cyst, cystic adenoma, cystic craniopharyngioma and epidermoid cyst when neuroimaging shows a sellar tumor with a cystic appearance (2, 5, 12, 14-16). Furthermore, when a greyish-white edematous tissue is detected in the suprasellar region on autopsy, forensic pathologists should take into account this entity, dissect the pituitary gland and perform a culture and histological study. This case provides useful information for clinicians to avoid a lethal outcome.
Figure legends:

Fig. 1. Postmortem computed tomography (CT) image of the brain.

A sagittal image showing a sellar mass with cystic changes (arrow heads) and suprasellar extension (arrows).

Fig. 2. Gross appearance of the pituitary abscess.

(a) Pituitary tumor with a self-destruction accompanied by yellowish-white creamy pus (arrow).

(b) Formalin-fixed tissue showing a cystic lesion of about 3.0 cm diameter covered with a tan to grey capsule-like tissue (scale bar: 1.0 cm).

Fig. 3. Microscopic findings of the intrasellar portion of the pituitary lesion (HE staining, scale bars: (a) 2 mm, (b-e) 50 μm)

(a) Horizontal section showing an abscess with peripheral hemorrhage and a remaining pituitary adenoma (left upper region). (LICA and RICA, left and right internal carotid artery, respectively)

(b) (* in a) Neutrophilic aggregation in the central region and Gram-negative cocci phagocytosis by neutrophils (arrow) (insets: Gram staining).
(c)** in a) Localized granulation tissue with fibrin accumulations detected in a portion of the abscess.

(d) (# in a) Pituitary adenoma adjacent to the abscess composed of polyhedral cells with acidophilic and chromophobic cytoplasm. Immunoreactive for synaptophysin (inset).

(e)## in a) Atrophic glands of normal pituitary glands with fibrosis in the capsule-like tissue.

Fig. 4. Microscopic findings of the suprasellar portion of the pituitary lesion (HE staining, scale bars: (a) 2 mm, (b) 100 μm, (b) 50 μm)

(a)Coronal section showing the brain parenchyma compressed upward by the suprasellar lesion and neutrophil spreading into the subarachnoid cistern (#).

(LICA and RICA, left and right internal carotid artery, respectively)

(b) * in a) Low power view of the boundary between the lesion and the brain showing a massive parenchymal infiltration of neutrophils.

(c) ** in a) Excessive infiltration of neutrophils in the hypothalamic region.
References


Fig. 2.