Primary cerebellopontine angle craniopharyngioma in a patient with Gardner syndrome

Case report and review of the literature


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The authors report on the case of a craniopharyngioma arising in the cerebellopontine angle (CPA) in a patient with Gardner syndrome. Although familial adenomatous polyposis (FAP) is associated with intracranial neoplasms, the current case is only the third reported craniopharyngioma in a patient with Gardner syndrome. Two of these tumors, including that of the current case, originated in the CPA, an unusual location for craniopharyngiomas. The literature concerning FAP and its associations with intracranial neoplasia, as well as the pathogenesis of craniopharyngiomas in the posterior fossa, is discussed.

KEY WORDS • craniopharyngioma • cerebellopontine angle • polyposis • Gardner syndrome • Turcot syndrome

C RANIOPHARYNGIOMAS are benign, partly cystic epithelial tumors and account for 1.2 to 4.6% of all intracranial tumors.13 They are most frequently located in the suprasellar region and often have an intrasellar component. In this paper, we report on a case in which a craniopharyngioma developed de novo in the CPA; the patient also was found to have Gardner syndrome. Although craniopharyngiomas are not generally associated with any of the syndromes that predispose an individual to cancer, this is the third craniopharyngioma reported in a patient with FAP. The first report described a suprasellar craniopharyngioma.2 In the second reported case, the craniopharyngioma developed primarily from the CPA, as did the tumor in the current case.15 Both the occurrence of craniopharyngiomas in patients with FAP and their origin in the CPA are rare events. However, it is unclear whether possessing the genetic abnormalities associated with FAP in any way predisposes an individual to a craniopharyngioma in an unusual location.

Case Report

History and Examination. This 31-year-old man presented with a 4-month history of intermittent headaches, nausea, and vomiting as well as a 1-week history of blurred vision and truncal ataxia. On examination, he was alert and oriented. He was ataxic, but showed no other signs of cerebellar dysfunction. There was no papilledema or nystagmus. His cranial nerves were intact. There were no focal motor or sensory deficits in his upper or lower extremities. Five well-demarcated subcutaneous swellings were observed: four on the skull (in the right preauricular, right occipital, left parietal, and left occipital regions) and one on the lower thoracic region. These were nontender, hard, nonmobile, nonerythematous, rounded lesions, each measuring approximately 4 cm in diameter.

It was noted that the patient’s brother was known to have Gardner syndrome. The brother had facial and truncal subcutaneous swellings very similar to those found in our patient and had previously undergone a complete proctocolectomy for colonic adenomatous polyposis. The results of a recent colonoscopy performed in our patient showed several rectal and colonic adenomatous polyps. Results of an esophagastroduodenoscopy were unremarkable.

A computed tomography scan of the patient’s brain revealed a cystic lesion in the posterior cranial fossa, with well-defined walls and an enhancing mural nodule. There was a degree of obstructive hydrocephalus secondary to compression of the fourth ventricle. An MR image exposed a large, heterogeneous, partially cystic, right-sided mass in the CPA. Following administration of gadolinium, both patchy peripheral enhancement and extension of the mass into the anterior aspect of the right middle cerebellar peduncle were revealed (Fig. 1). On midsagittal MR imaging, the mass was revealed to extend to the foramen magnum (Fig.
2). There was no evidence of a sellar or suprasellar lesion, and there was no tumor extension around the clivus.

Operation and Postoperative Course. After a brief course of high-dose corticosteroids, a suboccipital posterior fossa craniotomy was performed. Brown, viscous fluid resembling engine oil was released from the cystic part of the tumor. The lesion was adherent to the surrounding cerebellum and at several points around its circumference there was no clear cerebellum–tumor plane. A near-total resection of the lesion was achieved. The patient made a good postoperative recovery, with resolution of his symptoms. There were no new postoperative neurological deficits.

An open biopsy procedure and excision of one of the left occipital subcutaneous masses were subsequently performed and revealed a hard and fibrous lesion involving the galea and subcutaneous tissue, separate from the skull bone.

Histopathological Examination. Under examination, the posterior fossa lesion showed areas of basaloid epithelium with focal squamous differentiation as well as islands of necrotic keratin. Fragments of dura mater included in the resected tissue demonstrated infiltration and replacement by tumor cells. Invasion of the cerebellum was also evident. These findings were consistent with a diagnosis of adamantinomatous craniopharyngioma (Fig. 3).

Histological examination of the left occipital subcutaneous mass revealed a benign appearance consistent with a diagnosis of fibroma (Fig. 4). This, together with the family history and the findings on colonoscopy, confirmed that our patient had Gardner syndrome.

Discussion

Our case is the third reported instance of craniopharyngioma in a patient with FAP. Two of these patients, including ours, had extracolonic manifestations and were therefore diagnosed with Gardner syndrome. In both of these patients, the craniopharyngioma developed de novo in the CPA.

Gardner Syndrome, Turcot Syndrome, and FAP

Familial adenomatous polyposis is a syndrome in which hundreds of precancerous colonic polyps can develop. People with FAP are predisposed to colon cancer, and by the age of 35 years, 95% of them will have polyps. The condition is inherited in an autosomal dominant manner and is caused by mutations in the APC gene on chromosome 5q. It is diagnosed clinically in individuals with greater than 100 colorectal adenomatous polyps or in those with fewer than 100 polyps and a first-degree relative with FAP. The APC protein has been localized to the nucleus, cell membrane, and cytoskeleton in human epithelial cells; it is a tumor suppressor, maintains normal apoptosis, and plays a role in maintaining chromosomal stability.

In the past, patients with FAP who had extracolonic features were treated as having a distinct phenotype labeled Gardner syndrome. These features included polyps in the upper gastrointestinal tract, congenital hypertrophy of the retinal pigment epithelium, dermal fibromas, osteomas, dental anomalies, and desmoid tumors. Although several FAP kindreds both with and without extracolonic features have been described, FAP and Gardner syndrome may occur in sibling relationships and may even be associated with identical pathological mutations in the APC gene.

Turcot syndrome is characterized clinically by the concomitance of a primary brain tumor and multiple colorectal adenomas. There are two distinct types. In Type I, which was found in up to two-thirds of the patients in the original genetic study, there is a mutation in the APC gene and the CNS tumor is a medulloblastoma. Type II is due to a mutation in the mismatch repair genes that leads to hereditary nonpolyposis colorectal cancer, and its CNS component is a glioblastoma multiforme. Other malignant tumors of the CNS also have been described, however, in patients with Turcot syndrome, including ependymomas and fibrillary astrocytomas. More recently, a CPA epidermoid cyst and
a frontal meningioma—both benign intracranial tumors that are not necessarily of a neuroepithelial origin—were described in two members of the same family; both patients were diagnosed previously with Gardner syndrome.\textsuperscript{1,4}

It is clear that the risk of extracolonic tumors such as hepatoblastoma, carcinoma of the papillary thyroid, carcinoma of the upper gastrointestinal tract, and medulloblastoma is increased in patients with FAP.\textsuperscript{17} The experience of our patient, as well as others,\textsuperscript{2,4,15} suggests that this increased risk also applies to people with benign intracranial tumors. This brings the uniqueness of Type 1 Turcot syndrome into question. The underlying genetic disorder is FAP and this leads to a predisposition to neoplasia in several tissues.

None of the genetic abnormalities known to occur in patients in whom craniopharyngiomas develop are similar to those occurring in patients with FAP or Gardner or Turcot syndromes. Only eight cases of craniopharyngioma have been analyzed for genetic changes; abnormalities were found in only two cases, and those involved chromosomes 2 and 12, not 5q as is the case with FAP.\textsuperscript{8,10,12} Our patient had a family history of Gardner syndrome and fulfilled the clinical criteria for the syndrome himself. Clearly, it was expected that he carried the autosomal dominant \textit{APC} mutation in his germ line. Therefore, that mutation also should have been present in the craniopharyngioma. The significance of this with regard to the growth of the neoplasm and its location is unclear.

**Posterior Fossa Craniopharyngiomas**

Craniopharyngiomas in this location are rare and have been categorized into three distinct types: 1) large craniopharyngiomas extending from the suprasellar region to the posterior fossa;\textsuperscript{16} 2) craniopharyngiomas recurrent in the posterior fossa after surgery for a sellar or parasellar craniopharyngioma;\textsuperscript{14,15} and 3) craniopharyngiomas that arise de novo in the posterior fossa.\textsuperscript{1,7,15}

Three cases of de novo posterior fossa craniopharyngiomas have been reported.\textsuperscript{1,7,15} In one case, the tumor filled most of the fourth ventricle but also extended into the left CPA.\textsuperscript{1} The tumors in the other two cases were localized to the CPA. All three patients were young, presenting at 17,\textsuperscript{7} 23,\textsuperscript{1} and 29\textsuperscript{15} years of age, respectively. These patients presented with headache and other signs of raised intracranial pressure as well as ataxia, unilateral hearing loss,\textsuperscript{7,15} and progressive neurological signs related to lower cranial nerve dysfunction.\textsuperscript{15} The duration of symptoms was 3 years in one patient\textsuperscript{1} and 1 year in the other two patients. Our patient had experienced headaches for only 4 months; his presentation was precipitated by nausea, vomiting, blurred vision, and severe ataxia.

It is unclear how craniopharyngiomas, known to arise from remnants of the Rathke pouch, can develop in rare cases as primary lesions in the posterior fossa. It is possible that the epithelial remnants from which craniopharyngiomas develop may be incorporated within other midline brain regions during development;\textsuperscript{2} this process may not be necessarily limited to the suprasellar region. In the suprasellar region, the relationship of the epithelial cell nests to the arachnoid and pia mater depends on their location at the 5th week of gestation, when the pia mater of the diencephalic vesicle develops.\textsuperscript{2} If the nests are in contact with the infundibular area at this stage, the pia mater separates them from the mesoderm of the Rathke pouch, resulting in an intraparenchymal craniopharyngioma. If the nests remain adherent to the Rathke pouch, an extraparenchymal tumor with varying relationships to the arachnoid mater is formed. In contrast to the two previous case reports describing extraaxial CPA craniopharyngiomas,\textsuperscript{7,15} the tumor we describe was partially intraaxial, with invasion of cerebellar tissue. This suggests that the variation in the relationship of craniopharyngiomas to the pia mater and arachnoid mater is not restricted to the suprasellar location.

**Conclusions**

In this article, we report a case that is the third instance of a primary CPA craniopharyngioma and the second instance of a craniopharyngioma that arose in that location in a patient with Gardner syndrome. This could be due to chance, but both the CPA location and the occurrence of craniopharyngioma in a patient with FAP are clearly very rare events. We do not understand how a mutation on the \textit{APC} gene could influence the location, and indeed the development, of a craniopharyngioma.

This case confirms the high variability of extracolonic
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neoplasms, both benign and malignant, in patients with FAP. From a neurosurgical perspective, it is important to recognize that these patients and their families are at increased risk of having tumors develop in the CNS. The extent to which the family members of these patients should be investigated is currently unclear.

References


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