frontiers in Oncology

TYPE Case Report
PUBLISHED 20 April 2026
DOI 10.3389/fonc.2026.1780123

Check for updates

OPEN ACCESS

EDITED BY
Supriya Mallick,
All India Institute of Medical Sciences, India

REVIEWED BY
Maria-Mihaela Pop,
University of Medicine and Pharmacy Iuliu Hatieganu, Romania
Miguel Afonso Filipe,
Braga Hospital, Portugal

*CORRESPONDENCE
Shaolei Guo
guoshaol@mail.sysu.edu.cn
Bing Liao
liaob@mail.sysu.edu.cn

†These authors share first authorship

RECEIVED 03 January 2026
REVISED 04 April 2026
ACCEPTED 06 April 2026
PUBLISHED 20 April 2026

CITATION
Lin J, Lin J, Xie H, Hu L, Liao B and Guo S (2026) Primary intracranial adenocarcinoma associated with an epidermoid cyst: a case report and literature review. *Front. Oncol.* 16:1780123. doi: 10.3389/fonc.2026.1780123

COPYRIGHT
© 2026 Lin, Lin, Xie, Hu, Liao and Guo. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

Primary intracranial adenocarcinoma associated with an epidermoid cyst: a case report and literature review

Jiayi Lin[1†], Jianhang Lin[2†], Haiqing Xie[2], Liu Hu[1], Bing Liao[1*] and Shaolei Guo[2*]

[1]Department of Pathology, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, China, [2]Department of Neurosurgery, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, China

Intracranial epidermoid cysts are rare benign congenital lesions. Although malignant transformation is uncommon, most reported cases have involved squamous cell carcinoma. To our knowledge, transformation into adenocarcinoma has not previously been described. We present a 56-year-old man with a cerebellopontine angle lesion that demonstrated atypical contrast enhancement and mixed signals on SWI. The lesion was surgically resected, and postoperative histopathological examination revealed a poorly differentiated adenocarcinoma associated with a residual epidermoid cyst. Immunohistochemistry, including negative CK5/6 staining, excluded squamous cell carcinoma and common metastatic origins. Postoperative PET-CT showed no extracranial primary lesions. This appears to be the first well-documented case of primary intracranial adenocarcinoma associated with an intracranial epidermoid cyst. Careful radiologic evaluation and comprehensive immunohistochemical analysis are critical when atypical features are encountered. Further accumulation of similar cases is needed to better elucidate the mechanisms, biological behavior, and prognostic implications of this possible transformation process.

KEYWORDS
adenocarcinoma, cerebellopontine angle, intracranial epidermoid cysts, intracranial tumor, malignant transformation

Introduction

Intracranial epidermoid cysts are rare, benign congenital lesions, thought to arise from ectodermal inclusions during neural tube closure. They are most commonly located in the cerebellopontine angle (CPA) and parasellar region, accounting for approximately 1% of all intracranial tumors (1). Although histologically benign, epidermoid cysts are locally invasive and may encase or compress adjacent neurovascular structures, resulting in a range of neurological symptoms depending on their location and size (2).

Malignant transformation of intracranial epidermoid cysts is exceedingly rare, with the vast majority of reported cases progressing to squamous cell carcinoma (SCC) (3). This process is often associated with chronic inflammation, prior surgical intervention, or repeated cyst rupture, which may contribute to epithelial instability and carcinogenesis (4, 5). By contrast, adenocarcinomatous change appears to be exceptionally rare, and no

well-documented cases of primary intracranial adenocarcinoma associated with an intracranial epidermoid cyst were identified in our review.

Herein, we present a rare case of a 56-year-old man with a lesion radiologically consistent with a CPA epidermoid cyst, which was histopathologically diagnosed as a poorly differentiated adenocarcinoma with residual epidermoid cyst. We further review the existing literature on malignant transformation of epidermoid cysts and discuss potential mechanisms, histopathological challenges, and diagnostic considerations.

Case presentation

A 56-year-old man without significant history of tumor presented with a 2-month history of progressive left-sided hearing loss and tinnitus, followed by dizziness, unsteady gait, and numbness over the left side of the face. Neurological examination revealed a positive Romberg sign. No other focal neurological deficits were noted. CT revealed an irregular, slightly hyperdense lesion in the left cerebellopontine angle, with patchy calcifications and no evidence of bony destruction (Figures 1A, B). CT perfusion (CTP) demonstrated predominantly low perfusion within the lesion (Figure 1C). MRI demonstrated a 24×28 mm mass in the left cerebellopontine angle, hyperintense on T1-weighted imaging and showed mixed high and low signal intensities on T2-FLAIR and T2-SPACE sequences (Figures 1D–F). Contrast-enhanced MRI revealed focal areas of marked enhancement within the lesion (Figure 1G). SWI demonstrated internal mixed signals suggestive of calcification or microhemorrhage (Figure 1H). The mass compressed cranial nerves VII and VIII and displaced the adjacent brainstem. Radiologically, a diagnosis of epidermoid cyst was favored.

The patient subsequently underwent microsurgical resection via a retrosigmoid approach. Intraoperatively, the tumor was found to

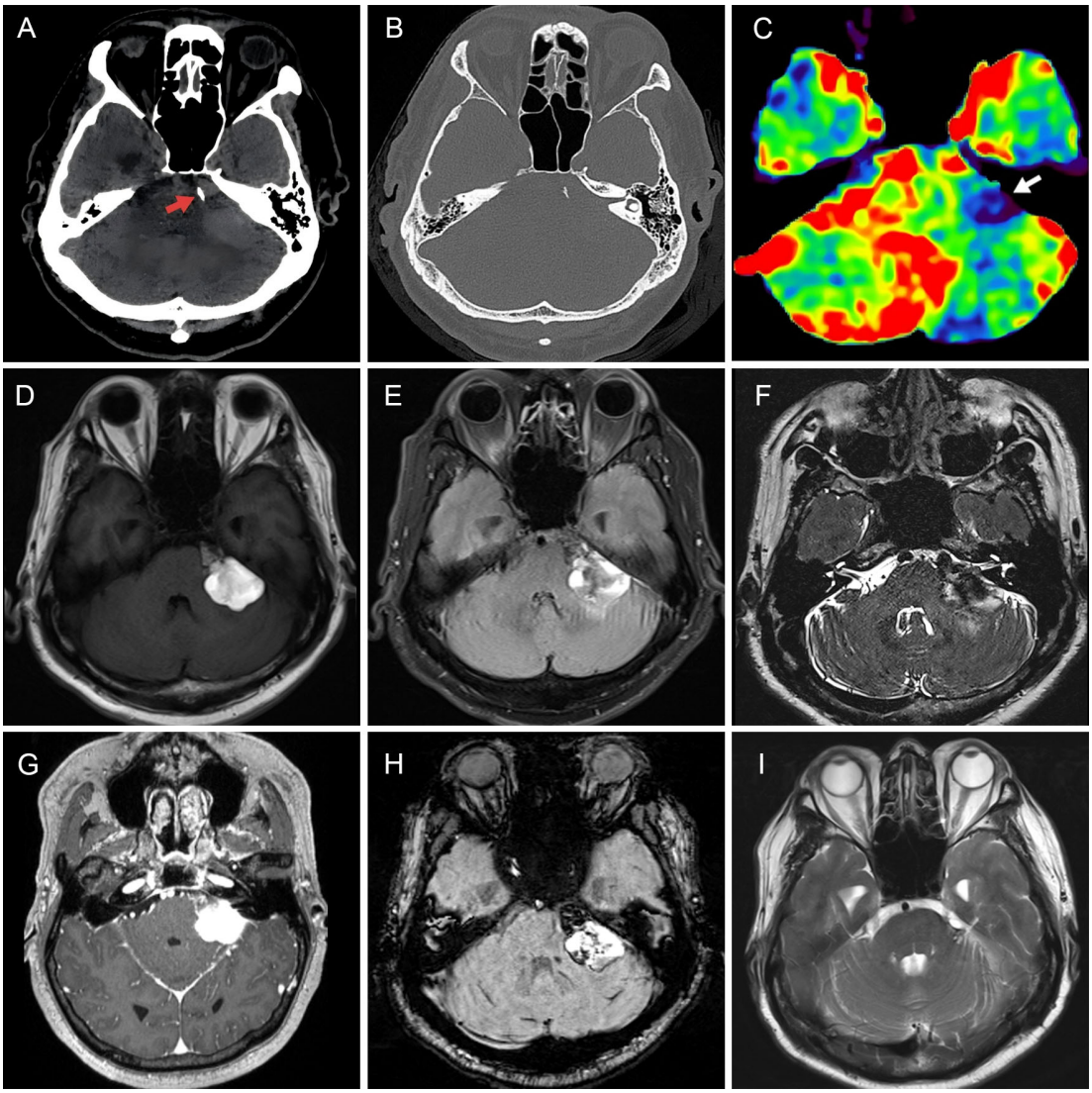


FIGURE 1
Preoperative and 8-month postoperative imaging. **(A, B)** Axial CT showing an irregular slightly hyperdense lesion with patchy calcifications in the left CPA (red arrows); no bony erosion. **(C)** CT perfusion indicating low perfusion in the lesion (white arrow). **(D–F)** MRI showing a 24 × 28 mm irregular CPA mass with hyperintensity on T1WI and mixed signals on T2-FLAIR and T2-SPACE. **(G)** Contrast-enhanced MRI demonstrating focal enhancement. **(H)** SWI revealing heterogeneous internal signals. **(I)** Follow-up MRI at 8 months confirming complete resection without recurrence.

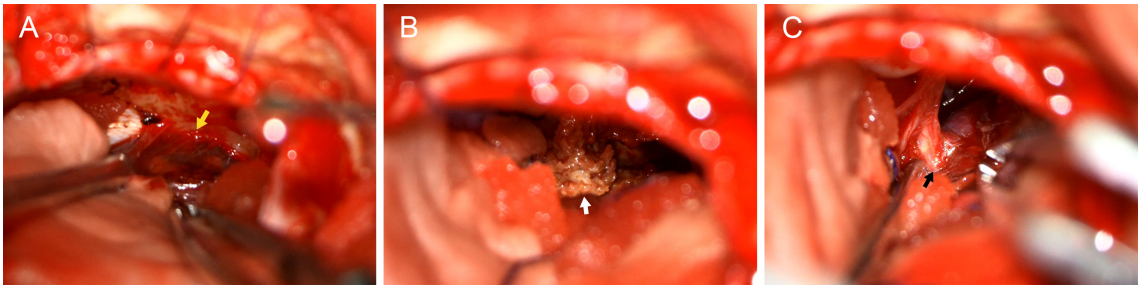


FIGURE 2
Intraoperative findings. **(A)** Cystic fluid with dark red, old hemorrhagic content (yellow arrow). **(B)** Grayish-white, cholesteatoma-like solid component (white arrow). **(C)** Tumor capsule adherent to cranial nerves VII and VIII (black arrow).

have both cystic and solid components. The cystic portion contained dark red, old hemorrhagic fluid, whereas the solid component consisted of grayish-white, cholesteatoma-like tissue (Figures 2A, B). The tumor capsule was tightly adherent to cranial nerves VII and VIII (Figure 2C). Intraoperative frozen section analysis showed edematous tissue with areas of collagenization, foamy cell formation, and hemosiderin deposition. A small number of epithelial cells and abundant eosinophilic keratinized material derived from squamous epithelium were noted. Some of the cells showed an increased nuclear/cytoplasmic ratio with atypia. The initial impression was consistent with an epidermoid cyst or epithelial neoplasm.

Subsequently, the surgical specimen was thoroughly sampled, fixed in formalin, and embedded in paraffin for sectioning. Histological examination revealed a cyst wall–like structure composed of fibrous tissue, with focal calcification, hemorrhage, and abundant eosinophilic keratinous material. Importantly, Carcinomatous tissue was observed infiltrating the cyst wall in a nested pattern (Figure 3A). The surface of the cyst wall was lined by stratified squamous epithelium. Within the cystic cavity, abundant eosinophilic keratinous material derived from squamous epithelium was present, along with a few shedded fragment of benign squamous epithelium and malignant tumor cell nests with obvious atypia (Figure 3B). In some tissue fragments, benign squamous epithelium and malignant adenocarcinoma components were identified simultaneously within the same cystic cavity. The malignant cells showed proliferation along the cyst lining, and in some areas, they appeared to extend directly beneath the benign squamous epithelium, accompanied by infiltrative growth into the deeper cyst wall. The malignant component showed diffuse infiltration, with tumor cells forming small nets and exhibiting an increased nuclear-to-cytoplasmic ratio, prominent nucleoli, and marked cellular

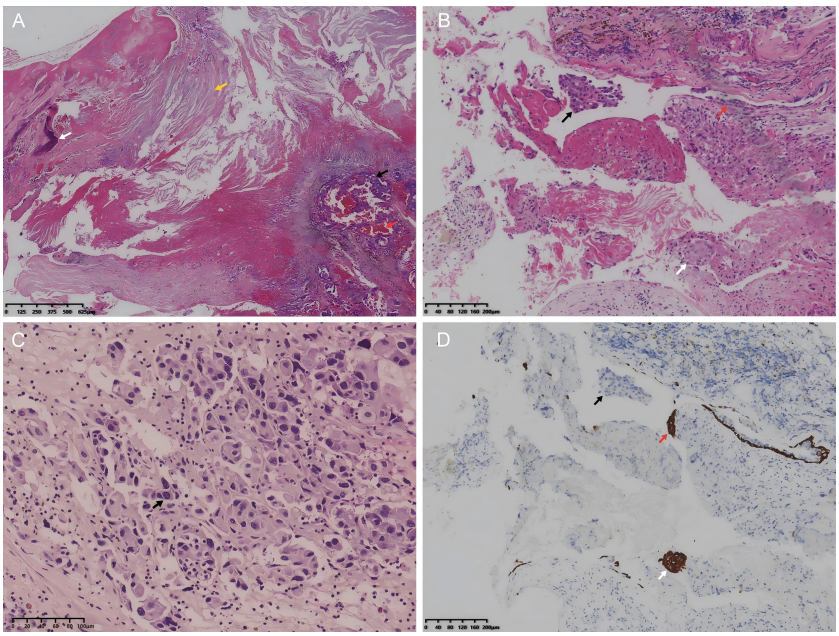


FIGURE 3
Hematoxylin and eosin (H&E) staining and CK5/6 immunohistochemistry. **(A)** H&E staining (×4) showing cyst wall and malignant tumor tissue (black arrow), with focal calcification (white arrow), hemorrhage (red arrow), and eosinophilic keratinous material in the lumen (yellow arrow). **(B)** H&E staining (×10) showing stratified squamous epithelium lining on the cyst wall (red arrow), a few shedded fragment of benign squamous epithelium (white arrow), and malignant tumor cells nest with obvious atypia (black arrow). **(C)** H&E staining (×20) showing tumor cells with marked nuclear atypia (black arrow). **(D)** CK5/6 immunohistochemistry (×10) showing diffuse cytoplasmic positivity in benign squamous epithelial cells (red and white arrows), while malignant tumor cells are negative (black arrow).

atypia (Figure 3C). These findings support the coexistence of an epidermoid cyst and a malignant epithelial neoplasm.

Immunohistochemically, the malignant tumor cells were strongly positive for CK (Figure 4A), CK7(Figure 4B), and CK19 (Figure 4C) in the cytoplasm, indicating an adenocytic epithelial origin. P53 showed diffuse strong nuclear positivity, suggesting a possible TP53 gene mutation (Figure 4D). CK20 was focally positive. The malignant tumor cells were negative for TTF-1 (Figure 4E), Napsin A, SATB2, CDX2(Figure 4F), NKX3.1, PSA, Synaptophysin, Chromogranin A, CK5/6(Figure 4G), and P40 (Figure 4H), excluding pulmonary adenocarcinoma, gastrointestinal adenocarcinoma, prostatic adenocarcinoma, neuroendocrine neoplasm, squamous cell carcinoma and urothelial carcinoma origins. The benign squamous epithelium lining on the cyst wall or shedded within the cyst lumen were diffusely positive for CK5/6 in the cytoplasm (Figure 3D), whereas the malignant tumor cells were negative, further supporting adenocarcinomatous differentiation in a lesion associated with an epidermoid cyst. The Ki-67 proliferation index of the malignancy was estimated at 25% (Figure 4I), indicating moderate proliferative activity. These immunohistochemical results of the malignant tumor were consistent with a diagnosis of poorly differentiated adenocarcinoma.

Based on the hematoxylin-eosin morphology and immunohistochemical results, the findings support a diagnosis of an epidermoid cyst and a poorly differentiated adenocarcinoma. These findings support the possibility of malignant transformation in association with the epidermoid cyst.

A PET-CT scan performed immediately after surgery revealed no abnormal uptake in the lung, gastrointestinal tract, or other organs, further ruling out a metastatic origin. The patient subsequently underwent three courses of postoperative radiotherapy. At the 8-month follow-up, MRI demonstrated no evidence of local tumor recurrence (Figure 1I), and a follow-up PET-CT confirmed that there were no extracranial primary lesions or systemic disease. Taken together, the clinical history, imaging findings, histology, and immunohistochemistry support the diagnosis of a poorly differentiated adenocarcinoma associated with an epidermoid cyst and suggest a possible transformation process. The patient continues to undergo regular follow-up, with no evidence of extracranial malignancy identified to date.

Discussion

A literature search of PubMed was conducted for articles published between January 2000 and April 2025 using the terms “intracranial epidermoid cyst” OR “intracranial epidermoid cysts” AND (“malignant transformation” OR “carcinoma” OR “adenocarcinoma”). Only publications reporting histopathologically confirmed malignant transformation of primary intracranial epidermoid cysts were included. Fifty-four articles were identified, and 63 eligible cases were included after screening. The reviewed cases showed that malignant transformation most commonly

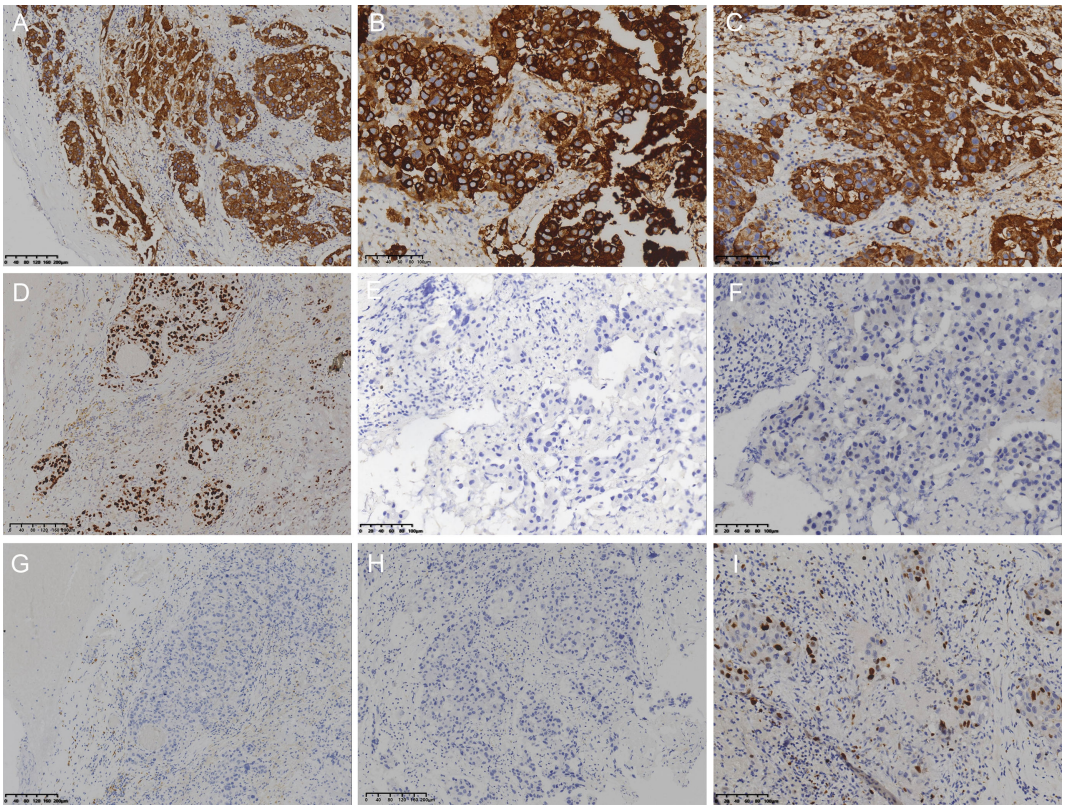


FIGURE 4
Immunohistochemical features. Tumor cells show strong cytoplasmic positivity for CK **(A)**, CK7 **(B)**, and CK19 **(C)**; diffuse nuclear positivity for P53 **(D)**; and are negative for TTF-1 **(E)**, CDX2 **(F)**, CK5/6 **(G)**, and P40 **(H)**. Ki-67 **(I)** staining shows a proliferation index of approximately 25%.

resulted in squamous cell carcinoma, whereas no well-documented case of primary intracranial adenocarcinoma arising from an intracranial epidermoid cyst was identified during the past 25 years.

Intracranial epidermoid cysts, while histologically benign, may cause considerable neurological morbidity due to their location and mass effect. Malignant transformation is exceedingly rare, with the majority of reported cases evolving into squamous cell carcinoma (SCC). Occasionally, undifferentiated carcinoma, poorly differentiated carcinoma, or sarcomatoid carcinoma have been documented (6–8). However, no well-documented case showing this pattern of adenocarcinomatous differentiation in association with an intracranial epidermoid cyst was identified in our review.

Our review of the literature over the past 25 years identified only a limited number of malignant transformation cases, predominantly involving SCC (Table 1). In contrast, the present case involved a cerebellopontine angle lesion was histopathologically diagnosed as a poorly differentiated adenocarcinoma. Residual benign squamous epithelium was observed within the lesion, suggesting a possible phenotypic transition from squamous to glandular differentiation. To our knowledge, this appears to be the first well-documented case of primary intracranial adenocarcinoma associated with an intracranial epidermoid cyst. This finding expands the recognized malignant potential of these lesions and suggests a more complex pathological evolution than previously appreciated.

Histologically, the malignant components in this case consisted predominantly of poorly differentiated epithelial cells with marked nuclear atypia, prominent nucleoli, and moderate eosinophilic cytoplasm. Focal areas showed a mucinous background, and residual benign squamous epithelium was also observed, suggesting a possible malignant phenotypic transition from squamous to glandular differentiation. Immunohistochemically, the malignant tumor cells showed strong diffuse positivity for CK, CK7and CK19, focal positivity for CK20, and strong nuclear overexpression of P53. The Ki-67 proliferation index was estimated at 25%, indicating moderate proliferative activity. These findings support the diagnosis of a poorly differentiated adenocarcinoma.

Importantly, both CK5/6 and P40—markers commonly used to identify squamous differentiation—were negative, effectively excluding squamous cell carcinoma or urothelial carcinoma. Meanwhile, a neuroendocrine neoplasm was also excluded, as both synaptophysin and chromogranin A were negative. These findings further support an adenocarcinoma. Immunomarkers associated with lung adenocarcinoma (TTF-1, Napsin A), gastrointestinal origin (CDX2, SATB2), and prostate or breast origin (PSA, NKX3.1, GCDFP-15, ER, PR, AR) were all negative. The patient had no significant history of tumor, and postoperative PET-CT imaging showed no evidence of extracranial primary lesions, further supporting a primary intracranial tumor rather than metastatic disease.

Taken together, the clinical, radiological, histological, and immunophenotypic findings support the interpretation of a primary intracranial adenocarcinoma associated with a preexisting epidermoid cyst and are compatible with a possible malignant transformation process. The absence of detectable extracranial malignancy on PET-CT, combined with the lack of immunohistochemical evidence supporting common primary sites, further reinforces this interpretation. In this context, the coexistence of benign squamous epithelium and malignant glandular components may reflect a process of epithelial transformation.

In previously reported cases, malignant transformation of intracranial epidermoid cysts has most commonly occurred in the cerebellopontine angle or posterior fossa, with squamous cell carcinoma (SCC) being the predominant histological subtype. In a systematic review of 94 studies encompassing 135 cases, Eatz et al (3) found that the vast majority of malignancies arising from epidermoid cysts were classified as SCC. In most reports, the diagnosis relied primarily on hematoxylin and eosin (H&E) morphology and limited immunohistochemical (IHC) markers, without a comprehensive panel to definitively determine tumor origin. In addition to SCC, rare cases of adenosquamous carcinoma have been described. Jain et al. (9) reported a 5-year-old girl with a large temporal lobe mass histologically diagnosed as poorly differentiated adenosquamous carcinoma, which recurred despite radical resection, chemotherapy, and radiotherapy. Histopathologically, the tumor was predominantly squamous with limited glandular differentiation, suggesting malignant transformation within a preexisting epidermoid or dermoid cyst. These observations highlight that although SCC remains the predominant histological outcome of malignant transformation, glandular differentiation may represent an underrecognized but clinically important pathway of tumor evolution (10).

The mechanisms underlying malignant transformation in epidermoid cysts remain poorly understood, and current theories are largely extrapolated from pathological observations and analogous conditions. Chronic inflammation is considered a key contributing factor. Repeated rupture, infection, or long-standing residual cysts may trigger chronic inflammation, leading to epithelial instability and DNA damage, which in turn promotes dysplasia and malignant transformation (5, 11, 12). Glandular metaplasia of squamous epithelium under inflammatory stress has been observed in middle ear cholesteatomas and chronic suppurative otitis media (13); similar pathways are well described in Barrett's esophagus and pancreatic intraductal neoplasms (14, 15). In our case, the histological presence of both squamous and glandular components suggests a possible phenotypic transition. Besides, immunohistochemical findings showed strong nuclear positivity for P53, indicating a potential TP53 mutation—an early and common event in epithelial tumorigenesis, associated with genomic instability and evasion of apoptosis (16). Moreover, hypointense foci on susceptibility-weighted imaging (SWI), suggestive of chronic microhemorrhage or calcification, imply a hypoxic and oxidative stress environment, which has been implicated in promoting prooncogenic signaling and genetic alterations (17). Taken together, chronic inflammation, molecular alterations such as TP53 mutation, and a hypoxic microenvironment may act synergistically in the

TABLE 1 Summary of reported cases of malignant transformation of intracranial epidermoid cysts in the past 25 years.

Author(Year)	Age/Sex	Location	Histology	IHC profile
Lin et al. (2025) (23)	55/M	CPA	SCC	P63(+), P40(+), CK5/6(+), P53(+)
Elsarraj et al. (2025) (11)	61/M	CPA	SCC	P40+, Calretinin (-), SOX-10 (-)
Harary et al. (2025) (24)	55/F	CPA	SCC	PD-L1 CPS <1%
Alsadi et al. (2025) (25)	59/M	CPA	SCC	N/A
Yang et al. (2024) (18)	61/F	Pre-pontine cistern	SCC	CK(AE1/AE3)(+), GATA3(+), Ki-67 20%
Zhang et al. (2023) (26)	58/M	Right frontoparietal lobe, right lateral ventricle	SCC	N/A
Narasimhaiah et al. (2023) (5)	39/M	CPA	SCC	P63(+), MIB-1 40%
Eatz et al. (2023) (3)	67/F	CPA	SCC	N/A
Sakamoto et al. (2022) (19)	59/F	CPA	SCC	P53(+), P16(+)
Gabay et al. (2022) (27)	61/M	CPA	SCC	β-catenin (-), BRAF V600E(-)
Zuo et al. (2021) (28)	39/M	CPA	SCC	Not reported
	54/F	Suprasellar region	SCC	Ki-67 40%
	43/M	CPA	SCC	Ki-67 30%
	44/M	CPA	SCC	Ki-67 60%
	51/M	CPA	SCC	Ki-67 30%
	48/M	CPA	SCC	Ki-67 10%
	61/M	CPA	SCC	Ki-67 50%
	61/M	CPA	SCC	Ki-67 90%
	60/M	CPA	SCC	Ki-67 60%
Yanagawa et al. (2021) (7)	69/F	Caudal region of cerebellar vermis	Undifferentiated carcinoma	CK(+), P40 (-), CK5/6 (-), CDX-2 (-), TTF-1 (-), p53(+)
Demuth et al. (2019) (29)	67/F	CPA	SCC	N/A
Nagata et al. (2019) (30)	77/F	CPA	SCC	N/A
Fereydonyan et al. (2019) (31)	30/M	Left middle cerebellar peduncle	SCC	N/A
Cuoco et al. (2019) (32)	71/M	CPA	SCC	CK5/6(+)
Chen et al. (2019) (33)	43/M	CPA	SCC	CK(AE1/AE3) (+)
Liu et al. (2018) (34)	20/M	Left lateral ventricle	SCC	P63(+), P40(+), CK5/6(+), EMA(+), Pan-CK(+), P53 (-), GFAP (-), CK20 (-), Vimentin (-), S100 (-)
Suematsu et al. (2018) (35)	54/M	CPA	SCC	N/A
Badat et al. (2018) (36)	70/NA	CPA	SCC	P40(+), P16(+)
Ou et al. (2018) (37)	71/F	Right posterolateral cerebellar convexity	SCC	N/A
Solanki et al. (2017) (38)	47/F	CPA	SCC	N/A
Seif et al. (2017) (39)	83/M	Intracranial extradural, left posterior fossa	SCC	N/A
Roh et al. (2017) (40)	53/F	CPA	SCC	N/A
Ozutemiz et al. (2017) (20)	64/M	the posterior horn of the left lateral ventricle	SCC	N/A
Mascarenhas et al. (2017) (41)	35/F	CPA	SCC with areas of poorly differentiated sarcomatoid elements	CK5/6(+), P63(+), AE1/3(+), CK5/6(+) (focal), P63 (+) (focal), CD34(-), S100(-), desmin(-), GFAP(-), CD31(-), myogenin(-)
Raheja et al. (2016) (42)	54/F	Brainstem, CPA	SCC	N/A

(Continued)

TABLE 1 Continued

Author(Year)	Age/Sex	Location	Histology	IHC profile
	37/F	Brainstem, CPA	infiltrative, poorly differentiated carcinoma most consistent with SCC	N/A
Pikis et al. (2016) (43)	77/M	CPA	SCC	N/A
Ding et al. (2016) (44)	55/F	Left temporal region and prepontine area	SCC	N/A
Chourmouzi et al. (2015) (45)	39/F	CPA	SCC	N/A
Vellutini et al. (2014) (46)	43/F	CPA	SCC	N/A
Kaplan et al. (2013) (10)	73/F	CPA	SCC with focal adenosquamous differentiation	N/A
Chon et al. (2012) (47)	43/M	CPA	SCC	pan-cytokeratin(+)
Raghunathan et al. (2011) (8)	60/M	CPA	SCC and Sarcomatoid Carcinoma	SCC component: CK5/6(+), pan-cytokeratin(+), EMA(+), P63(+), P53(+); Sarcomatoid component: Vimentin(+), SMA (+), focal MSA (+), P53(+)
Lakhdar et al. (2011) (48)	52/M	CPA	SCC	P53(+)
Kano et al. (2010) (49)	64/F	CPA	SCC	N/A
Hao et al. (2010) (50)	61/F	Right CPA, prepontine cistern, temporoparietal lobe	SCC	N/A
Ge et al. (2009) (51)	50/M	Right temporal lobe	SCC	N/A
Kim et al. (2008) (12)	72/F	Brain stem	SCC	N/A
Agarwal et al. (2007) (52)	45/M	Posterior fossa midline	SCC	CK(AE1/AE3) (+), MIB-1 index 42%
Kodama et al. (2007) (53)	67/M	CPA	poorly differentiated SCC	N/A
Pagni et al. (2007) (54)	65/F	Pineal region	SCC	N/A
Tamura et al. (2006) (55)	56/F	CPA	SCC	CK7 (+), MIB-1 index 47.9%
Michael et al. (2005) (56)	45/M	CPA	SCC	CK6 (+), CK8 (+)
Guan et al. (2004) (57)	42/F	Left frontotemporal region	SCC	N/A
Kadashev et al. (2003) (58)	47/F	The third ventricle and medial portions of temporal lobes	SCC	N/A
Jain et al. (2003) (9)	5/F	Right posterior temporal lobe	Poorly differentiated adenosquamous carcinoma	CK7(+), CAM5.2(+), keratin903(focal +), CEA+, MIB-1 >90%
Akar et al. (2003) (59)	N/A	CPA	SCC	N/A
Link et al. (2002) (60)	57/F	CPA	SCC	N/A
Tsugu et al. (2001) (61)	47/M	Cerebellar vermis, left cerebellar hemisphere, cisterna magna	SCC	MIB-1 index 10.9%
Nawashiro et al. (2001) (62)	46/M	Left temporal lobe and basal cisterns	Recurrent intracranial epidermoid cyst with malignant transformation (carcinomatous component)	N/A
Khan et al. (2001) (63)	53/M	Cystic lesion anterior to pons	SCC	N/A
Asahi et al. (2001) (6)	55/F	CPA	Poorly differentiated carcinoma	EMA (focal +), Keratin (-), AFP (-), HCG (-), PLAP (-), GFAP (-), MIB-1 index 30%
Sawan et al. (2001) (64)	66/M	Front of the pons/ brainstem	SCC	N/A

rare malignant transformation of epidermoid cysts. Nevertheless, further studies are needed to validate these proposed mechanisms.

At the molecular level, comparative analysis of the squamous and adenocarcinoma components would be valuable for assessing their clonal relationship and further clarifying the mechanism of malignant transformation. In particular, next-generation sequencing (NGS) may help determine whether the two components share key genetic alterations, which would provide additional support for a common origin and evolutionary progression within the same lesion. Although such analysis was not performed in the present case, it represents an important direction for future investigation.

In terms of radiological features, distinguishing malignant transformation from a complicated but benign epidermoid cyst is particularly important. Malignant transformation is more likely to be associated with nodular or irregular contrast enhancement, development of a solid component, perilesional edema, and invasive involvement of adjacent neurovascular structures (18–20). In contrast, benign epidermoid cysts complicated by inflammation or hemorrhage may show signal heterogeneity or limited enhancement, but they usually lack a discrete enhancing solid component and other aggressive features (21, 22). In the present case, the lesion retained a typical cerebellopontine angle location for an epidermoid cyst; however, several atypical findings raised concern for a malignant process, including focal marked enhancement, mixed susceptibility signals suggestive of calcification or chronic hemorrhage, intraoperative identification of both cystic and solid components, and tight adherence to adjacent cranial nerves. These findings do not by themselves prove malignant transformation, but they are less typical of a benign complicated cyst and therefore support preoperative suspicion of an associated malignant process.

From a diagnostic perspective, this case expands the known spectrum of epidermoid cyst malignant transition, suggesting that transformation may not be confined to squamous differentiation but may also include glandular components. It highlights the importance of maintaining diagnostic vigilance even in radiologically typical lesions. Intraoperative findings such as abnormal tissue texture, significant cytologic atypia on frozen section, or atypical enhancement patterns should prompt a comprehensive IHC evaluation, and molecular analysis when necessary.

Ongoing documentation and systematic review of such rare cases are essential to deepen our understanding of the malignant transformation potential of epidermoid cysts. Establishing multi-institutional collaborative databases will further help delineate their pathological evolution and improve diagnostic and therapeutic strategies.

Several limitations should be acknowledged. First, although extensive clinical and radiological evaluation did not reveal any extracranial primary tumor, the possibility of an occult extracranial primary lesion cannot be entirely excluded. Second, molecular analysis was not performed to compare the genetic profiles of the squamous and adenocarcinoma components, which could have provided additional evidence regarding clonality and the mechanism of malignant transformation. Third, the relatively short follow-up limits long-term assessment.

Conclusion

We report an exceedingly rare case of a poorly differentiated adenocarcinoma associated with an intracranial epidermoid cyst, with findings that support the possibility of malignant transformation. This case suggests that the malignant transformation potential of epidermoid cysts may not be limited to squamous differentiation and highlights the possibility of glandular transformation within these lesions. Our findings underscore the importance of maintaining suspicion for an associated malignant process when an epidermoid cyst shows atypical imaging or intraoperative features despite an otherwise benign radiological appearance. Comprehensive histopathological and immunohistochemical evaluation as well as postoperative PET-CT is essential for accurate diagnosis and for ruling out metastatic disease. Further accumulation of such rare cases is warranted to elucidate their underlying molecular mechanisms, clinical behavior, and prognostic characteristics.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material. Further inquiries can be directed to the corresponding authors.

Ethics statement

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article. Written informed consent was obtained from the participant/patient(s) for the publication of this case report.

Author contributions

JYL: Data curation, Investigation, Writing – original draft. JHL: Data curation, Investigation, Writing – original draft. HX: Data curation, Writing – original draft. LH: Data curation, Writing – original draft. BL: Resources, Supervision, Writing – review & editing. SG: Resources, Supervision, Writing – review & editing, Conceptualization, Funding acquisition.

Funding

The author(s) declared that financial support was received for this work and/or its publication. This work was supported by Basic and Applied Basic Research Foundation of Guangdong Province (2023A1515220098).

Conflict of interest

The author(s) declared that this work was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The author(s) declared that generative AI was not used in the creation of this manuscript.

Any alternative text (alt text) provided alongside figures in this article has been generated by Frontiers with the support of artificial intelligence and reasonable efforts have been made to ensure accuracy, including review by the authors wherever possible. If you identify any issues, please contact us.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

References

1. Gader G, Hdhili H, Mansour W, Ali KB, Badri M, Zammel I. Huge intraventricular epidermoid cyst: A case report. *Radiol Case Rep*. (2025) 20:3319–22. doi: 10.1016/j.radcr.2025.03.046

2. Kiss-Bodolay D, Hautmann X, Lee KS, Rohde V, Schaller K. Intracranial epidermoid cyst: A volumetric study of a surgically challenging benign lesion. *World Neurosurg*. (2024) 185:e1129–e1135. doi: 10.1016/j.wneu.2024.03.035

3. Eatz TA, Elarjani T, Chen SH, Lu VM, Wu EM, Saad AG, et al. Malignant transformation of an intracranial epidermoid cyst 25 years after initial surgery: A case report and systematic review. *World Neurosurg*. (2023) 177:e52–e65. doi: 10.1016/j.wneu.2023.05.039

4. Kwon SM, Kim JH, Kim Y-H, Hong SH, Kim CJ. Treatment and survival outcomes of primary intracranial squamous cell carcinoma. *World Neurosurg*. (2019) 125:e1–e9. doi: 10.1016/j.wneu.2018.11.252

5. Narasimhaiah D, Nair P, Kesavadas C, Poyuran R. Rapid Malignant transformation of an intracranial epidermoid cyst: Report of a case. *Neuropathology*. (2023) 43:268–72. doi: 10.1111/neup.12884

6. Asahi T, Kurimoto M, Endo S, Monma F, Ohi M, Takami M. Malignant transformation of cerebello-pontine angle epidermoid. *J Clin Neurosci*. (2001) 8:572–4. doi: 10.1054/jocn.2000.0856

7. Yanagawa N, Nishiya M, Sato Y, Sugimoto R, Osakabe M, Uesugi N, et al. Undifferentiated carcinoma arising from intracranial epidermoid cyst. *Pathol Int*. (2021) 71:281–3. doi: 10.1111/pin.13071

8. Raghunathan A, Barber SM, Takei H, Moisi MD, Mukherjee AL, Rivera AL, et al. Primary intracranial sarcomatoid carcinoma arising from a recurrent/residual epidermoid cyst of the cerebellopontine angle: A case report. *Am J Surg Pathol*. (2011) 35:1238–43. doi: 10.1097/PAS.0b013e318223ee29

9. Jain R, Gujar S, McKeever P, Robertson P, Mukherji S. Imaging findings associated with childhood primary intracranial squamous cell carcinoma. *AJNR Am J Neuroradiol*. (2003) 24:109–11.

10. Kaplan SE, Modest MC, Farrell CJ, Artz GJ. Squamous cell carcinoma arising in a remnant of an extirpated cerebellopontine angle epidermoid tumor: Case report and literature review. *J Neurol Surg B Skull Base*. (2013) 74:A281. doi: 10.1055/s-0033-1336404

11. Elsarraj HS, Hogan K. Cytologic diagnosis of squamous cell carcinoma arising from a recurrent cerebellopontine angle epidermoid cyst in a 61-year-old male. *Diagn Cytopathol*. (2025) 53:E87–E91. doi: 10.1002/dc.25450

12. Kim M-S, Kim O-L. Primary intracranial squamous cell carcinoma in the brain stem with a cerebellopontine angle epidermoid cyst. *J Korean Neurosurg Soc*. (2008) 44:401–4. doi: 10.3340/jkns.2008.44.6.401

13. Magliocca KR, Vivas EX, Griffith CC. Idiopathic, infectious and reactive lesions of the ear and temporal bone. *Head Neck Pathol*. (2018) 12:328–49. doi: 10.1007/s12105-018-0952-0

14. Barchi A, Dell'Anna G, Massimino L, Mandarino FV, Vespa E, Viale E, et al. Unraveling the pathogenesis of barrett's esophagus and esophageal adenocarcinoma: The "omics" era. *Front Oncol*. (2025) 14:1458138. doi: 10.3389/fonc.2024.1458138

15. Chen X, Sun F, Wang X, Feng X, Aref AR, Tian Y, et al. Inflammation, microbiota, and pancreatic cancer. *Cancer Cell Int*. (2025) 25:62. doi: 10.1186/s12935-025-03673-6

16. Kennedy MC, Lowe SW. Mutant p53: It's not all one and the same. *Cell Death Differ*. (2022) 29:983–7. doi: 10.1038/s41418-022-00989-y

17. Chen N, Xu L, Bi Z, Wu J. Hypoxia-inducible factor-1α contributes to the proliferation of cholesteatoma keratinocytes through regulating endothelin converting enzyme 1 expression. *Laryngoscope Investig Otolaryngol*. (2024) 9:e1233. doi: 10.1002/lio2.1233

18. Yang T, Hu J, Li L, Xu H, Zhang C, Huang Z, et al. The imaging dynamic changes in the Malignant transformation of an epidermoid cyst: A case report and literature review. *Front Neurol*. (2024) 15:1349044. doi: 10.3389/fneur.2024.1349044

19. Sakamoto H, Akimoto J, Tsutsumi M, Ken KM, Ichimasu N, Kohno M. Radiopathological characteristics of Malignant transformation of an epidermoid cyst in the cerebellopontine angle: A case report. *Surg Neurol Int*. (2022) 13:135. doi: 10.25259/SNI_1226_2021

20. Ozutemiz C, Ada E, Ersen A, Ozer E. Imaging findings of an epidermoid cyst with Malignant transformation to squamous cell carcinoma. *Turk Neurosurg*. (2017) 27:312–5. doi: 10.5137/1019-5149.JTN.12722-14.0

21. Ahuja S, Shankar M, Mankotia DS, Shankar KB, Zaheer S. Epidermoid cyst of central nervous system: A case series and review of literature. *Int J Surg Case Rep*. (2024) 115:109293. doi: 10.1016/j.ijscr.2024.109293

22. Jamjoom DZ, Alamer A, Tampieri D. Correlation of radiological features of white epidermoid cysts with histopathological findings. *Sci Rep*. (2022) 12:2314. doi: 10.1038/s41598-022-06167-x

23. Lin T, Ding L. Primary intracranial squamous cell carcinoma arising in epidermoid cysts: A case report and review of literature. *Med (Baltimore)*. (2025) 104:e42094. doi: 10.1097/MD.0000000000042094

24. Harary PM, Hori YS, Kassu R, Persad ARL, Tayag A, Ustrzynski L, et al. Paired molecular profiling of Malignant transformation of an epidermoid cyst for potential genetic drivers: Illustrative case. *J Neurosurg Case Lessons*. (2025) 9:CASE24849. doi: 10.3171/CASE24849

25. Alsadi H, Dahlstrom K, Summers K, Camarata PJ, Werth K. Intracranial epidermoid cyst with Malignant degeneration and leptomeningeal carcinomatosis: Illustrative case. *J Neurosurg Case Lessons*. (2025) 9:CASE24738. doi: 10.3171/CASE24738

26. Zhang X, Zhan A, He D, Wei Z, Pan Y, Li X. Epidermoid cyst in atypical intracranial areas transformed to epidermoid carcinoma: A case report. *J Int Med Res*. (2023) 51:3000605221148146. doi: 10.1177/03000605221148146

27. Gabay S, Serafimova M, Raz M, Roth J. Concurrent occurrence of squamous cell carcinoma in a cerebellopontine angle epidermoid cyst: A case report and review of the literature. *Surg Neurol Int*. (2022) 13:500. doi: 10.25259/SNI_726_2022

28. Zuo P, Sun T, Wang Y, Geng Y, Zhang P, Wu Z, et al. Primary squamous cell carcinomas arising in intracranial epidermoid cysts: A series of nine cases and systematic review. *Front Oncol*. (2021) 11:750899. doi: 10.3389/fonc.2021.750899

29. Demuth S, Lasry DE, Obaid S, Letourneau-Guillon L, Chassé M, Bélanger K, et al. Pseudo-chemical meningitis and the Malignant transformation of an epidermoid cyst. *Can J Neurol Sci*. (2019) 46:642–4. doi: 10.1017/cjn.2019.235

30. Nagata K, Kiyofuji S, Umekawa M, Yokoyama M, Sora S. malignant transformation of cerebellopontine angle epidermoid cyst:A case report. *No Shinkei Geka*. (2019) 47:1173-1178. doi: 10.11477/mf.1436204095

31. Fereydonyan N, Taheri M, Kazemi F. Cerebellar squamous cell carcinoma due to Malignant transformation of cerebellopontine angle epidermoid cyst, report an interesting case and review the literature. *Prague Med Rep*. (2019) 120:95–102. doi: 10.14712/23362936.2019.14

32. Cuoco JA, Rogers CM, Busch CM, Apfel LS, Entwistle JJ, Marvin EA. Intracranial squamous cell carcinoma arising from a cerebellopontine angle epidermoid cyst remnant four decades after partial resection. *Front Oncol*. (2019) 9:694. doi: 10.3389/fonc.2019.00694

33. Chen Z, Araya M, Onishi H. Proton beam therapy for Malignant transformation of intracranial epidermoid cyst. *BMJ Case Rep*. (2019) 12:e229388. doi: 10.1136/bcr-2019-229388

34. Liu X, Chen Z, Dong Y, He X, Pan X, Tong D. Primary intracranial squamous cell carcinoma arising de novo: A case report and review of the literature. *World Neurosurg*. (2018) 120:372–81. doi: 10.1016/j.wneu.2018.08.067

35. Suematsu Y, Takeishi G, Yokogami K, Uehara H, Gi T, Yamashita A, et al. a case of Malignant transformation of epidermoid cyst with cerebrospinal fluid dissemination. *No Shinkei Geka*. (2018) 46:509–14. doi: 10.11477/mf.1436203760

36. Badat N, Cholet C, Hervé G, Pyatigorskaya N, Trunet S, Dormont D, et al. Malignant transformation of epidermoid cyst with diffuse leptomeningeal carcinomatosis on skull base and trigeminal perineural spread. *J Neuroradiol*. (2018) 45:337–40. doi: 10.1016/j.neurad.2018.07.002

37. Ou A, Heslin R, Kowalska A, Coyle P. Rare Malignant transformation of an epidermoid cyst (P6.101). *Neurology*. (2018) 90:P6.101. doi: 10.1212/WNL.90.15_supplement.P6.101

38. Solanki SP, Maccormac O, Dow GR, Smith S. Malignant transformation of residual posterior fossa epidermoid cyst to squamous cell carcinoma. *Br J Neurosurg*. (2017) 31:497–8. doi: 10.3109/02688697.2015.1125445

39. Seif B, Pourkhalili R, Shekarchizadeh A, Mahzouni P. Malignant transformation of an intracranial extradural epidermoid cyst into squamous cell carcinoma presented with cerebrospinal fluid leakage. *Adv BioMed Res*. (2017) 6:16. doi: 10.4103/2277-9175.200791

40. Roh TH, Park YS, Park YG, Kim SH, Chang JH. Intracranial squamous cell carcinoma arising in a cerebellopontine angle epidermoid cyst: A case report and literature review. *Med (Baltimore)*. (2017) 96:e9423. doi: 10.1097/MD.0000000000009423

41. Mascarenhas A, Parsons A, Smith C, Molloy C, Jukes A. Malignant squamous cell carcinoma arising in a previously resected cerebellopontine angle epidermoid. *Surg Neurol Int*. (2017) 8:186. doi: 10.4103/sni.sni_99_17

42. Raheja A, Eli IM, Bowers CA, Palmer CA, Couldwell WT. Primary intracranial epidermoid carcinoma with diffuse leptomeningeal carcinomatosis: Report of two cases. *World Neurosurg*. (2016) 88:692.e9–692.e16. doi: 10.1016/j.wneu.2015.11.039

43. Pikis S, Margolin E. Malignant transformation of a residual cerebellopontine angle epidermoid cyst. *J Clin Neurosci*. (2016) 33:59–62. doi: 10.1016/j.jocn.2016.04.008

44. Ding S, Jin Y, Jiang J. Malignant transformation of an epidermoid cyst in the temporal and prepontine region: Report of a case and differential diagnosis. *Oncol Lett*. (2016) 11:3097–100. doi: 10.3892/ol.2016.4368

45. Chourmouzi D, Papadopoulou E, Karkavelas G, Drevelegas A. Imaging findings of an epidermoid cyst undergoing Malignant transformation. *J Belg Soc Radiol*. (2015) 99:42–5. doi: 10.5334/jbr-btr.829

46. Vellutini EAS, de Oliveira MF, Ribeiro APC, Rotta JM. Malignant transformation of intracranial epidermoid cyst. *Br J Neurosurg*. (2014) 28:507–9. doi: 10.3109/02688697.2013.869552

47. Chon K-H, Lee J-M, Koh E-J, Choi H-Y. Malignant transformation of an epidermoid cyst in the cerebellopontine angle. *J Korean Neurosurg Soc*. (2012) 52:148–51. doi: 10.3340/jkns.2012.52.2.148

48. Lakhdar F, Hakkou EM, Gana R, Maaqili RM, Bellakhdar F. Malignant transformation six months after removal of intracranial epidermoid cyst: A case report. *Case Rep Neurol Med*. (2011) 2011:525289. doi: 10.1155/2011/525289

49. Kano T, Ikota H, Kobayashi S, Iwasa S, Kurosaki S, Wada H. Malignant transformation of an intracranial large epidermoid cyst with leptomeningeal carcinomatosis: Case report. *Neurol Med Chir (tokyo)*. (2010) 50:349–53. doi: 10.2176/nmc.50.349

50. Hao S, Tang J, Wu Z, Zhang L, Zhang J, Wang Z. Natural Malignant transformation of an intracranial epidermoid cyst. *J Formos Med Assoc*. (2010) 109:390–6. doi: 10.1016/S0929-6646(10)60068-X

51. Ge P, Luo Y, Fu S, Ling F. Recurrent epidermoid cyst with Malignant transformation into squamous cell carcinoma. *Neurol Med Chir (Tokyo)*. (2009) 49:442–4. doi: 10.2176/nmc.49.442

52. Agarwal S, Rishi A, Suri V, Sharma MC, Satyarthi GD, Garg A, et al. Primary intracranial squamous cell carcinoma arising in an epidermoid cyst–a case report and review of literature. *Clin Neurol Neurosurg*. (2007) 109:888–91. doi: 10.1016/j.clineuro.2007.07.026

53. Kodama H, Maeda M, Hirokawa Y, Suzuki H, Hori K, Taki W, et al. MRI findings of Malignant transformation of epidermoid cyst: Case report. *J Neuro-Oncol*. (2007) 82:171–4. doi: 10.1007/s11060-006-9255-5

54. Pagni F, Brenna A, Leone BE, Vergani F, Isimbaldi G. Malignant epidermoid cyst of the pineal region with lumbar metastasis. *Neuropathology*. (2007) 27:566–9. doi: 10.1111/j.1440-1789.2007.00820.x

55. Tamura K, Aoyagi M, Wakimoto H, Tamaki M, Yamamoto K, Yamamoto M, et al. Malignant transformation eight years after removal of a benign epidermoid cyst: A case report. *J Neuro-Oncol*. (2006) 79:67–72. doi: 10.1007/s11060-005-9117-6

56. Michael LM, Moss T, Madhu T, Coakham HB. Malignant transformation of posterior fossa epidermoid cyst. *Br J Neurosurg*. (2005) 19:505–10. doi: 10.1080/02688690500495356

57. Guan L, Qi X, Zhang J, Xu K, Cui L, Zhang Q. MRI manifestation of brain squamous cell carcinoma followed by intracranial epidermoid cyst–a case report. *Zhonghua Yi Xue Za Zhi*. (2005) 85:1006–7. doi: 10.3760/j:issn:0376-2491.2005.14.024

58. Kadashev BA, Shkarubo AN, Korshunov AG, Murusidze NA, Taniashin SV. Malignant transformation of epidermoid cyst. *Zh Vopr Neirokhir Im N N Burdenko*. (2003) (1), 38–40.

59. Akar Z, Tanriover N, Tuzgen S, Kafadar AM, Kuday C. Surgical treatment of intracranial epidermoid tumors. *Neurol Med Chir (Tokyo)*. (2003) 43:275–80. doi: 10.2176/nmc.43.275. discussion 281.

60. Link MJ, Cohen PL, Breneman JC, Tew JM. Malignant squamous degeneration of a cerebellopontine angle epidermoid tumor. Case report. *J Neurosurg*. (2002) 97:1237–43. doi: 10.3171/jns.2002.97.5.1237

61. Tsugu H, Fukushima T, Hayashi S, Iwaasa M, Matsuda T. Squamous cell carcinoma arising in an intracranial dermoid cyst–case report. *Neurol Med Chir (Tokyo)*. (2001) 41:213–6. doi: 10.2176/nmc.41.213

62. Nawashiro H, Higo R, Tokumaru AM, Tsuzuki N, Shima K. Diffusion-weighted MRI of an intracranial epidermoid with Malignant transformation. *Neuroradiology*. (2001) 43:891. doi: 10.1007/s002340100612

63. Khan RB, Giri DD, Rosenblum MK, Petito FA, DeAngelis LM. Leptomeningeal metastasis from an intracranial epidermoid cyst. *Neurology*. (2001) 56:1419–20. doi: 10.1212/wnl.56.10.1419

64. Sawan B, Vital A, Loiseau H, Dousset V, Strub D, Vital C. Squamous cell carcinoma developing in an intracranial prepontine epidermoid cyst. *Ann Pathol*. (2000) 20:258–60.