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Case Report

Cerebellopontine angle craniopharyngioma in familial adenomatous polyposis

Sayantan Bose[1], James Balogun[1], Daniel du Plessis[2], Matthew Bailey[1], Fiona Lalloo[3], Omar Pathmanaban[1]

Departments of [1]Neurosurgery and [2]Cellular Pathology, Salford Royal NHS Foundation Trust, Salford, [3]Department of Clinical Genetics, Saint Mary's Hospital, Manchester, United Kingdom.

E-mail: *Sayantan Bose - bosesayantan0@gmail.com; James Balogun - jamesabalogun@gmail.com; Daniel du Plessis - daniel.duplessis@nca.nhs.uk; Matthew Bailey - matthew.bailey@nca.nhs.uk; Fiona Lalloo - fiona.lalloo@mft.nhs.uk; Omar Pathmanaban - omar.pathmanaban@nca.nhs.uk

***Corresponding author:**
Sayantan Bose,
Department of Neurosurgery,
Salford Royal NHS Foundation Trust, Salford, United Kingdom.

bosesayantan0@gmail.com

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ABSTRACT

Background: Craniopharyngiomas are benign tumors arising in the sellar and suprasellar regions. Although ectopic tumors do occur, it is usually due to local spread or recurrent tumors. Purely ectopic cerebellopontine angle (CPA) or 4th ventricle tumors are extremely rare and have been found to be significantly associated with familial adenomatous polyposis (FAP), a genetic disorder.

Case Description: Only four cases of ectopic CPA craniopharyngioma associated with FAP have been reported to date. Here, we present the 5th case of ectopic CPA craniopharyngioma on a background of FAP. The previously described cases have been elaborated as well.

Conclusion: CPA tumor with a background of FAP should raise a differential diagnosis of craniopharyngioma, and similarly, a CPA primary ectopic craniopharyngioma may raise suspicion of underlying APC gene mutation.

Keywords: 4th ventricle craniopharyngioma, Cerebellopontine angle craniopharyngioma, Ectopic craniopharyngioma, Familial adenomatous polyposis, Gardner syndrome

INTRODUCTION

Craniopharyngiomas are benign brain tumors with a point prevalence of 0.5–2 cases/million population, and they constitute 2–5% of all intracranial tumors.[13] There are two distinct histologic types – adamantinomatous, which has a bimodal age distribution with a peak at 5–15 years and a second peak at 45–60 years, and papillary type, which is rare in the younger age group.[3,15] The tumors arise from the remnants of Rathke's pouch, usually located in the suprasellar region but, exceptionally, have been described to occur anywhere along the tract of an incompletely involuted hypophyseal-pharyngeal duct.[10,21] Tumor extension to the anterior, middle, or posterior cranial fossa can occur.[4,25] There can be a recurrence of tumors locally or in ectopic sites through cerebrospinal fluid dissemination or surgical tract implantation, but primary ectopic tumors are extremely rare.[7] Varying radiological and intraoperative classification schemes have been essentially for sellar/suprasellar locations, though some tumors have been reported in the posterior fossa[1,8,11,20] and even fewer in cerebellopontine angle (CPA).[2,12,23,28,29] CPA craniopharyngioma has been reported in only 13 cases until now as summarized in table 1, with a further six cases described within fourth ventricle. 4/13 CPA tumors and 3/6 fourth ventricle

tumors were associated with familial adenomatous polyposis (FAP) due to an underlying *APC* pathogenic variant.

We report a patient with FAP and an ectopic CPA craniopharyngioma, adding to the potential CPA craniopharyngioma predisposition in FAP.

CASE REPORT

A 47-year-old male, known to have FAP with a confirmed pathogenic variant of *APC* on genetic testing aged 19, had declined recommended colorectal surveillance for a number of years. He presented with rectal bleeding, following which he was diagnosed with numerous colorectal polyps and a rectal adenocarcinoma. A screening positron emission tomography (PET) scan demonstrated areas of high FDG uptake in the colon and showed an area of photopenia in the posterior cranial fossa and a mass effect on the brain stem [Figure 1]. Brain magnetic resonance imaging (MRI) was performed, which demonstrated a large, well-defined cystic lesion at the left CPA. The lesion had an isointense signal on T1-weighted images (WI) [Figure 2] and a high signal on both T2WI and fluid-attenuated inversion recovery images [Figure 3]. Marginal microcalcifications on computed tomography (CT) and gradient echo blooming artifacts were seen, and there were multiple craniofacial and paranasal sinus osteomas [Figure 4].

He underwent a retrosigmoid approach and gross total excision of the tumor, including the capsule, with intraoperative monitoring of cranial nerves. Adherent choroid plexus at Foramen of Luschka was observed and resected with tumor *en bloc*. The histology of the tumor was composed of stratified squamous epithelium showing architectural features of an adamantinomatous craniopharyngioma [Figure 5].

He remained neurologically intact postoperatively without any new deficits and has been subsequently reviewed in the clinic and continues to remain well. A postoperative MRI scan is shown in Figure 6, confirming gross total excision.

DISCUSSION

Craniopharyngiomas located outside of the usual embryological locations of the Rathke's pouch are not common, and CPA is particularly unusual. The presence of craniopharyngiomas at CPA has been theorized to include the migration and entrapment of squamous cells into the posterior fossa from the suprasellar location.[23] Another proposed hypothesis is that they may originate from residual metaplastic squamous epithelium in the adenohypophysis and anterior infundibulum.[16] There have been four case reports identified craniopharyngiomas located in CPA and three-fourth ventricle tumors in patients with FAP and its variant Gardner Syndrome before

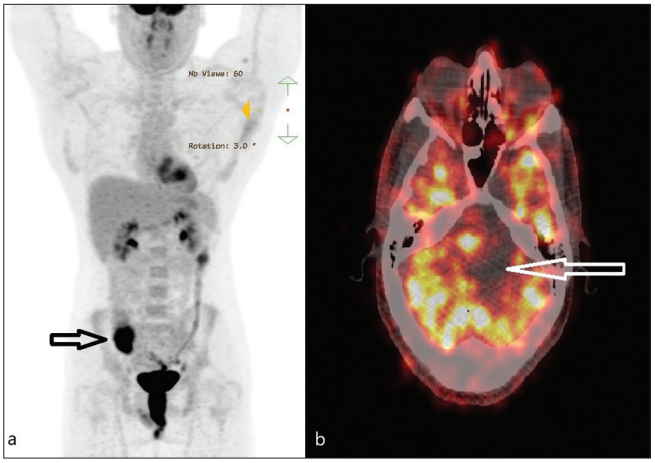

Figure 1: (a) Positron emission tomography (PET) scan showing "hot spot" in caecum (arrow) and anorectum and a few more focal activities in the colon on coronal view. (b) Axial section shows photopenia (arrow) on the left side of the posterior cranial fossa.

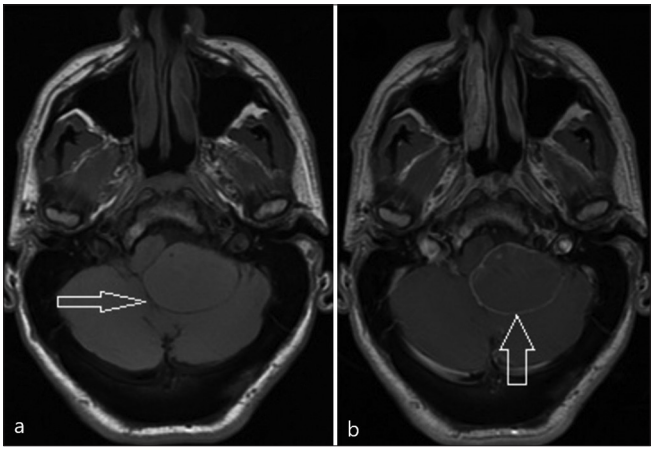

Figure 2: (a) Isointense signal on T1-weighted images at the left cerebellopontine angle, causing mass effect (arrow) to brainstem and cerebellum. (b) Post IV contrast thin marginal enhancement (arrow) with mildly thickened septae at the lower anterior part.

our report [Table 1]. It is, therefore, possible that *APC* related pathways are implicated in craniopharyngioma of the posterior fossa. Out of the two main histologic variants of craniopharyngiomas all patients reported with CPA craniopharyngioma with background of FAP were histologically adamantinomatous.

Patients with craniopharyngioma can present with several clinical features, including endocrine dysfunction in the form of pan-hypopituitarism, selective hormone deficiency, or posterior pituitary/stalk dysfunction. With the increasing size of tumor, patients may present with features of raised intracranial pressure from obstructive hydrocephalus or with a disturbance in behaviour or mentation due to the effect on hypothalamus, frontal and temporal lobes.

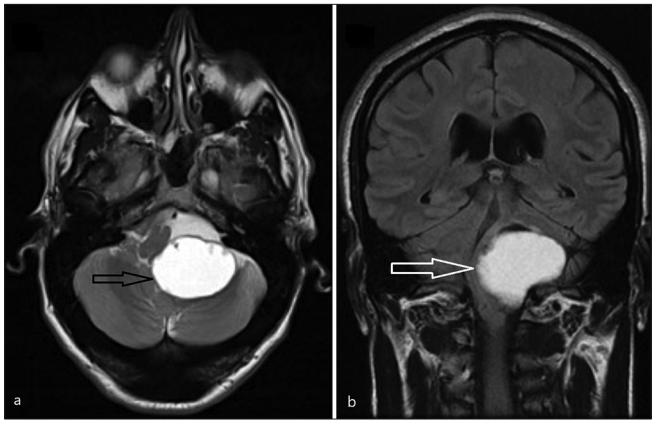

Figure 3: (a) Both T2-weighted images and (b) fluid-attenuated inversion recovery (FLAIR) show high signals in the lesion (arrows). At maximum dimension, the lesion measures about 46 × 31 × 42 mm.

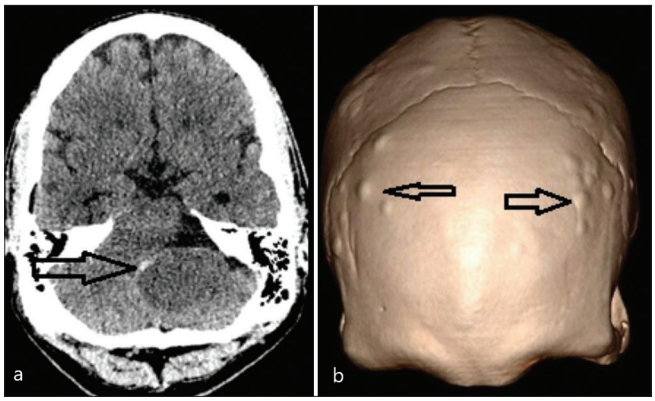

Figure 4: (a) Computed tomography (CT) scan showing marginal calcifications (arrow). (b) 3D reconstruction of the same scan shows multiple craniofacial osteomas (arrows).

As with any CPA tumor, there can be deficits of multiple cranial nerves. It is interesting to note that our patient was asymptomatic, while in earlier reports, the patients presented with features of raised intracranial pressure, cerebellar, and cranial nerve II, V, VI, VII, VIII, IX, and X symptoms. Screening protocol, including a PET-CT scan at the time of his diagnosis of colorectal cancer, incidentally identified the current lesion.

Nearly all adamantinomatous craniopharyngiomas are driven by somatic mutations in the *CTNNB1* gene (encoding β-catenin) that affect β-catenin production.[6] Papillary craniopharyngiomas practically always harbor a somatic V600E variant in BRAF.[6] Both *APC* and *CTNNB1* genes are closely related to the WNT/β-catenin pathway, which is responsible for embryonic development and adult cellular homeostasis through multiple functions such as cellular proliferation, cell polarity, and migration.[19] β-catenin, which is continuously produced in the cytoplasm, is also degraded continuously by Axin-mediated phosphorylation

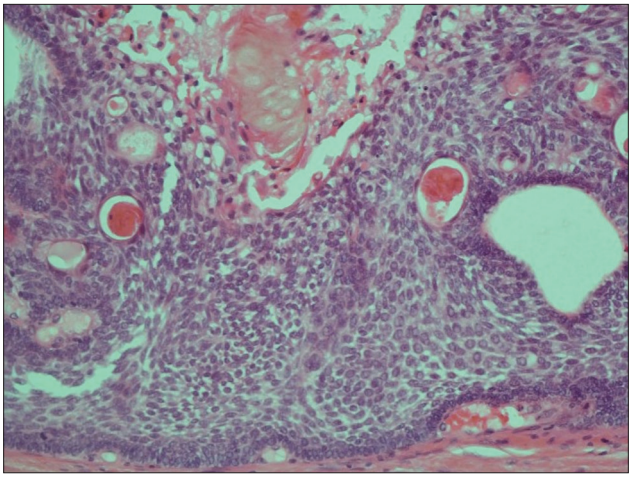

Figure 5: Histology consistent with an adamantinomatous craniopharyngioma characterized by stratified squamous epithelium with a well-defined basal layer and wet keratin. (Hematoxylin and Eosin (H&E), original magnification ×200).

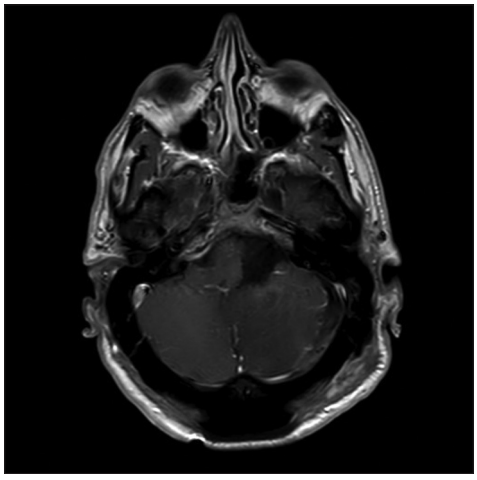

Figure 6: Postoperative post-contrast T1-weighted magnetic resonance imaging (MRI) showing gross total resection.

and APC-mediated ubiquitination, thus maintaining an equilibrium. Axin complex consists of the proteins Axin, the tumor suppressor APC gene product, casein kinase 1, and glycogen synthase kinase 3.[19] When WNT ligands bind to cell membrane G-protein coupled receptors, there is the deactivation of Axin complex-mediated β-catenin degradation; thus, β-catenin accumulates in the cytoplasm and reaches the nucleus. β-catenin in the nucleus activates DNA bound transcription factors of the T-cell factor/Lymphoid enhancer factor family (TCF/LEF family) and causes WNT target gene expression.[19]

In FAP, the germline pathogenic variant in *APC* coupled with a second hit somatic mutation results in the lack of β-catenin degradation. In sporadic adamantinomatous

Table 1: Reported patients with isolated CPA or 4th ventricle craniopharyngiomas.

Year	Authors	Age/Sex	Presenting symptoms	Location	Extent of Resection	Histology	Outcomes	Associated syndrome
1984[2]	Altinors *et al.*	14/M	Right-sided hearing loss, diplopia, and neck pain	CPA	Total	Papillary	Excellent	NA
1990[12]	Gokalp and Mertol	17/F	Headache, vomiting, loss of hearing, and ataxia	CPA	Total	Not mentioned	Excellent	NA
1996[4]	Bashir *et al.*	23/M	Headache, neck pain, dizziness, ataxia, and nystagmus	4th ventricle	Near total	Papillary	Excellent	NA
2002[18]	Link *et al.*	29/M	Headache, vomiting, tinnitus, hearing loss, dysphagia, CN V, VI, VII, VIII, IX, and X deficit	CPA	Near Total	ACP	Transient worsening in his difficulty with swallowing but excellent in the long term.	Gardner Syndrome (FAP)
2006[3]	Aquilina *et al.*	31/M	Headache, visual blurring, truncal ataxia, and scalp swellings,	CPA	Near Total	ACP	Excellent	Gardner Syndrome (FAP)
2007[25]	Shah *et al.*	12/F	Headache, diplopia, ataxia, and left CN VI palsy	4th ventricle	Total	ACP	Excellent	NA
2007[23]	Powers *et al.*	12/F	Headache, nausea, vomiting	CPA	Near total	ACP	Well Post op, Left V, VI, and VII affected	NA
2009[29]	Yan *et al.*	54/F	Headache, tinnitus, deficit of right cranial nerves V, VI, VII, VIII, IX, and X, left hemiparesis, ataxia	CPA	Subtotal	ACP	Poor dysphasia, hemiparesis, pneumonia	NA
2010[28]	Yilmaz *et al.*	14/M	Right ear hearing loss, diplopia, neck pain, and right CN V, VII	CPA	Total	Not mentioned	Not mentioned	NA
2011[5]	Bozbuga *et al.*	34/M	Scalp lesions, tinnitus, hearing impairment	CPA	GTR	Not mentioned	Excellent	Gardner Syndrome (FAP)
2012[26]	Sharma *et al.*	26/F	Headache	CPA	Total	Papillary	Excellent	NA
2012[16]	Khalatbari *et al.*	40/M 22/M 28/M	• Tinnitus, left hearing loss, diplopia, headache, CN VI, and VII palsy • Headache, vomiting, diplopia, tinnitus, ataxia, left hearing loss, and CN VI and VII palsy • Headache, vomiting, and diplopia	CPA	Total	ACP	Excellent	NA
2014[17]	Kim *et al.*	31/M	Headache, Dizziness	CPA	Near Total	ACP	Excellent	Gardner Syndrome (FAP)
2015[22]	Pena *et al.*	20/M	Headache	4th ventricle	GTR	ACP	Excellent	Gardner syndrome (FAP)

(*Contd...*)

Table 1: (*Continued*).

Year	Authors	Age/Sex	Presenting symptoms	Location	Extent of Resection	Histology	Outcomes	Associated syndrome
2016[24]	Salgado *et al.*	29/M	Jaw osteomas, CN VI, VII palsy	4th ventricle	Total	ACP	Not mentioned	Gardner syndrome (FAP)
2018[1]	Algahtani *et al.*	24/M	Headache, ataxia, vomiting, reduced consciousness, and CN VI, VII palsy	4th ventricle	Total	ACP	Excellent	NA
2021[27]	Uemura *et al.*	63/F	Headache	4th ventricle	Total	ACP	Excellent	FAP
2021 (This case)		47/M	Asymptomatic	CPA	GTR	ACP	Excellent	Gardner Syndrome (FAP)

GTR: Gross total resection, ACP: Adamantinomatous craniopharyngioma, CN: Cranial nerve, CPA: Cerebellopontine angle, FAP: Familial adenomatous polyposis, NA: Not available

craniopharyngioma, which is caused by somatic *CTNNB1* mutation, there is production of mutated β-catenin. This is resistant to degradation by Axin complex or *APC*, thus causing accumulation of β-catenin in the cytoplasm and nucleus.[14] Gorelyshev *et al*. found previously undescribed *APC* pathogenic variants in two blood-related patients with familial adamantinomatous craniopharyngioma.[14] They did not identify a variant in *CTNNB1* in either of them; instead, the tumourigenic event in *APC* gene was described as a two-hit *APC* mechanism. There was no mention of FAP in their article, but the patient's mother did have multiple colonic polyps.

Safe maximal surgical excision has been recommended in the treatment of craniopharyngiomas. Gross total excision has been noted to reduce the risk of recurrence.[9] Almost all the patients reported having near or complete excision and did well postoperatively with minimal deficits from which they fully recovered, affirming the safety of surgery for tumors in this location in these patients. Complete resection may allow adjuvant radiotherapy to be delayed or prevented, which minimizes late side-effects in young people with a genetic tumor predisposition. Close imaging surveillance is required.

CONCLUSION

Craniopharyngioma in CPA is rare. We have described a report of a CPA craniopharyngioma in a man with FAP in addition to the few previously reported cases. Craniopharyngioma should be included as a differential diagnosis of CPA/4th ventricle tumors in FAP patients. Likewise, a CPA/4th ventricle craniopharyngioma should also raise suspicion of underlying FAP and may warrant investigation. Early diagnosis and safe maximal resection are the keys to a favorable outcome.

Ethical approval

The Institutional Review Board approval is not required.

Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

REFERENCES

1. Algahtani AY, Algahtani HA, Jamjoom AB, Samkari AM, Marzuk YI. *De novo* craniopharyngioma of the fourth ventricle: Case report and review of literature. Asian J Neurosurg 2018;13:62-5.
2. Altinörs N, Senveli E, Erdoğan A, Arda N, Pak I. Craniopharyngioma of the cerebellopontine angle. Case report. J Neurosurg 1984;60:842-44.
3. Aquilina K, O'Brien DF, Farrell MA, Bolger C. Primary cerebellopontine angle craniopharyngioma in a patient with Gardner syndrome. Case report and review of the literature. J Neurosurg 2006;105:330-3.

4. Bashir EM, Lewis PD, Edwards MR. Posterior fast craniopharyngioma. Br J Neurosurg 1996;10:613-5.
5. Bozbuga M, Turan Suslu H, Hicdonmez T, Bayindir C. Primary cerebellopontine angle craniopharyngioma in a patient with Gardner syndrome. J Clin Neurosci 2011;18:300-1.
6. Brastianos PK, Taylor-Weiner A, Manley PE, Jones RT, Dias-Santagata D, Thorner AR, *et al*. Exome sequencing identifies BRAF mutations in papillary craniopharyngiomas. Nat Genet 2014;46:161-5.
7. Carleton-Bland N, Kilday JP, Pathmanaban ON, Stivaros S, Kelsey A, Kamaly-Asl ID. Ventricular metastatic dissemination of a paediatric craniopharyngioma: Case report and literature review. Br J Neurosurg 2017;31:474-7.
8. Connolly ES Jr., Winfree CJ, Carmel PW. Giant posterior fossa cystic craniopharyngiomas presenting with hearing loss. Report of three cases and review of the literature. Surg Neurol 1997;47:291-9.
9. Dandurand C, Sepehry AA, Asadi Lari MH, Akagami R, Gooderham P. Adult craniopharyngioma: Case series, systematic review, and meta-analysis. Neurosurgery 2018;83:631-41.
10. Fernandez-Miranda JC, Gardner PA, Snyderman CH, Devaney KO, Strojan P, Suárez C, *et al*. Craniopharyngioma: A pathologic, clinical, and surgical review. Head Neck 2012;34:1036-44.
11. Gökalp HZ, Egemen N, Ildan F, Bacaci K. Craniopharyngioma of the posterior fossa. Neurosurgery 1991;29:446-8.
12. Gökalp HZ, Mertol T. Cerebellopontine angle craniopharyngioma. Neurochirurgia (Stuttg) 1990;33:20-1.
13. Gooderham P, Akagami R, Asadi Lari MH, Sepehry AA, Dandurand C. Adult craniopharyngioma: Case series, systematic review, and meta-analysis. Neurosurgery 2018;83:631-41.
14. Gorelyshev A, Mazerkina N, Medvedeva O, Vasilyev E, Petrov V, Ryzhova M, *et al*. Second-hit APC mutation in a familial adamantinomatous craniopharyngioma. Neuro Oncol 2020;22:889-91.
15. Haupt R, Magnani C, Pavanello M, Caruso S, Dama E, Garrè ML. Epidemiological aspects of craniopharyngioma. J Pediatr Endocrinol Metab 2006;19:289-93.
16. Khalatbari MR, Borghei-Razavi H, Samadian M, Moharamzad Y, Schick U. Isolated primary craniopharyngioma in the cerebellopontine angle. J Clin Neurosci 2012;19:1516-9.
17. Kim MS, Kim YS, Lee HK, Lee GJ, Choi CY, Lee CH. Primary intracranial ectopic craniopharyngioma in a patient with probable Gardner's syndrome. J Neurosurg 2014;120:337-41.
18. Link MJ, Driscoll CL, Giannini C. Isolated, giant cerebellopontine angle craniopharyngioma in a patient with Gardner syndrome: Case report. Neurosurgery 2002;51:221-5; discussion 225-6.
19. MacDonald BT, Tamai K, He X. Wnt/β-catenin signaling: Components, mechanisms, and diseases. Dev Cell 2009;17:9-26.
20. Novák Z, Chrastina J, Feitová V, Lzicarová E, Říha I. Minimally invasive treatment of posterior fossa craniopharyngioma by means of navigated endoscopy. Minim Invasive Neurosurg 2008;51:165-8.
21. Ohmori K, Collins J, Fukushima T. Craniopharyngiomas in children. Pediatr Neurosurg 2007;43:265-78.
22. Pena AH, Chaudhry A, Seidman RJ, Peyster R, Bangiyev L. Ectopic craniopharyngioma of the fourth ventricle in a patient with Gardner syndrome. Clin Imaging 2016;40:232-6.
23. Powers CJ, New KC, McLendon RE, Friedman AH, Fuchs HE. Cerebellopontine angle craniopharyngioma: Case report and literature review. Pediatr Neurosurg 2007;43:158-63.
24. Salgado JA, de Mesa FG, Ledezma JJ, Méndez ML, Sansinenea IP, de Lope-Llorca AR, *et al*. Craneofaringioma ectópico y síndrome de Gardner: A propósito de un caso y revisión de la literatura. Neurocirugía 2017;28:97-101. (In Spanish)
25. Shah GB, Bhaduri AS, Misra BK. Ectopic craniopharyngioma of the fourth ventricle: Case report. Surg Neurol 2007;68:96-8.
26. Sharma M, Mally R, Velho V, Hrushikesh K. Primary isolated cerebellopontine angle papillary craniopharyngioma. Neurol India 2012;60:438-9.
27. Uemura H, Tanji M, Natsuhara H, Takeuchi Y, Hoki M, Sugimoto A, *et al*. The association of ectopic craniopharyngioma in the fourth ventricle with familial adenomatous polyposis: Illustrative case. J Neurosurg Case Lessons 2022;3:CASE21572.
28. Yilmaz C, Altinors N, Sonmez E, Gulsen S, Caner H. Rare lesions of the cerebellopontine angle. Turk Neurosurg 2010;20:390-7.
29. Yan Y, Tang WY, Yang G, Zhong D. Isolated cerebellopontine angle craniopharyngioma. J Clin Neurosci 2009;16:1655-7.

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