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

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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 a 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.

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; Neu rological Symptom.

Case 2

Case 2

Case 2 is a 60 year-old male, discovered dead in his own home. The 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.
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 53.9 kg. 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 1.125 g), forming uncal and tonsillar herniations (Figures 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 1.5×1.5×0.5 cm 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 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.
The subject’s height was 164 cm with a weight of 50.6 kg. On the right side of the back, there was a subcutaneous tumor of 2.5×2×2 cm (8.6 g) connected to the pituitary gland (Figure 5a). The cause of death in Case 1 was determined to be traumatic hemorrhage around the base of the brain, and there was a bleed- ing tumor of 2.5×2×2 cm (8.6 g) connected to the pituitary gland (1.7 g) (Figures 5a).

**Postmortem Imaging:** In a postmortem CT, a hematoma of 50.6 kg. On the right side of the back, there was a subcutaneous tumor of 2.5×2×2 cm (8.6 g) connected to the pituitary gland (Figure 5a). The cause of death in Case 1 was determined to be traumatic 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).
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 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 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).
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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 intra-cranial 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 prosth, right central facial palsy with right hemiparesis, Weber's syndrome | - | 1977, Palmucci L |
| 4    | 14  | Female| Respiratory failure | Ventral pons | Intra-axial epidermoid | Urinary infeccion, 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 | Epidermid 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, intra-cranial 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 | Spondyloysis, absence of the buttocks | Right hemiparesis, ocu-lomotor, abducens and facial palsy, dysphagia, dysarthria, quadriplegia with Babinski's sign | 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, Morita 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 fractures, 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-
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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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 hemor-| 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 hemipare-sis, left hemiparesis, altered speech, Optic atrophy, right hypothyrosis | Detail unknown | 2008, Salinas-Lara C |
| 2    | 52  | Male        | Ischemic heart disease | Pituitary gland | PRL, GH, TSH positive | Details unknown | Details unknown | γ1.3 | 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, Mo- noka F (present case) |

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