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Epithelioid schwannoma of the vestibular nerve

T C Tan, P W Y Lam

ABSTRACT

Epithelioid schwannomas are rarely encountered intracranially, with only four cases involving the eighth nerve reported in the literature. Histological behaviour ranging from benign to aggressive has been described. We report a 45-year-old woman who presented with right-sided tinnitus and hearing impairment. Magnetic resonance imaging revealed a tumour in the right cerebellopontine angle with intracanalicular extension. The patient underwent retromastoid craniectomy with near-total tumour excision. Microscopical examination confirmed the diagnosis of epithelioid schwannoma of the vestibular nerve. Intraoperative findings of sharp circumscription, bland histological appearance, low proliferative activity, coupled with the indolent clinical course, point to the quiescent nature of the lesion in this case.

Keywords: acoustic nerve, epithelioid schwannoma, immunohistochemistry, magnetic resonance imaging, vestibular tumour

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INTRODUCTION

Epithelioid schwannomas mainly affect peripheral nerves, and are frequently malignant[1-4]. Cranial nerve involvement is uncommon[1,5-7]. We report a case of epithelioid schwannoma arising from the vestibular nerve. The diagnostic tools used in the identification of this entity, together with the therapeutic options, are discussed.

CASE REPORT

A 45-year-old woman presented with tinnitus for five years and progressive right-sided deafness for two years. There was no past or family history of neurofibromatosis. Physical examination revealed right-sided hearing impairment that was confirmed by pure tone audiometry. Magnetic resonance (MR) imaging confirmed an extra-axial tumour in the right cerebellopontine angle extending into the internal acoustic meatus, which enhanced heterogeneously after gadolinium administration (Fig. 1a).

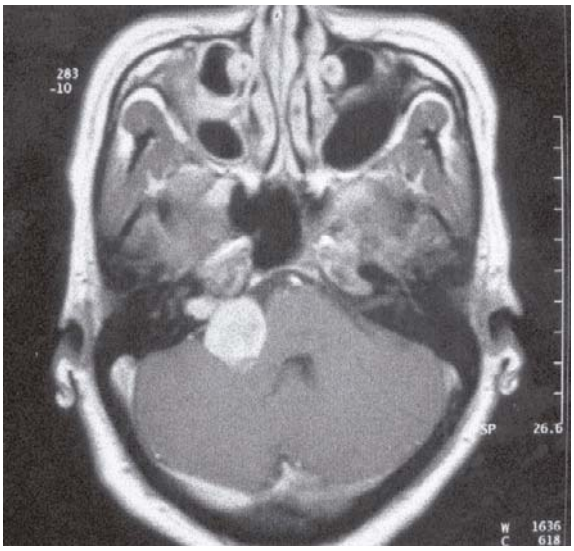

Fig. 1a Enhanced axial T1-W MR image shows a heterogeneous extra-axial tumour in the right cerebellopontine angle.

The patient underwent a retromastoid craniectomy. Intraoperatively, a yellow extra-axial tumour measuring 2.5cm in diameter was found arising from the eighth cranial nerve and extending into the internal acoustic meatus. Near-total tumour excision with facial nerve preservation was achieved. Microscopically, the tumour was composed of plump epithelioid cells with oval vesicular nuclei and abundant eosinophilic cytoplasm. Mitotic figures and necrosis were absent (Fig. 2a). Antoni A areas with palisading nuclei, and reticular Antoni B areas were present. Both the epithelioid and Schwann cells stained diffusely with S-100 protein (Fig. 2b). Staining for glial fibrillary acid protein (GFAP), Leu-7, epithelial membrane antigen (EMA), HMB-45, cytokeratin (CK) and CD68 (Fig. 2c) were negative. The Ki-67 labelling index was 4%. Neither the Schwann nor epithelioid cells displayed p53 immunoreactivity. Electron microscopy was performed. Intermediate cell junctions, fibrous long-spaced collagen and the presence of basal lamina material surrounding

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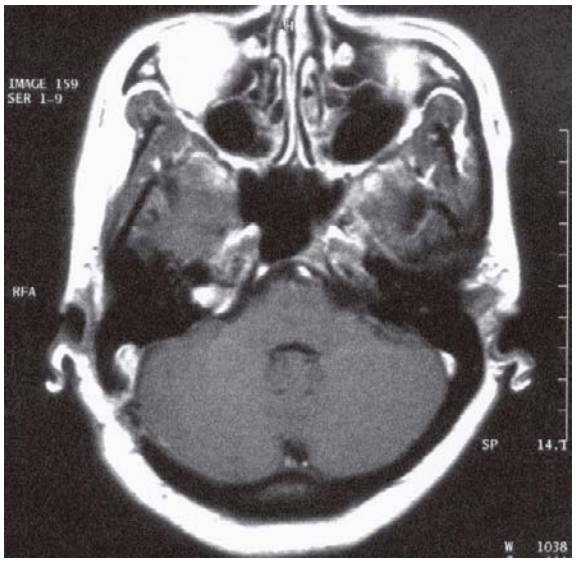

Fig. 1b Repeat MR image taken six months post-surgery shows a small tumour remnant measuring 8mm in the right internal acoustic meatus.

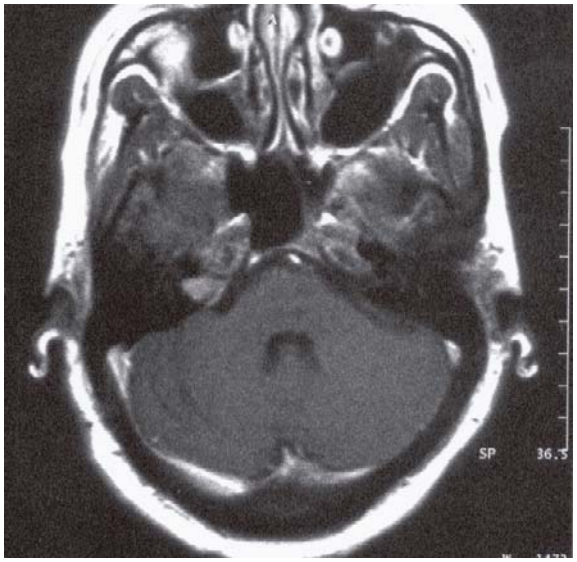

Fig. 1c Repeat MR image taken two years post-surgery shows that the size of the tumour remnant remains static.

tumour cells were demonstrated (Fig. 2d). The histology was compatible with benign epithelioid schwannoma of the vestibular nerve.

The post-operative period was uneventful, except for transient facial nerve palsy, which resolved after four months. Post-operative MR imaging performed six months later demonstrated a small 8mm tumour remnant in the right internal acoustic meatus (Fig. 1b). At follow-up MR imaging done two years later, the patient remained well, with no radiological evidence of recurrence (Fig. 1c).

DISCUSSION

Cranial nerve epithelioid schwannomas are rare. To date, four cases involving the acoustic nerve[1,5] and two cases in the trigeminal nerve have been reported[6,7]. Epithelioid schwannomas are well-recognised in association with peripheral nerves[1-4], and they account for 5% of all nerve sheath tumours in the body[4]. The presence of epithelioid cells in peripheral nerve schwannoma, designated as "epithelioid malignant change", are believed to represent the earliest morphological indication of malignant transformation[2,8].

Clinically, malignant epithelioid schwannoma of the peripheral nerves often exhibit aggressive behaviour with a history of rapid growth, pain, and possibly neurological deficit in the territory of the afflicted nerve[2]. The presentation of intracranial epithelioid schwannomas has been reported as ranging from indolent to malignant. Four epithelioid acoustic schwannomas described in the literature presented as conventional benign schwannoma with tinnitus and hearing loss[1,5]. However, facial palsy was noted in half of the patients[5]. Two reported cases involving the trigeminal nerve exhibited more aggressive behaviour, with multiple cranial nerve palsies[6], and lymph node metastasis[7].

Histological evidence of malignant schwannoma include local infiltration, metastases, anaplasia, high mitotic rate and necrosis[8-13]. Features of classic schwannoma such as Antoni A, B or Verocay bodies are usually absent[8]. Benign epithelioid schwannomas involving peripheral nerves have recently been described[14]. Immunohistochemistry has been employed in distinguishing between benign and malignant epithelioid schwannoma. Kindblom et al suggested a high proliferation index in excess of 10%, and p53 immunoreactivity as features of malignancy in peripheral nerve sheath tumors[14,15]. In contrast, benign schwannomas exhibited a proliferation index below 5% and absence of p53 immunoreactivity. S-100 protein immunostaining has also been used towards this end[11].

Diffuse staining for S-100 is believed to denote a benign pathology, as conventional malignant schwannomas show focal or weak reaction[16]. However, positive staining with S-100 cannot be used as the sole means of excluding malignancy, as it has been observed in up to 50% of malignant schwannomas[17]. The epithelioid cells resemble macrophages, and can be easily differentiated from the latter by the absence of staining with CD68. The lack of expression of cytokeratin and HMB-45 also favour the diagnosis of epithelioid schwannoma over malignant melanoma or carcinoma[4].

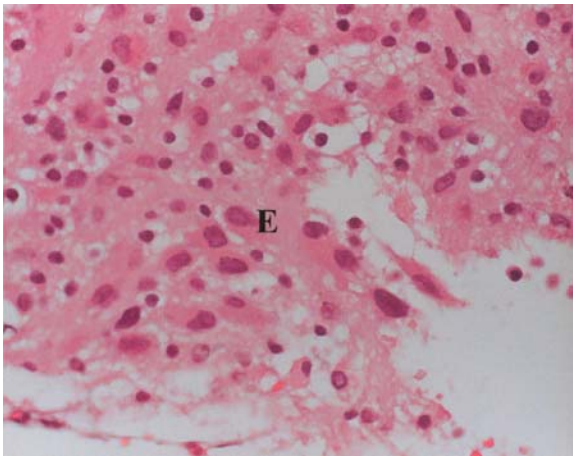

Fig. 2a Photomicrograph shows individual epithelioid cells (labelled as E) with vesicular nuclei and small nucleoli.A lymphocytic infiltrate is also present. (Haematoxylin & eosin, x 600).

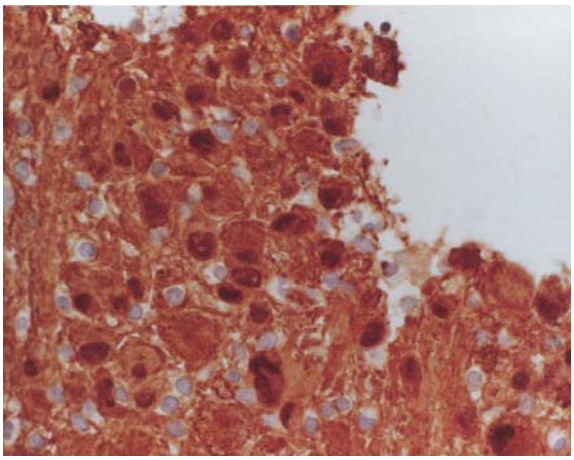

Fig. 2b Photomicrograph shows positive staining of epithelioid cells with S-100 protein (x 600).

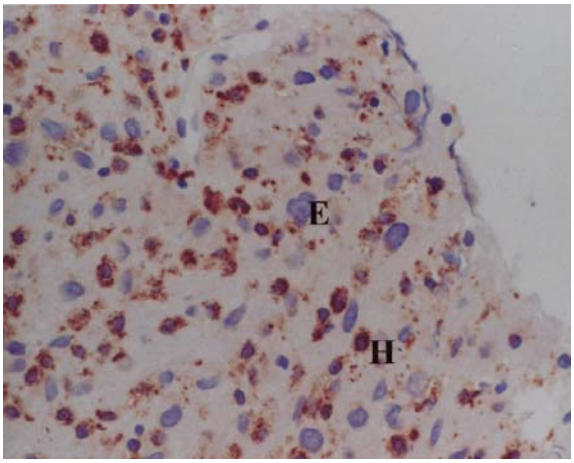

Fig. 2c CD 68 stain shows cytoplasmic staining of infiltrating histiocytes (labelled as H). Note the absence of reaction of the epithelioid cells (labelled as E) (x 600).

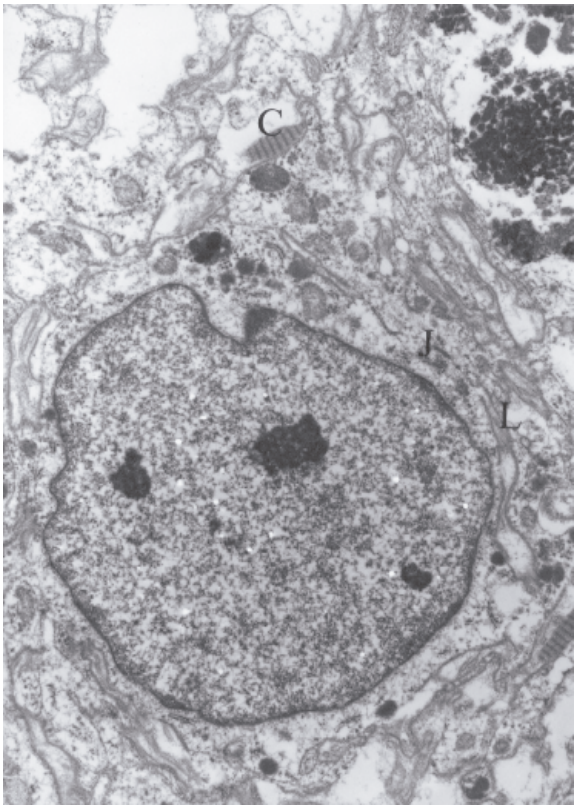

Fig. 2d Electron micrograph shows intermediate cell junctions (labelled as J), fibrous long-spaced collagen (labelled as C) and the presence of a basal lamina (labelled as L) surrounding the tumour cells (x10920).

The prognosis of epithelioid cranial nerve schwannoma is difficult to predict due to the paucity of cases in the literature. Of the four acoustic epithelioid schwannomas reported previously, one was described as benign, with no evidence of recurrence or metastases after five years[5]. Although the other three tumours were not clinically malignant, the short follow-up precluded understanding of their true nature[1]. The lesion in our patient appeared to be benign, as evidenced by the chronic symptoms, and absence of local brain invasion, mitoses, necrosis or nuclear pleomorphism on microscopical examination. In addition, the presence of Antoni A and B areas[1], uniform staining for S-100 in both the Schwann and epithelioid cells[16], low Ki-67 proliferative index[14,15], and negative p53 protein immunoreactivity[14,15] supported a more favourable prognosis.

Surgery remains the mainstay of treatment of epithelioid schwannoma[2,4,5,10,13,14]. Extent of resection depends on the degree of malignancy. Benign epithelioid schwannomas are managed by simple excision[2,4,5,14], while malignant variants may require more radical surgery[4,10], supplemented by adjuvant chemotherapy and radiation in cases of subtotal resection or metastatic spread[9,10,13]. As the biological potential of intracranial epithelioid schwannoma has not been fully elucidated, complete tumour extirpation with close follow-up is recommended.

In conclusion, cranial nerve epithelioid schwannoma may be benign or malignant. Differentiation between

benign and malignant variants is pivotal to the treatment plan because while the former can be managed with simple excision alone, the latter requires more radical resection with attendant high morbidity. We advocate thorough histological examination supplemented by immunohistochemical techniques such as S-100, Ki-67 proliferative index, CD68 and p53 immunostaining as simple and cost-effective measures in the diagnosis and grading of epithelioid schwannomas.

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REFERENCES

1. Kroh H, Matyja E, Marchel A. Epithelioid schwannomas of the acoustic nerve. Folia Neuropathol 2000; 38:23-7.
2. McMenamin ME, Fletcher CD. Expanding the spectrum of malignant change in schwannomas: epithelioid malignant change, epithelioid malignant peripheral nerve sheath tumor, and epithelioid angiosarcoma: a study of 17 cases. Am J Surg Pathol 2001; 25:13-25.
3. Enzinger FM, Weiss SW. Soft Tissue Tumors. 2nd ed. St Louis: Mosby, 1988.
4. Laskin WB, Weiss SW, Bratthaver GL. Epithelioid variant of malignant peripheral nerve sheath tumor (malignant epithelioid schwannoma). Am J Surg Pathol 1991; 15:1136-45.
5. Benhaiem-Sigaux N, Ricolfi F, Keravel Y, Poirer J. Epithelioid schwannoma of the acoustic nerve. Clin Neuropathol 1996; 15:231-3.
6. Franks AJ. Epithelioid neurilemmoma of the trigeminal nerve: an immunohistochemical and ultrastructural study. Histopathology 1985; 9:1339-50.
7. Stout AP. The malignant tumors of the peripheral nerves. Am J Cancer 1935; 25:1-36.
8. Sharma S, Abbott RI, Zagzag D. Malignant intracerebral nerve sheath tumor: a case report and review of the literature. Cancer 1998; 82:545-52.
9. Alvira MM, Mandybur TI, Menefee MG. Light microscopic and ultrastructural observations of a metastasizing malignant epithelioid schwannoma. Cancer 1976; 38:1977-82.
10. D'Argostino AN, Soule EH, Miller RH. Primary malignant neoplasms of nerves (malignant neurilemmomas) in patients without manifestations of multiple neurofibromatosis (von Recklinghausen's disease). Cancer 1963; 16:1003-14.
11. Burger PC, Scheithauer BW. Tumors of the peripheral nerve sheath. In: Atlas of Tumor Pathology, 3rd series, Fascicle 10. Washington, DC: AFIP,1994; 333-43.
12. Storm FK. Eiber FR, Mirra J, Morton DL. Neurofibrosarcoma. Cancer 1980; 45:126-9.
13. Trojanowski JQ, Kleinman GM, Proppe KH. Malignant tumors of nerve sheath origin. Cancer 1980; 46:1202-12.
14. Kindblom LG, Meis-Kindblom JM, Havel G, Busch C. Benign epithelioid schwannoma. Am J Surg Pathol 1998; 22:762-70.
15. Kindblom LG, Ahlden M, Meis-Kindblom JM, Stenman G. Immunohistochemical and molecular analysis of p53, MDM2, proliferating cell nuclear antigen and Ki67 in benign and peripheral nerve sheath tumors. Virchows Arch 1995; 427:19-26.
16. Jacque CM, Kujas M, Poreau A, et al. GFAP and S 100 protein levels as an index for malignancy in human gliomas and neurinomas. J Natl Cancer Inst 1979; 62:479-83.
17. Weiss SW, Langloss JM, Enzinger FM. Value of S-100 protein in the diagnosis of soft tissue tumors with particular reference to benign and malignant schwann cell tumors. Lab Invest 1983; 49:299-308.