

## Two Autopsy Cases Assessing the Association of Rare Tumors Adjacent to the Sella turcica with Cause of Death and a Review of the Literature

Case Report

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### Abstract

Case 1 is an 80 year-old female, who consumed alcohol in a bar, fell down the stairs upon returning home, and was later found deceased. A postmortem CT did not confirm the presence of a tumor. An autopsy confirmed diffuse subarachnoid hemorrhage and a tumor, with a white surface covered by microvasculature pressing on the optic chiasma. The cause of death was traumatic subarachnoid hemorrhage due to an injury to the head while under the influence of alcohol. However, given the formation of a tumor pressing on the optic nerve, a possible causal relationship between the epidermoid cyst and the head injury cannot be excluded. Case 2 is a 60 year-old male, discovered dead in his own home. The autopsy confirmed subarachnoid hemorrhage around the base of the brain, and there was a hematoma-like tumor connected to the pituitary gland. The cause of death was determined to be pituitary bleeding due to pituitary adenoma. As seen in these cases, it is possible that a tumor at the base of the brain, which is a difficult location for identification, would impact the process of death; therefore, studying the grade of tumor, stage, and its involvement in the cause of death are diagnostically critical in forensic autopsies.

**Keywords:** Epidermoid Cyst; Plurihormonal Pituitary Adenoma; Sella turcica; Forensic Pathology; Endocrinology; Neurological Symptom.

### Introduction

Tumors occurring adjacent to the sella turcica not only put pressure directly on the base of the cerebrum, brain stem, and cerebellum but also involve cranial nerves and blood vessels that penetrate the base of the skull [1, 2]. Therefore, in addition to the symptoms caused by pressure on adjacent cranial nerves, symptoms of intracranial hypertension are often the chief complaint [3]. As computed tomography (CT) and magnetic resonance imaging (MRI) became available, diagnosis of tumors in the sella turcica has become more accurate [4, 5]; however, understanding the properties of tumors and their relationship with surrounding tissues to examine the causal relationship with death is extremely important in forensic pathology. There have been only few reports on confirmed tumors adjacent to the sella turcica in forensic

science [4, 6-8]. In this report, we examined two cases in which tumors were macroscopically confirmed near the sella turcica based on forensic pathological evidence, and reviewed past case reports.

### Case Reports

#### Case 1

Case 1 was an unemployed 80 year-old female, who resided with her brother, sister, and brother-in-law and had a history of hypertension. The case subject returned home after consuming alcohol at a bar. In the early morning of the following day, the subject was found dead at the landing of a staircase lying on her back. The subject was not transferred to an emergency hospital. An autopsy was performed one and a half days after the death.

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**Postmortem Imaging:** A post-mortem head CT showed subcutaneous bleeding slightly to the left of the occipital region and a linear longitudinal fracture from the top of the head to the right forehead. The brain showed mild swelling, and a subarachnoid hemorrhage was found around the base of the brain (Figures. 1a and b).

**Autopsy Findings:** The subject's height was 145 cm, with a weight of 53.9kg. A subcutaneous hemorrhage of 30×15×0.9 cm was found in the occipital region with a crushed intradermal area of 4×4 cm. In the skull, we found sagittal suture dehiscence around the intradermal crushed area in the occipital region and a fracture line toward the frontal bone. A diffuse subarachnoid hemorrhage was identified on the surface of the brain, and the brain was swollen (the weight of brain was 1.125g), forming uncus and tonsillar herniations (Figure. 2a). A brain contusion was present at the bilateral base of the cerebellum; however, no macroscopic contusions were found on the lower surface of the frontal and temporal lobes. Also, a slightly hardened tumor with a white surface was detected pressing on the optic chiasma at the base of the brain. The tumor was 1.5×1.5×0.5cm and covered by

micro vessels extending from the surrounding main vessels with nearly-transparent mucus leaking when cut (Figure. 2b). Part of the tumor was in contact with the pituitary stalk, but no adhesion of the tumor to the pituitary gland was found. Also, no additional abnormalities were identified on major organs such as heart (370 g) and lung (left: 385 g, right: 615 g).

**Histological Examination:** The surface of the tumor was a cyst covered by epidermis-like keratinized stratified squamous epithelium. Immunostaining revealed that the stratified squamous epithelium of the tumor was positive for CK19 that stains keratin and for PDS5A that stains stratified squamous epithelium, and the tumor was histopathologically diagnosed as an epidermoid cyst (Figures. 3a-c).

**Toxicological Analysis:** Concentrations of 1.90 mg/mL and 2.35 mg/mL of ethyl alcohol was detected in the left intracardiac blood and urine, respectively. No drugs or toxic substances were detected in the blood.

**Postmortem Biochemistry:** There was no inflammation, liver dysfunction, or renal dysfunction. Pituitary gland hormones

Figure 1. Sagittal (a) and coronal (b) image of the head CT revealing a mass in the sella and subarachnoid hemorrhage in Case 1. The yellow arrow shows the tumor.

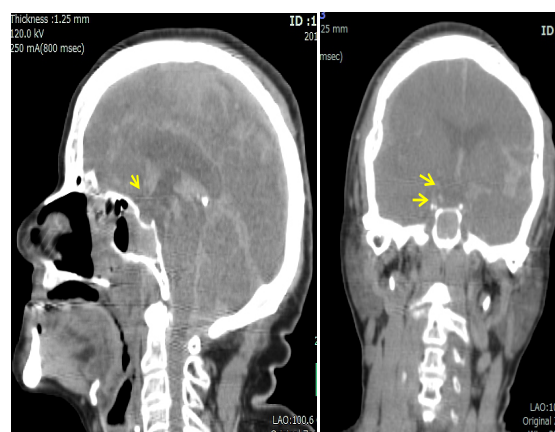


Figure 1a

Figure 1b

Figure 2. Panel (a) shows the base of the brain in Case 1. Panel (b) shows blood vessels at the base of the brain and the tumor after the formalin fixation. The yellow arrow shows a tumor.

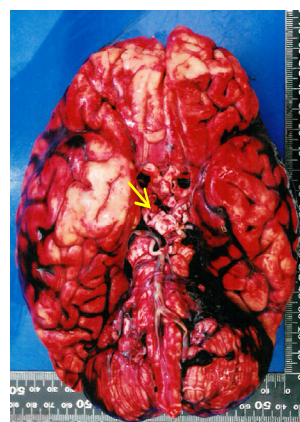


Figure 2a

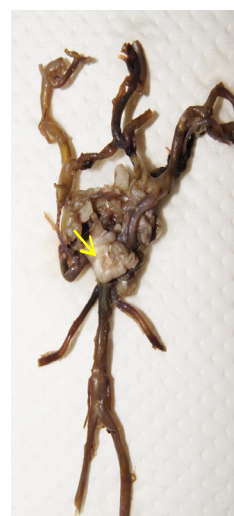


Figure 2b

**Figure 3. The Histopathological and Immunohistochemical Findings of the Tumor (a: Hematoxylin & eosin stain, b: anti-CK19 antibody, c: anti-PDS5A antibody, magnification×100).**

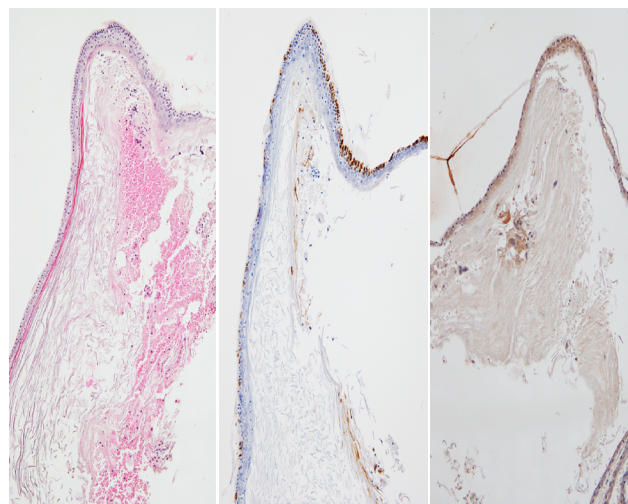


Figure 3a

Figure 3b

Figure 3c

measured using right intracardiac blood were as follows: adrenocorticotrophic hormone (ACTH): 2.0 pg/mL (forensic reference: median 10pg/mL, clinical reference: 7.2-63.3 pg/mL), growth hormone (GH): 0.52 ng/mL(forensic reference: median 7.0 ng/mL, clinical reference: < 2.47 pg/mL), thyroid stimulating hormone (TSH): 3.89  $\mu$ IU/mL (forensic reference: median 3.5  $\mu$ IU/mL, clinical reference: 0.34-4.04  $\mu$ IU/mL), prolactin (PRL): 13.23 ng/mL (forensic reference: median 20.0 ng/mL, clinical reference: 4.29-13.7 ng/mL), luteinizing hormone (LH): 0.95 mIU/mL (forensic reference: not established, clinical reference: 1.8-7.0 mIU/mL), and follicle stimulating hormone (FSH): 4.17 mIU/mL (forensic reference: not established, clinical reference: 5.2-14.4mIU/mL).

## Case 2

Case 2 was a male taxi driver in his 60s who lived alone. His medical history included hypertension and insomnia, and they had been on leave for the last several years. He was discovered lying in his living room and was estimated to have been deceased for several days.

**Postmortem Imaging:** In a postmortem CT, a hematoma of 2cm in diameter was discovered in the sella turcica at the base of the brain. Diffuse subarachnoid hemorrhage was confirmed through the cerebrum, centered around the base of the brain (Figures. 4a, and b). There was no fracture of the skull. There were multiple parallel fractures on the outer parts of the right dorsal ribs, and pneumothorax was present on the right side.

**Autopsy Findings:** The subject's height was 164cm with a weight of 50.6 kg. On the right side of the back, there was a subcutaneous intramuscular hemorrhage of 30×22×3 cm. In the same area, the third to tenth ribs on the right side showed parallel fractures. Some ends of the fractured ribs protruded into the thoracic cavity, forming a small contusion in the posterior surface of the right lower pulmonary lobe with bleeding in the surrounding area. The brain showed diffuse swelling (1.310 g). There was subarachnoid hemorrhage around the base of the brain, and there was a bleeding tumor of 2.5×2×2 cm (8.6 g) connected to the pituitary gland (1.7 g) (Figures. 5a).

**Histological Examination:** There was accumulation of acidophilic cells in the blood from the bleeding pituitary gland, presenting as pituitary adenoma (Figure 5b). The pituitary adenoma was positive for ACTH, TSH, and LH, and negative for PRL, GH, and FSH on immunostaining, suggesting a multiple hormone-producing tumor (Figure 6a-f).

**Toxicological Analysis:** Ethanol was not detected in the left or right intracardiac blood, and no other toxic substances were detected in the blood.

**Postmortem Biochemistry:** There were no findings of systemic inflammation, liver dysfunction, or renal dysfunction. Pituitary gland hormone levels, measured using right intracardiac blood, were used for reference only as several days had passed since death: ACTH: 2.0 pg/mL, GH: 0.28 ng/mL, TSH: 0.08  $\mu$ g/dL, PRL: 0.1 ng/mL, LH: 0.1 mIU/mL, and FSH 0.4: mIU/mL.

## Discussion

The cause of death in Case 1 was determined to be traumatic subarachnoid hemorrhage due to a contusion to the occipital region. Since the Case 1 subject was highly inebriated, there is a high likelihood that alcohol was involved in her death, but the epidermoid cyst found in this case was located at the chiasmatic groove and pressing on the optic nerve; therefore, it is possible that the subject was experiencing visual field impairment.

Epidermoid cysts comprise about 1% of brain tumors and have only been reported in eight autopsies published in international journals [9-16]. The ages of the subjects in these reports range from 4-66 years (median: 36 years), which is relatively young, and there were six males and two females. Only two of the eight cases had a clear and direct connection between the tumor and death [12, 16]. Among the eight reported cases, half of the patients had complications of malignant tumors, and these cases had a history of infections in their medical record [9, 16]. Though the details of a causal relationship between infection and malignant tumors are unknown, there are reports of infections spreading through the cerebrospinal fluid [17, 18]. Among the eight reported cases,

Figure 4. Sagittal (a) and coronal (b) image of the head CT revealing a mass in the sella and subarachnoid hemorrhage in Case 2. The yellow arrow shows a tumor.

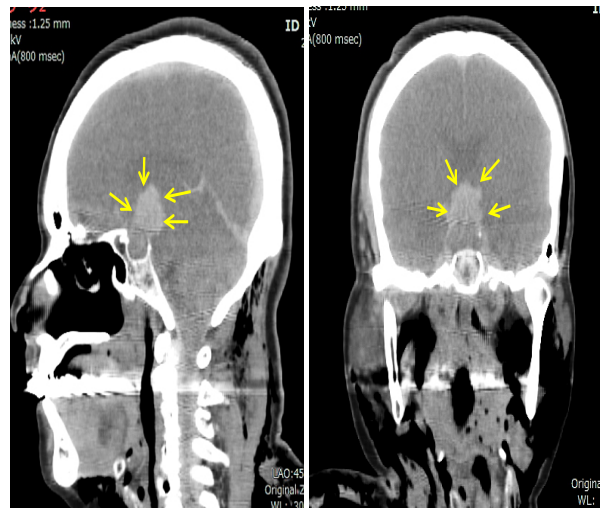


Figure 4a

Figure 4b

Figure 5. Panel (a) shows the base of the brain in Case 2 with a tumor among hematomas. Panel (b) shows the histopathological findings of the tumor (Hematoxylin & eosin stain, magnification × 20).

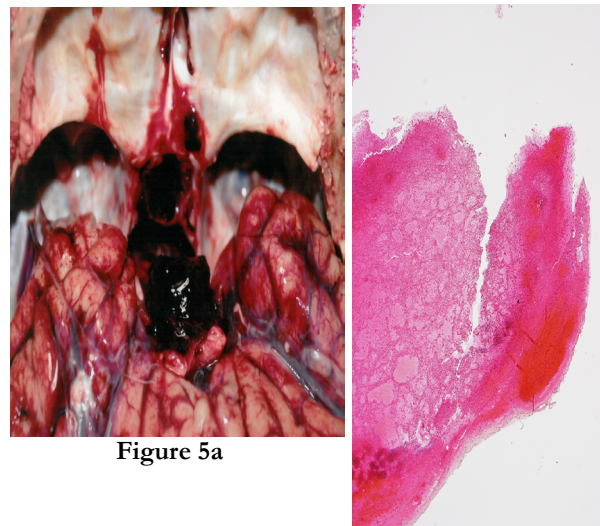


Figure 5a

Figure 5b

Figure 6. The immunohistochemical findings of the tumor (a: anti-ACTH antibody, b: anti-GH antibody, c: anti-PRL antibody, d: anti-TSH antibody, e: anti-FSH antibody, f: anti-LH antibody, magnification × 20).

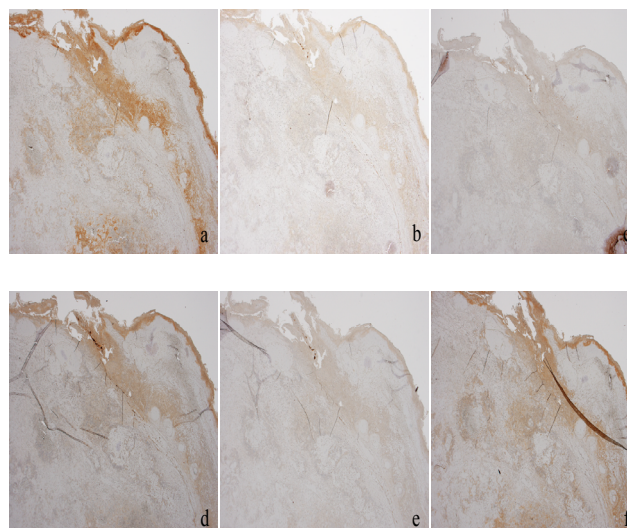


Figure 6

Table 1. Autopsy and clinical findings of brain epidermoid cyst.

Case	Age	Sex	Direct cause of death	Site of tumor	Histopathological findings	Medical history	Clinical symptom	Size of tumor (cm)	Reference
1	57	Male	Details unknown	Base of the brain and spinal meninges	Squamous cell carcinoma	Herpes zoster on the right chest	Headache, motor disturbance of the left leg, difficulty in micturition and defecation, peripheral facial palsy, hypoesthesia of the lower half of the body, motor paralysis of the lower limb, increase protein, stiffness of the neck, kerning's sign	-	1955, Yamanaka A
2	4	Male	Details unknown	Anteriorly in the parapontine part of the right cerebello-pontine angle	Cyst-derived intracranial epidermoid carcinoma	Details unknown	Irritable, fearful, headache, weakness on the left side of the face, right side poorly, unsteady on feet, head and neck pain, blurring of the optic disk, diminished right corneal reflex, diminished right eyelid closure, Absent gag reflexes, tongue deviation, to right, left Babinski sign, right pupil smaller	3×2×2	1976, Wong SW
3	31	Male	Details unknown	The left cerebral hemisphere extending basally from the frontal lobe to the cerebellum and the brain stem and determining left cerebellar atrophy and a right cerebellar hernia through the occipital foramen	Epidermoid cyst	Details unknown	Lethargy, gait trouble, slurred speech, headache, prostration, blurring of the left optic disk, left nystagmus, left ptosis, right central facial palsy with right hemiparesis, weber's syndrome	-	1977, Palmucci L
4	14	Female	Respiratory failure	Ventral pons	Intra-axial epidermoid	Urinary infection, hereditary spherocytosis	Right hemiparesis, fever, irritability, lethargy, anorexia, dysarthria, dysphagia, right facial weakness, increased right stretch reflexes	1.5×2.0×1.0	1978, Schwartz JF
5	38	Male	Myocardial infarction	Suprasellar, near the optic-chiasm area	Epidermoid cyst	Chest pain, Hyperphagia	Details unknown	8×7.5	1981, Rhodes RH
6	34	Female	Extensive burns	The left parietal lobe one cm deeper to the central sulcus	Epidermoid cyst	Details unknown	Fainting attacks	4×4	1997, Logani KB
7	66	Male	Details unknown	Front of the brain stem encasing the basilar artery	Squamous cell carcinoma	Details unknown	Fatigue, low back pain, weight loss, deterioration of neurological signs, intracranial hypertension	3×1	2000, Sawan B
8	49	Male	Cardiorespiratory failure as a result of brainstem involvement	Pons	Proliferation of atypical squamous epithelial cells corresponding to poorly differentiated squamous cell carcinoma	Spondylolysis, abscess of the buttocks	Right hemiparesis, oculomotor, abducens and facial palsies, dysphagia, dysarthria, quadriplegia with Babinski's signs	2×1	2003, Shirabe T
9	83	Female	Traumatic subarachnoid hemorrhage	Chiasmatic groove	Epidermoid cyst	Hypertension	Details unknown	1.5×1.5×0.5	2017, Morioka F (present case)

the location of the tumor was often at the base of the brain, particularly in the brain stem, and the main clinical symptoms were those of the central nervous system, which were observed even in tumors measuring only about 1 cm in size.

The pituitary gland adenoma in Case 2 was an extrasellar extension that protruded from the sella turcica according to the radiological diagnostic classification [19], and diffuse bleeding had spread from the pituitary adenoma at the base of the brain. On the other hand, injuries on the back included multiple rib frac-

tures, lung contusion, and pneumothorax, but the thoracic cavity was not open to the air, and there were no subcutaneous emphysema or injuries to large vessels. In addition to the delayed death that Case 2 presents, the lung contusion was also localized. Macroscopically, the lung contusion did not have valvular findings or extreme mediastinal displacement; therefore, there was no rationale to assert that pneumothorax was the primary condition. The direct cause of death in Case 2 was determined to be pituitary gland bleeding caused by the pituitary adenoma. The lung injury and pneumothorax caused by multiple rib fractures from contu-

Table 2. Autopsy and Clinical Findings of Plurihormonal Pituitary Adenoma.

Case	Age	Male/ Female	Direct cause of death	Site of tumor	Histopathological findings	Medical history	Clinical symptom	Size of tumor (cm)	Reference
1	42	Female	Pituitary apoplexy due to mucormycosis	Sella turcica, pituitary gland, right lung	GH, FSH, LH positive, Necrosis and hemorrhage consistent with apoplexy	Hypertension, type 2 diabetes mellitus, Cushing's syndrome due to an ACTH-producing tumor	Stress-related lumbar pain, facial and lower limb edema, itching, skin darkening, left hemiparesis, left hemiplexy, altered speech, Optic atrophy, right hypoesthesia	Detail unknown	2008, Salinas-Lara C
2	52	Male	Ischemic heart disease	Pituitary gland	PRL, GH, TSH positive	Details unknown	Details unknown	ϕ1.3	2007, Kim JH
3	31	Female	Acute myelogenous leukemia	Pituitary gland	PRL, Thyrotropin, α-subunit positive	Details unknown	Details unknown	Detail unknown	1990, Scheithauer BW
4	64	Male	Pituitary gland bleeding	Pituitary gland	ACTH, GH, TSH, PRL, LH, FSH positive	Hypertension, insomnia	Details unknown	2.5×2×2	2017, Morioka F (present case)

sion to the right side of the back were not the direct causes of death, but may have played a role.

Approximately 40% of pituitary adenomas, such as the one found in Case 2, are considered nonfunctional adenomas [20]. As for functional adenomas, about 30% of all pituitary adenomas are prolactin-producing tumors, which occur approximately eight times more frequently in females than in males [21]. In addition, about 20% of pituitary adenomas are growth hormone-producing tumors, while other types of pituitary tumors are reported to be extremely rare [22]. The pituitary gland adenoma seen in Case 2 is classified as a plurihormonal adenoma, an adenoma producing multiple hormones, based on the Kovacs classification and has an incidence rate of less than 1% [23]. This is the first reported case of a plurihormonal adenoma with production of ACTH, TSH, and LH. Clinical symptoms of pituitary adenoma include headaches due to cerebral compression, visual field impairment due to optic nerve compression, and symptoms related to the hormones produced [24]. Prolactin-producing tumors result in symptoms such as lactation, amenorrhea syndrome, visual impairment, and visual field impairment [25]. However, reports of plurihormonal adenoma autopsy cases are limited to three existing reports, and its low incidence rate does not allow for a detailed understanding of factors such as symptoms and gender ratio. Since optic nerve compression is confirmed in the present case, the patient likely had symptoms of optic nerve impairment, such as visual field impairment, prior to death; however, the medical history only indicated hypertension.

There was no history of treatment for Cases 1 or 2, and only hypertension was noted in the medical history of both subjects. These two cases resulted in an autopsy due to traumatic findings. However, since the tumors were at the base of the brain, which is difficult to diagnose, they may have played a role in their deaths. Therefore, we consider that examining the malignancy and stages of the tumors, their relationship with surrounding tissues, and their involvement in the death of the subject, in addition to examining possible foul play, is diagnostically important in forensic autopsies.

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