Case Report

Sudden Death in Giant Pituitary Adenomas: Two Case Reports with Literature Review

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Abstract

Pituitary macroadenomas are rare tumors constituting <1% of intracranial tumors. The giant macroadenomas are even rarer and have the potential to cause fatality due mostly to mass effects within the intracranial space. Most cases are nonfunctional and are either null cell adenomas or gonadotroph adenomas in which symptoms may have been ignored by the patient. Sudden deaths from intracranial tumors are uncommon and pituitary adenomas are very rarely associated with unexpected deaths. Here, we present two cases of giant pituitary adenomas both of which were undiagnosed before demise of the patient. The autopsy report showed no other findings except the sellar tumor. Immunohistochemistry of both tumors showed null cell adenoma.

Keywords: Giant adenoma, null cell, pituitary

Introduction

Intracranial tumors are divided into benign and malignant, but unlike in other parts of the body, all intracranial tumors are malignant in behavior.[1] This is due to their mass effect which raises the intracranial pressure within the unyielding cranium with eventual compromise of vital centers in the brain. However, with recent technological advances in diagnosis of intracranial neoplasm, most tumors are detected before death.[1-3] Thus, sudden deaths from intracranial tumors are uncommon. Most cases that occur are due to metastatic tumors, gliomas, and meningiomas.[3-5] The gliomas are usually high grade and often infiltrate adjacent parts of the brain. Meningiomas are more common in females and may grow more rapidly during pregnancy due to hormonal effects.[4]

Although pituitary adenomas are the third most common intracranial neoplasm, sudden death due to the tumor is rare.[3-5] Most pituitary adenomas are small and confined to the sellar region while the larger tumors are rare.[6] Pituitary adenomas are surgically classified into micro- and macroadenomas. The microadenomas are <10 mm in diameter while macroadenomas are >10 mm in diameter with some extending beyond the sella turcica.[5,7] Macroadenomas constitute <0.5% in the population according to several studies done using magnetic resonance imaging (MRI).[6,8] Even more rare forms of macroadenomas are the giant macroadenomas which may exceed 4 cm in size. These are tumors which usually extend out of the sellar cavity either into the intracranial cavity or into the sphenoid and pharynx.[7,9,10] Most giant macroadenomas are nonfunctioning tumors which mainly cause symptoms via compression of surrounding structures.[7,11] Rarely giant pituitary adenomas have been known to cause sudden death with discovery of the tumor at autopsy.[3] Here, we report two giant pituitary adenomas found at autopsy of patients who presented with sudden death.

Case Reports

Case 1

A 35-year-old female trader presented to the emergency department of our hospital with a 1-month history of altered sensorium and 4 days of fever. There was no headache, seizures, or loss of consciousness. There was a history of anorexia and loss of weight. Three years before presentation,

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she had sudden bilateral loss of vision and amenorrhea and was seen at the ophthalmology clinic but later defaulted before any diagnostic procedure could be done. Main findings on examination were the cardiovascular system with a blood pressure of 210/130 mmHg. She was drowsy with no sign of meningeal irritation. Examination of the eyes revealed no light perception and normal depth of the anterior chambers of both eyes. The pupils were 4 mm and unreactive to light. Both lenses were clear and the discs were markedly pale with distinct margins. Kestenbaum sign was markedly positive and there was mild arteriolar narrowing. Examination of the other systems revealed no abnormality. Two days into her admission before an MRI could be done, she had a respiratory arrest and could not be resuscitated.

At autopsy, the main findings were in the intracranial cavity with the brain weighing 1100 g. The cerebral hemispheres are bilaterally symmetrical. The leptomeningeal vessels are mildly congested. There is a large tumor within the interpeduncular fossae measuring 6 cm × 5 cm and splaying the arterial circle of Willis [Figure 1]. There is also expansion of the sella turcica. There is moderate-to-severe cerebral edema with flattening of the gyri and narrowing of the sulci.

Microscopically, the tumor showed fairly uniform cells with round-to-oval nuclei and scanty eosinophilic to amphophilic cytoplasm which were disposed of in sheets, trabecular, and sinusoidal patterns in keeping with pituitary adenoma [Figure 2]. Immunohistochemical studies showed no staining for prolactin, growth hormone, adrenocorticotropic hormone, thyroid-stimulating hormone, follicle-stimulating hormone (FSH), and luteinizing hormone. The MIB index was 0.2%. The final diagnosis of a null cell giant pituitary adenoma was made [Figure 3].

Case 2

A 56-year-old female clerical officer presented at the emergency department of the hospital with a day history of altered sensorium and coma. Ten days previously, she had suddenly been unable to walk and had become anorexic 4 days later. She had a 2-year history of loss of vision before presentation. At presentation, she had a Glasgow coma score of 5/15. There was an equinovarus deformity of the left leg. The pulse rate was 80 beats/min and blood pressure was 210/100 mmHg. Other systems were essentially normal. An initial assessment of a hemorrhagic stroke was made. However, the patient had a cardiopulmonary arrest 3 h into admission and could not be resuscitated.

At autopsy, all the systems were grossly normal except for the brain which showed a giant tumor extending above the sella turcica with a right lateral extension altogether measuring 8 cm in diameter. There is a marked expansion of the sella turcica.

Histology of the tumor showed an epithelial neoplasm disposed of in sheets and showing papillary fronds in areas and pseudorosettes [Figure 4]. The cells have moderated eosinophilic cytoplasm and round-to-oval nuclei. The overall features were in keeping with a pituitary adenoma. The cells were mainly nonstaining to all the pituitary antibodies except for focal areas of staining for FSH and a MIB index of 0.4% [Figure 5].

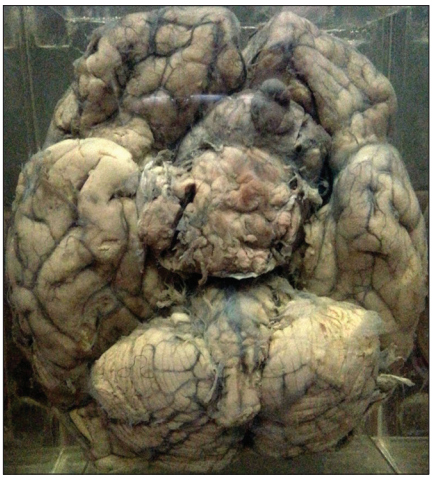

Figure 1: Cerebral hemispheres with a large tumor in the interpeduncular fossa, overlying the arterial circle of Willis

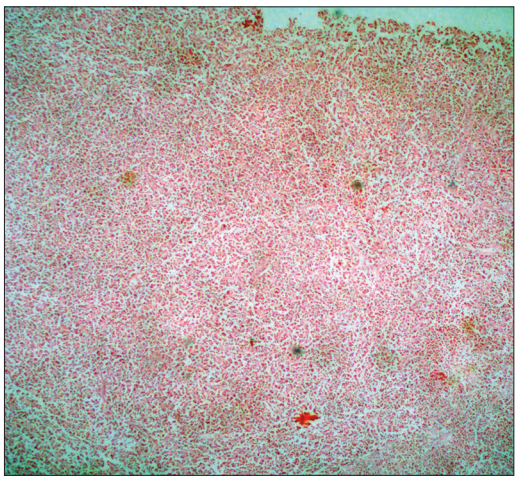

Figure 2: Pituitary adenoma with cells arranged in sheets

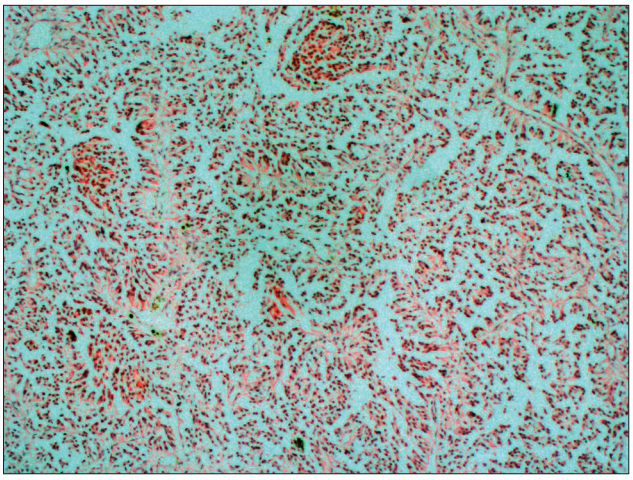

Figure 3: Papillary fronds in tumour from second patient with areas of pseudo rosettes

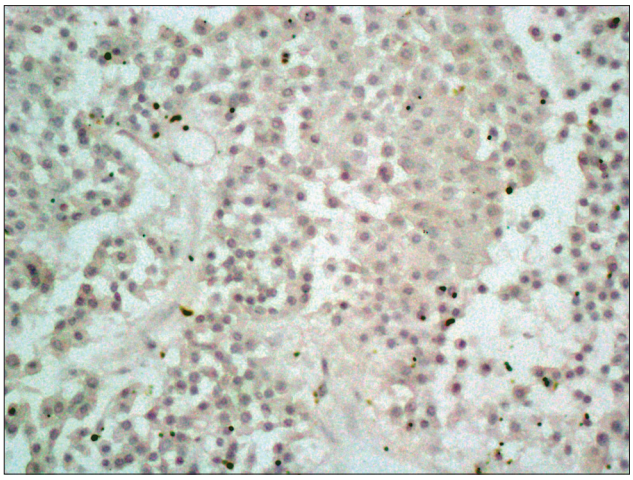

Figure 4: Null cell adenoma seen in the first patient showing negative staining

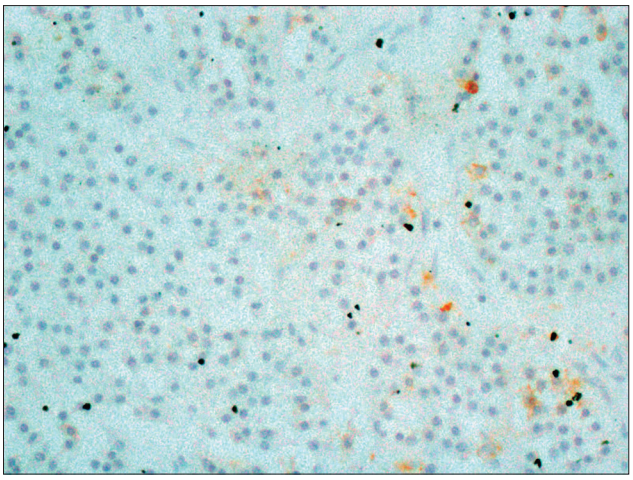

Figure 5: Null cell adenoma seen in the second patient with occasional cells staining for follicle-stimulating hormone

Discussion

Symon and Jakuwoski defined giant pituitary adenomas as tumors measuring 4 cm above the sphenoid bone and extending in any direction.[9] The pathological classification of pituitary adenomas was initially based on their staining patterns on hematoxylin and eosin. This method has however been found to be inaccurate and confers no prognostic or therapeutic advantage in management. There were also significant overlaps between the different groups both in morphology and clinical behavior.[7,10,12] At present, the WHO have classified pituitary adenomas into six main groups based on their immunohistochemical staining pattern which is based on the hormone elaborated by the tumor cells.[10,13]

Although prolactinomas are the most common type of pituitary adenomas, most of the giant pituitary adenomas are either gonadotroph adenomas or null cell adenomas.[7] These variants of adenomas are often not functional, and the symptoms they cause are either ignored by the patient or may cause misdiagnosis allowing the growth of the tumor to giant sizes.[14] The two patients in our report had nonfunctioning adenomas with one of them showing focal staining for FSH. Some scholars regard gonadotroph adenomas as nonfunctioning adenomas based on the fact that many of the tumors stain for the hormone histologically but do not show raised plasma levels of the hormone. Those tumors that show hypersecretory activities have no clinical effects in the patients and are largely ignored.[11,14] Most null cell adenomas have however been shown to have both morphological and molecular patterns of gonadotroph adenomas.[12,15]

With modern diagnostic instruments, incidental pituitary adenomas are more commonly detected and radiological studies showed an estimated prevalence of 22.5%.[6] Autopsy studies have however shown a prevalence of 14%.[6] In our environment, studies from various centers gave an incidence of 16.8%–18% with a slight male predominance although different tumor types have varying sex predilections.[16-18] It is generally less common in children and shows a peak age of occurrence ranging between 30 and 60 years.

The most common symptoms seen in patients with pituitary adenomas are headaches and visual symptoms which the two index patients had.[19-21] The visual symptoms occurred due to the raised intracranial pressure and pressure effect on the optic chiasma which lies above the pituitary fossa. Varying degrees of visual affectation are seen in patients with pituitary adenoma depending on the part of the optic chiasma that the tumor is impinging on. These include bitemporal hemianopia, bitemporal quadrantanopia, and impaired visual acuity and there may be optic nerve atrophy.[20,22] Some giant adenomas may erode into the sphenoid sinus with communication into the upper airway and cerebrospinal fluid rhinorrhea.[5,22]

One of the feared complications of pituitary macroadenomas is pituitary apoplexy which results from a vascular accident in the tumor with resulting infarctive necrosis. It is a surgical emergency with patients presenting with sudden severe rise in intracranial pressure with loss of consciousness and death if not treated rapidly. Histologically, the tumor shows marked hemorrhagic necrosis with few viable areas of tumor being seen in some cases. Although the two index cases in this report died suddenly, the histological appearance of the tumor in both the cases showed no features of infarction.

Other symptoms seen in patients with pituitary adenomas include amenorrhea, galactorrhea, loss of libido in men, and other symptoms which may be pointers to oversecretion of a hormone.[21] The amenorrhea may be due to symptoms from hypersecretion of hormones particularly gonadotropins and prolactins or due to pressure effects on the hypothalamus.[19,22] Interestingly, both patients presented with symptoms of severe hypertension which warranted the diagnosis of intracerebral hemorrhage in one of the patients. Hypertension in these patients may be manifestations of raised intracranial pressure which may be seen in conditions causing a mass effect in the cranial cavity.[23]

Symptomatic pituitary adenomas are generally more common in the female population.[10] Studies have shown the increased

incidence of functioning tumors in young females compared to males.[10] However, null cell adenomas are more common in elderly individuals with a slight male predominance. They are said to be rare in patients <40 years of age, an age bracket in which one of the patients described here is found.[24] Some have ascribed this to the fact that pituitary adenomas often cause a derangement of the normal hormonal cycle in females which prompts a visit to the hospital. The lack of these warning signs in older females may cause the tumor to remain undetected for a much longer period.[14] In men, the tumor may also cause loss of libido, a symptom which is often disregarded by the patient.[14]

Pituitary adenomas are sometimes associated with genetic diseases such as McCune–Albright syndrome and Carney's complex.[13] McCune–Albright syndrome is known to also include skeletal lesions, particularly fibrous dysplasia, precocious puberty, spotty pigmentation of the skin, and endocrine tumors.[13] The second patient presented with a deformity of one of the limbs but none of the other signs diagnostic of McCune-Albright syndrome, such as spotty skin pigmentation, was seen in her neither was a history of precocious puberty elicited. In McCune–Albright syndrome, the pituitary adenomas are usually functioning unlike the tumor in this index patient.[13] In patients with an associated genetic predisposition, the tumors are often seen at an earlier age and the most common adenomas seen are growth hormone adenomas and prolactinomas. Most often, other lesions associated with such syndrome complexes include neuroendocrine tumors, central and peripheral nervous tumors, and skin pigmentation.[13]

Conclusion

Giant macroadenomas are rare pituitary tumors which are usually not functional but have the potential to cause mortality due to their mass effects and pressure on surrounding structures. The differential diagnosis of patients with unexplained headache and long-term visual symptoms and signs should include this tumor type.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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