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Dumbbell-shaped C-2 psammomatous melanotic malignant schwannoma

Case report and review of the literature

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✓The authors present the case of a dumbbell-shaped malignant psammomatous melanotic schwannoma of the upper cervical spine involving the C-2 sensory root. The family of the patient had a history of other malignant stromal tumors, without the Carney complex genetic pattern. The 30-year-old female patient complained of experiencing cervical pain and cervical muscle contractions for 6 months, and was admitted to the hospital. The cervical T_1-weighted magnetic resonance (MR) images revealed the presence of a slightly hyperintense C2–3 intra–extradural lesion, moderately enhancing, which had eroded and enlarged the intervertebral foramen. The patient workup also included computed tomography scans and angiography. A posterior approach was used to perform a C2–3 hemilaminectomy, including opening of the dura mater and gross-total removal of the lesion. Histopathological examination of the lesion revealed it to be a malignant psammomatous melanotic schwannoma. The cerebrospinal MR image of the patient obtained at the 12-month follow-up examination demonstrated the presence of tumor progression into the subarachnoid space at the C-3 level. The strong malignancy potential of the lesion must be considered in the future management of the patient, especially due to the presence in the family of other stromal tumors such as gastrointestinal-stromal tumors and malignant melanomas. The authors review all the literature concerning melanotic schwannomas and report 105 cases of melanotic schwannoma that were not related to the Carney complex. The particular focus of their review is on the characteristics of the malignant progression of melanotic schwannoma, such as local recurrences, metastasis, and survival rate.

Key Words • dumbbell-shaped schwannoma • malignant melanotic schwannoma • psammomatous schwannoma • Carney complex

Melanotic schwannoma is a rare neuroectodermal tumor originating from the Schwann cells of the nerve sheaths, accounting for less than 1% of primary peripheral nerve sheath tumors. It was first described in 1932 by Millar and colleagues,[53] who reported one case involving the thoracic sympathetic ganglion. A melanotic schwannoma is a pathological variant that can be sporadic or part of the Carney complex, a dominantly inherited syndrome characterized by spotty skin pigmentation, endocrine overactivity, and myxomas.[12,13] The melanotic schwannoma of the Carney complex is a psammomatous melanotic schwannoma; approximately 50% of psammomatous melanotic schwannomas are characterized by the Carney complex. Dumbbell-shaped psammomatous melanotic schwannomas are extremely rare, and in the literature, only one dumbbell-shaped melanotic schwannoma has been reported as located in the dorsal spine and having benign features.[20]

Abbreviations used in this paper: CT = computed tomography; GIST = gastrointestinal tumor; MR = magnetic resonance; VA = vertebral artery.

Case Report

History and Examination. This 30-year-old woman who experienced right cervical pain and cervical muscle contractures for six months was admitted to our hospital. An MR image of the cervical spine revealed the presence of a dumbbell-shaped lesion localized in the right C2–3 vertebral foramen, extending into the extravertebral space for approximately 2 cm. The lesion compressed and dislocated the cervical spinal cord and had eroded and enlarged the vertebral foramen. The lesion was slightly hyperintense on T_1-weighted MR images, and highly hypointense on T_2-weighted spin echo images, with moderate contrast enhancement after injection of gadolinium (Figs. 1–3). The

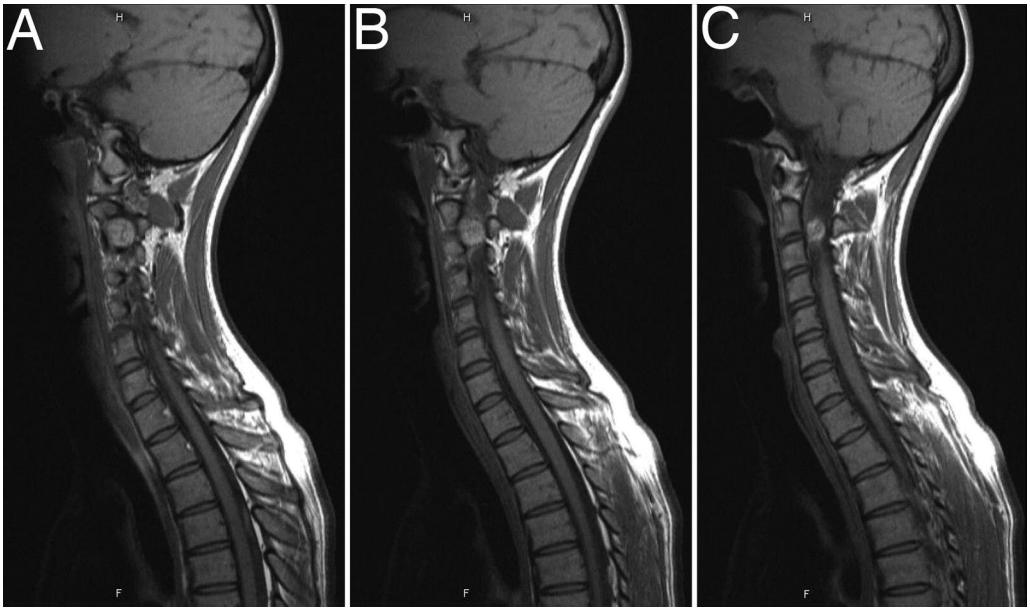

FIG. 1. Sagittal T_1-weighted MR images showing a dumbbell-shaped C2–3 hyperintense enhancing lesion.

preoperative workup included a CT bone window scan and angiography. The CT scan revealed that the vertebral foramen was enlarged, but its edges were smooth and regular. The vertebral angiography study showed that the VA was slightly lateralized but not compressed. The neurological examination results showed slight muscle weakness in the right arm (Medical Research Council Grade 4) with hyperesthesia in the right occipitocervical region.

The family history of the patient was positive for other malignant stromal tumors. Specifically, the patient's father had undergone an operation to treat a GIST and was currently receiving chemotherapy with imatinib. The patient's sister underwent an operation for a small malignant melanoma in her left shoulder, which did not contain satellite lymph nodes.

Operative Course. A posterior approach to the surgery was planned for the C2–3 hemilaminectomy using radioscopic control. A right-sided dumbbell-shaped intra–extradural mass was found, black in color and smooth in aspect, which had enlarged the vertebral foramen and greatly thickened its edges. The hemilaminectomy procedure was therefore extended with a foraminotomy and complete removal of the lateral peduncles of C2–3 to completely free the extradural mass. The tumor was embedded in the external stromal layer of the VA, so a great deal of work was used to debride the mass itself from the venous plexus of the VA. The midline opening of the dura mater revealed the residual intradural portion, originating from the dorsal root of C-2. Gross-total resection was achieved by sacrificing the C-2 dorsal root.

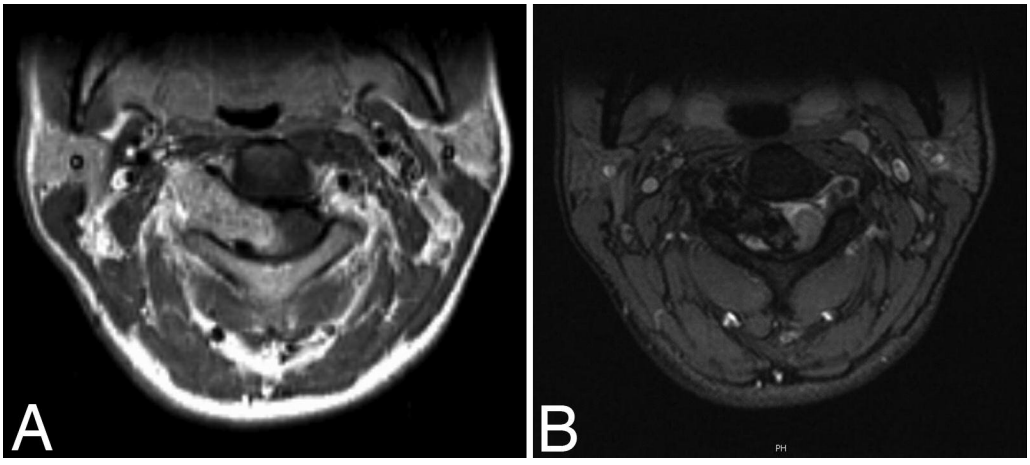

FIG. 2. Axial MR images showing a C2–3 intra–extradural lesion hyperintense after T_1-weighted gadolinium-enhanced imaging (A) and hypointense after T_2-weighted spin echo imaging (B).

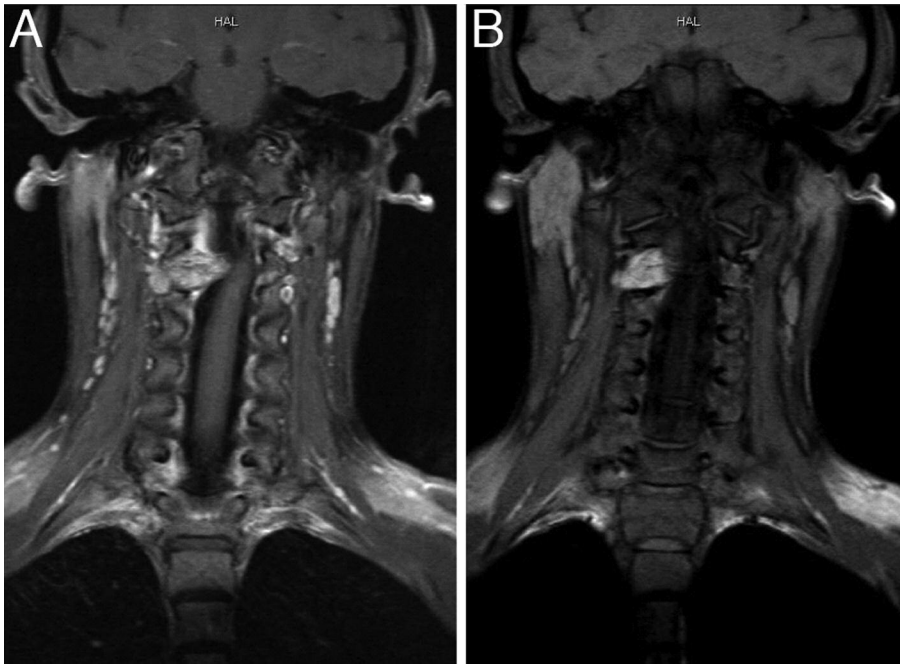

FIG. 3. Coronal T_1-weighted MR images with (A) and without (B) gadolinium enhancement showing the dumbbell-shaped C2–3 enhancing lesion.

Histopathological Analysis and Postoperative Course. Histopathological examination of the tumor revealed polygonal neoplastic cells with severe nuclear pleomorphism, atypia, and macronucleoli; wide cytoplasm with diffuse melanin granules; and high mitotic activity (5 × 10 hpf). The stroma also included sprinkle cells and psammomatous bodies. Immunohistochemical staining was positive for HMB-45, S100, and tyrosinase, and negative for melanin A. The proliferation index Ki 67 was quite high (12%), and neurofilaments and glial fibrillary acidic protein were positive in the neural fibers. Malignant psammomatous melanotic schwannoma was diagnosed in the patient (Fig. 4).

The clinical workup was completed with a thorough dermatologic examination, heart ultrasonography, endocrinological evaluation and hormone administration, ocular ultrasonography, and a total-body CT scan, to exclude the Carney complex. The same workup was performed in the patient's immediate relatives. All examinations showed negative results for the Carney complex. The genetic evaluation of the family was negative for mutations of the Carney complex gene (*PRKAR1-α*) located on 17q22-24. The postoperative MR image of the cervical spine revealed the complete removal of the lesion, and a complete craniospinal MR imaging study was performed to exclude the presence of drop metastasis.

The postoperative course was uneventful, with complete resolution of the cervical pain and good healing of the surgical wound. The patient used a Philadelphia collar for 1 month. She was encouraged to receive radiotherapy due to the high malignant potential of the lesion, but she refused because of the high risk of radiation-induced lesions. Therefore a clinical radiological follow up was planned, and the craniospinal MR images obtained 3 and 6 months postoperatively did not reveal any relapse or drop metastasis (Fig. 5). Unfortunately, the craniospinal MR image obtained 12 months after surgery revealed signs of tumor progression into the subarachnoid space at the C-3 level (Fig. 6).

Discussion

Psammomatous melanotic schwannomas were first described in 1932 by Millar,[53] who reported a case involving the sympathetic ganglion. In 1961 Hodson[34] reported this rare neurogenic tumor that affected the cranial nerves, alveolar nerves, palate, parotid gland, and neck. Subsequently, in 1985 Carney and colleagues[13] described an autosomal dominant syndrome characterized by a complex of spotty pigmentations of mucosa and skin, myxomas, and endocrine overactivity (particularly Cushing syndrome secondary to adrenocortical pigmented hyperplasia), and thyroid dysfunction, now known as the Carney complex.

Approximately 50% of patients with psammomatous melanotic schwannomas are affected by the Carney complex. The other 50% of psammomatous melanotic schwannomas are sporadic lesions, as are the nonpsammomatous melanotic schwannomas. Melanotic schwannomas are generally derived from spinal nerves and sympathetic ganglia, but extraneural locations have also been described. Intramedullary tumors are quite rare. The typical site of melanotic schwannomas is intraspinal extramedullary, especially in the thoracic region. Most melanocytic schwannomas are located at the vertebral foramen or the paravertebral sulcus.

Different theories exist regarding the histogenesis of this tumor. Schwann cells and melanocytes are both of neuroectodermal origin and melanocytes appear to migrate with Schwann cells.[5,55] Mandybur[48] suggested a melanomatous transformation of Schwann neoplastic cells. Janzer and Makek[38] and Killeen and coworkers[41] found that neoplastic

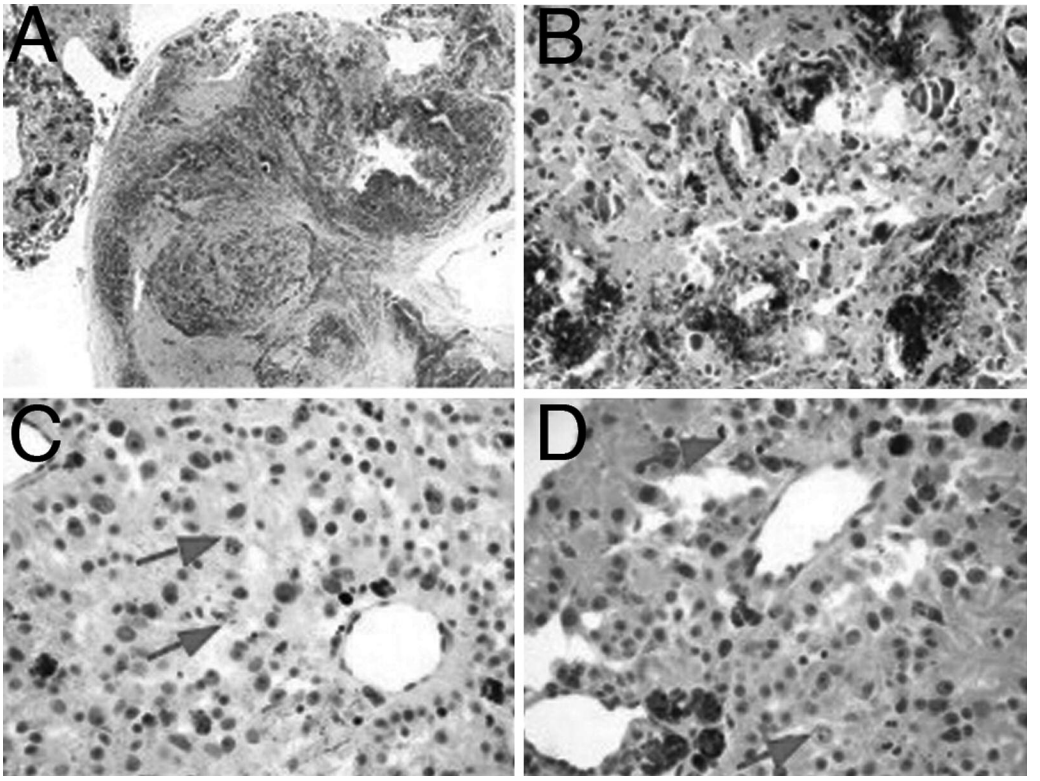

FIG. 4. Photomicrographs of the lesion. A: Low magnification of the lesion showing highly pigmented cells with nodular and fascicular architecture. B: Image of the lesion showing pigmentation with atypia, macronucleoli, and psammomatous bodies. C and D: Images showing melanotic pigmentation, nuclear atypia with macronucleoli, and mitosis (5 × 10 hpf). H & E, original magnification × 40 (A), × 200 (B), and × 400 (C and D).

cells of melanocytic schwannomas are capable of melanogenesis; McGravan,[51] Menneymer,[52] and Noubari[58] and their colleagues supported this theory with electron microscopy data, showing that Schwann cells produce melanin.

The biological behavior of melanocytic schwannomas remains unclear, because even lesions considered benign without mitosis, atypia, or necrosis may present with recurrence and/or metastasis, even after many years. In particular, in large literature reviews, Killeen and associates[41] described recurrence and/or metastasis in 24 and 10% of cases, respectively, with the worst prognosis for patients with incompletely excised tumors and tumors located in the cranial nerves; Vallat-Decouvelaere and colleagues[78] reported a 15% rate of recurrence and a 26.3% rate of metastasis for

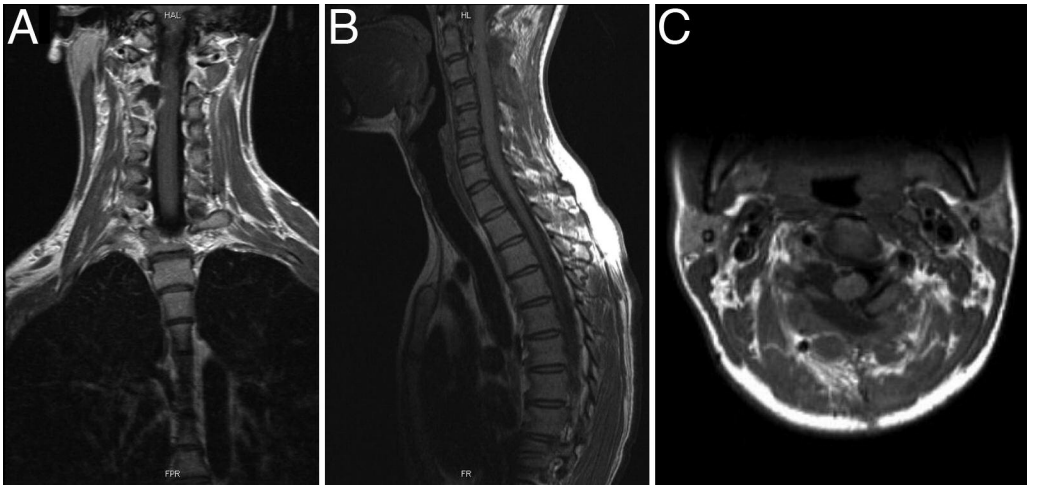

FIG. 5. Postoperative coronal (A), sagittal (B), and axial (C) T_1-weighted MR images obtained 6 months after surgery showing the gross-total removal of the lesion.

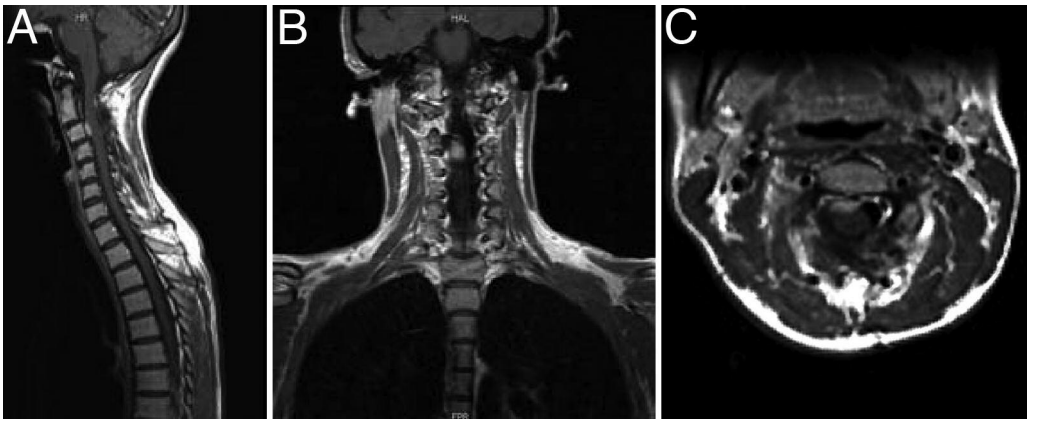

FIG. 6. Postoperative sagittal (A), coronal (B), and axial (C) T_1-weighted MR images obtained 12 months after surgery showing signs of the tumor progressing into the subarachnoid space at the C-3 level.

melanotic schwannomas; the lungs were the most common site for metastasis in this study. Vallat-Decouvelaere et al.[78] also concluded that a low mitotic count does not necessarily indicate a benign outcome, after reporting that of five patients with melanotic schwannomas without histopathological features of malignancy, mitosis, or a low mitotic rate, four died from tumor progression.

In patients with melanotic schwannomas, the percentage of malignant tumors is very low at the initial diagnosis, but the risk of possible malignant transformation of a melanotic schwannoma should be always taken into consideration. The follow up of these patients should be rigorous and focused not only on the primitive tumor regrowth but also on the meningeal drop metastasis and the remote locations, especially in the lungs. A recent review[20] on total spinal extramedullary melanotic schwannomas in the literature found 47 cases as of January 2006, but the authors of this review did not focus on malignancy, recurrences, metastasis, or survival rate.

We reviewed all the literature concerning melanotic schwannoma and found 105 cases that were not related to the Carney complex.[1–4,6–52,54,56–80] In particular, we were able to distinguish the primitive nonpsammomatous from the psammomatous melanotic schwannomas to focus on the cases of malignant melanotic schwannoma, indicated by the presence of a high level of mitosis, necrosis, pleomorphism, and nuclear atypia. This review also focused on patient follow up, the malignant progression of the tumor with local recurrences and metastasis, and the survival rate (Table 1).

We found that 15 of 105 melanocytic schwannomas[8,15,18,30,35,40–43,47,63,78] were psammomatous melanotic schwannomas not related to the Carney complex, and 90 were nonpsammomatous melanotic schwannomas.

Seventeen (16.2%) of 105 patients were given a diagnosis of a malignant tumor.[6,11,14,26,29,38,43,50,58,61,65,67,77,80] One patient presented with drop metastasis in the conus medullaris region, but the histological examination of the tumor revealed only benign features.[75]

Unfortunately, long-term follow-up data were available in only 72 of the reported cases, because 33 of the cases reviewed lacked a thorough follow up. Twenty-eight of the 72 patients had a malignant progression of their tumors and received adequate follow up.[8,9,16,19,38,41,44,45,47,50,52,58,62,65,66,75,78,80] Specifically, 12 patients had local recurrences, nine had metastasis or leptomeningeal spreading without local recurrence, and seven had both local recurrence and metastasis, resulting in a malignant progression rate of 26.7% compared with the total number of cases (105) with melanotic schwannomas. If only the population with malignant progression and long-term follow up is considered, the malignant progression rate was 38.9%.

We were not able to obtain sufficient data to calculate a survival rate after 12 or 24 months; we can only state that at 12 months, 63 of 105 patients (or 63 of the 72 patients with available follow-up data) were still alive, and among these, 38 were disease free. At 24 months the number of patients still living was 48, 26 of whom were also disease free.

If only the population with psammomatous schwannomas is considered, four of these patients had tumors that progressed to malignancy.[8,44,47,78] One patient with a psammomatous schwannoma, with histopathological findings of malignancy at diagnosis, was disease free 1 year after surgery.[43] Five of the 15 patients with psammomatous schwannomas were disease free for longer than 1 year after surgery;[40–43,63] for one of these patients the follow-up period lasted 5 years, and for another 6 years. Five patients did not have any follow up. Therefore, the percentage of malignant progression of psammomatous tumors (26.7%) was identical to the percentage of tumors that underwent malignant progression in the entire group of melanotic schwannomas, suggesting that the characteristic of a psammomatous or nonpsammomatous tumor does not have a prognostic value. The finding of a psammomatous schwannoma is mandatory for the exclusion of the Carney complex.

Thus, considering the biological behavior of this tumor, which can undergo malignant progression and cerebrospinal fluid seeding despite its benign histological features, treatment with complete excision and a strict follow up of the patient is mandatory, particularly in those lesions with malignant features at presentation, such as in the patient in this report. In particular, in this patient's family, the current presence of GIST, malignant melanoma, and malignant psammomatous melanotic schwannoma could indicate a genetic abnormality, different and separate from the Carney complex.

We would like to emphasize that in the literature[75] we

TABLE 1

*Summary of cases of melanotic schwannoma not related to the Carney complex in which there was evidence of malignant progression**

Authors & Year	Patient Age (yrs) & Tumor Type	Site			Malignant at 1st Diagnosis	Survival, FU
		Spinal Extramedullary	Spinal Intramedullary	Extraspinal		
Acciarri et al., 1999	44, NP		T2–3		no	ND
Aprile et al., 2000	70, NP	L-3			no	ND
Bagchi et al., 1975	40, NP	T6–7			no	ND
Belak et al., 2001	44, NP	dorsal			no	discharged 8 days postop
Bosman et al., 1995	43, NP	L4–5			yes	ND
Bouziani et al., 1994	46, NP	lumbar			no	alive, DF 2 yrs
Buhl et al., 2004	28, P	L5–S1 & multiple small lesions			no	intracranial mets after 30 mos
Bunc et al., 2004	NP	T12–L1–2			no	recur 13 yrs postop; alive 3 yrs after 2nd op
Burns et al., 1983	51, NP			gastric antrum	no	alive, DF 22 mos
Capote et al., 2006	75, NP			neck, lt carotid space	yes	alive, DF 15 mos
Christensen, 1986	55, NP	lumbar			yes	alive, DF 4 yrs
Claessens et al., 2003	45, P			subcutaneous	no	no recur
Cornejo et al., 1992	36	L3–4			no	recur 18 mos postop
Culhaci et al., 2003	52, NP	multiple paraspinal			no	alive DF 6 mos
Cummings et al., 2000	51, P	S-2			no	pt declined op
Dastur et al., 1967	38, NP			acoustic nerve	no	recur 8 mos postop; died after 2nd op; cerebellar mets at autopsy
De Cerchio et al., 2006	53, NP	T9–10			no	alive, DF 24 mos
Di Bella et al., 1997	46, NP	L-3			no	alive, DF 16 mos
Di Gregorio et al., 1984	70, NP	sacral			no	alive, DF 2 yrs
Ducastelle et al., 1981	10			index finger	no	alive, DF 6 yrs 6 mos
	15			femur		alive, DF 18 mos
Erlandson, 1985	36	L5–S1			no	alive, DF 92 mos
Font & Truong, 1984	45			shoulder	no	alive, DF 7 yrs
Gelfand et al., 1977	14, NP			rt atrium	yes	alive, DF 14 mos
Ghadially, 1983	23	S-2			no	ND
Goasguen et al., 2003	66	C2–3			no	ND
Gratz et al., 1991	62			mandible	yes	ND
	79			maxilla	yes	ND
Grayson & Hale, 1998	23, P			abdominal wall	no	ND
Graziani et al., 1988	40, NP	T-3			no	ND
Gregorios et al., 1982	45	T-2			no	ND
Hisaoka et al., 1991	52, NP	thoracolumbar			no	ND
Hodson, 1961	27, NP			lt mandible	no	ND
Hollinger et al., 1999	47, P	T-12			no	alive, DF after 1 yr
Iizuka et al., 1988	58, NP	T-10			no	ND
Jaffer & Woodruff, 2000	44, NP	paraspinal		pleural fluid	no	ND
Janzer & Makek, 1983	24, NP			intraoral	yes	recur 3 mos later; op & 2nd recur 17 mos later; died 2 yrs postop w/ mets at lymph nodes & liver
Katati et al., 2000	NP	multiple spinal			no	ND
Katenkamp et al., 1986	10, P			posterior mediastinum	no	alive, DF 2 yrs
Killeen et al., 1988	26, P	S-1			no	alive, DF 1 yr
	84, NP			parotid gland	no	died 7 mos later
Krichen et al., 1993	27, P	C6–7			no	alive, DF 6 yrs
Kuchelmeister et al., 2004	53, P	C5–6			yes	alive, DF 1 yr
Le Cam-Savin et al., 1995	35, NP	L-4			no	recur after 2 & 3 yrs; progression w/ pulmonary mets
Liessi et al., 1990	58, NP	thoracic spine			no	died; local spreading 2 yrs postop
	45, NP	thoracic spine			no	died; local spreading postop
	75, NP			head, pancreas	no	alive 7 mos; pt refused op
Lowman & Livolsi, 1980	17	T12–L1				alive, DF 14 yrs postop
	26	C-6				alive, DF 17 yrs
Ludvikova et al., 1997	56, P	spinal root			no	ND
	58, P	spinal root			no	local recur
Mandybur, 1974	59	T-7			no	recur 4 mos postop; radiological recur 16 mos postop

(continued)

TABLE 1 *(continued)*

Marchese & McDonald, 1990	72, NP		cervical		no	ND
Marco et al., 1998	34, NP	cervical			yes (necrosis)	mets 2 yrs postop; died 5 yrs after 1st op
	21, NP	superior mediastinum			yes (necrosis)	died from mets 10 mos postop
McGavran et al., 1978	12, NP	T-2			no	alive, DF 5 yrs
	49, NP	C-8			no	alive, DF 2 yrs
Mennemeyer et al., 1979	23, NP	L-1			no	recur 62 mos later
	25, NP	T-7			no	alive, DF 2 yrs
	36, NP	S-1			no	alive, DF 9 mos
Miller et al., 1986	74			acoustic nerve	no	alive, DF 9 mos
Napoli & De Domenico, 1987	NP	spinal			no	alive, DF 3 yrs
Ngaage et al., 2002	47, NP			esophagus	no	ND
Noubari et al., 1998	35, NP	T5–6 (infiltration of surrounding structures)			yes	died 3 mos later of disease progression
Parent et al., 1987	63	S-1			no	ND
Paris et al., 1979	49, NP	C-8			no	alive, DF 4 yrs
Parker et al., 1980	18	dorsal			yes	ND
Peltier et al., 2005	34	C4–5			no	brain & spinal mets at 18 mos; died
	80	T7–8			no	alive, DF 5 yrs
	35	L3–4			no	recur & mets at 2 yrs, died
Prieto-Rodriguez et al., 1998	38, P	T-5			no	alive, DF 5 yrs
Ranjan et al., 1995	NP			cerebellum	no	ND
Robertson et al., 1983	42			lower lip, mental & alveolar nerves	yes	recur 20 mos later; alive, DF 1 yr after 2nd op
	46			rt cheek	yes	recur 18 mos later; died 9 yrs 6 mos postop
Santaguida et al., 2004	35, NP		C4–5		no	recur after 2 yrs; 2nd recur & mets after 2 yrs
Schmitz et al., 2005	42, NP	cervical & other small lesions			yes	alive, DF 1 yr
Schulz et al., 1965	32			buccal mucosa	no	alive, DF 12 yrs
Shields et al., 1994	21, NP			choroid	no	ND
Shillitoe, 1965	20			rt buttock	no	alive, DF 12 mos
Simansky et al., 2000	30, P			lt lung	no	ND
Sola-Perrez et al., 1994	63, NP		intramedullary		no	ND
Solomon et al., 1987	69, NP		cervicomedullary junction		no	ND
Stein et al., 1993	25, NP	L-5			no	alive, 48 mos
Tawk et al., 2005	61, NP	T-7 & drop mets conus			no	died 11 mos postop; meningeal mets
Theodossiou & Segditsas, 1971	34, NP			abdomen	no	ND
Thewes et al., 1997	NP			subcutaneous	yes	ND
Vallat-Decouvelaere et al., 1999	5 pts: 2 P (Cases 1 & 2, both w/ progression) & 3 NP	spinal roots			no	3 pts died (1 w/ recur & mets after 6 yrs; 1 died from mets after 6 yrs; 1 died from mets after 3 yrs); 1 pt w/ mets, alive after 7 yrs; 1 pt alive, DF 6 yrs
Webb, 1982	53			dorsum of lt foot	no	ND
Zhang et al., 2005	5, NP	spinal roots			no	at 2 yrs: 2 pts w/ local recur; 1 w/ subcutaneous mets & 1 w/ local recur & mets; 7 pts DF after 2 yrs; 2 pts lost to FU
	NP			cranial nerve	no	at 2 yrs: 2 pts w/ local recur; 1 w/ subcutaneous mets & 1 w/ local recur & mets; 7 pts DF after 2 yrs; 2 pts lost to FU
	NP			greater omentum	yes	
	3, NP			subcutaneous tissue	no	
	NP			mesentery	no	
	NP			bone	no	
	NP			mediastinum	no	

* DF = disease free; FU = follow up; mets = metastasis; ND = no data available; NP = nonpsammomatous; P = psammomatous; pt = patient; recur = recurrence.

found, both in melanotic schwannomas and in tumors such as GISTs and malignant melanomas, positivity for the CD117 marker (c-kit). This marker is important for oncology treatments as the target of imatinib, a chemotherapeutic agent already used in chronic myelogenous leukemia as well as in GIST, with excellent results. The mechanism of action of imatinib consists of a competitive inhibition of a tyrosine kinase associated with CD117 and other receptors. In patients with GIST, such as in the father of the patient in this report, the efficacy of imatinib depends on the levels of expression of CD117. Imatinib is now used in clinical trials for malignant melanoma and the expression of CD117 has recently been reported in malignant melanotic schwannomas. In our patient, the CD117 marker in neoplastic cells was absent. Nevertheless, it could be interesting to investigate if other markers exist in different stromal tumors, especially to be considered as targets for other therapeutic agents.

References

1. Acciarri N, Padovani R, Riccioni L: Intramedullary melanotic schwannoma. Report of a case and review of the literature. **Br J Neurosurg 13:**322–325, 1999
2. Aprile I, Scott CA, Cervesato D, Beltrami CA, Meo A, Fabris G: Two rare lumbar tumors with unusual MRI characteristics. **Neuroradiology 42:**458–461, 2000
3. Bagchi AK, Sarkar SK, Chakraborti DP: Melanotic spinal schwannoma. **Surg Neurol 3:**79–81, 1975
4. Belak J, Vajo J, Boor A, Janik M, Sauka C, Lukac I, et al: A "dumbell" tumor of the mediastinum case report. **Rozhl Chir 80:** 572–574, 2001 (Abstract)
5. Bird CC, Willis RA: The histogenesis of pigmented neurofibromas. **J Pathol 97:**631–637, 1969
6. Bosman C, Boldrini R, Corsi A: Malignant melanotic schwannoma or schwannian melanoma? **Tumori 81:**208–212, 1995
7. Bouziani A, Kammoun N, Zidi B, Ben Hamadi F, Benzarti H, Khelil A, et al: [Melanotic schwannoma. A case with review of the literature.] **Arch Anat Cytol Pathos 42:**46–53, 1994 (Fr)
8. Buhl R, Barth H, Hugo HH, Mautner VF, Mehdorn HM: Intracranial and spinal melanotic schwannoma in the same patient. **J Neuroncol 68:**249–254, 2004
9. Bunc G, Kramberger S, Kovacic S, Seruga T, Vorsic M: Recurrent giant invasive thoracolumbar schwannoma. **Wien Klin Wochenschr 116 (2 Suppl):**93–96, 2004
10. Burns DK, Silva FG, Forde KA, Mount PM, Clark HB: Primary melanocytic schwannoma of the stomach. Evidence of dual melanocytic and schwannian differentiation in an extra-axial site in a patient without neurofibromatosis. **Cancer 52:**1432–1441, 1983
11. Capote A, Escorial V, Reina T, Munoz-Guerra MF, Nieto S, Naval L: Primary malignant schwannoma of the cervical plexus with melanocytic differentiation. **Int J Oral Maxillofac Surg 35:** 767–771, 2006
12. Carney JA: Psammomatous melanotic schwannoma: a distinctive, heritable, tumor with special associations, including cardiac myxoma and the Cushing syndrome. **Am J Surg Pathol 14:**206–222, 1990
13. Carney JA, Gordon H, Carpenter PC, Shenoy BV, Go VLW: The complex of myxomas, spotty pigmentation, and endocrine overactivity. **Medicine 64:**270–283, 1985
14. Christensen C: Malignant melanocytic schwannoma. A case report. **Acta Chir Scand 152:**385–386, 1986
15. Claessens N, Heymans O, Arrese JE, Garcia R, Oelbrandt B, Pierard GE: Cutaneous psammomatous melanotic schwannoma: non-recurrence with surgical excision. **Am J Clin Dermatol 4:** 799–802, 2003
16. Cornejo M, Pierrot D, Robine D, Lepreux JF, Baviera E, Merland JJ: [Intraspinal melanocytic schwannoma. About one case. Literature review.] **Rachis 4:**281–286, 1992 (Fr)
17. Culhaci N, Dikicioglu E, Meteoglu I, Boylu S: Multiple melanotic schwannoma. **Ann Diagn Pathol 7:**254–258, 2003
18. Cummings TJ, Liu K, Jordan LK III, Dodd LG: Fine-needle aspiration diagnosis of psammomatous melanotic schwannoma. **Diagn Cytopathol 23:**55–58, 2000
19. Dastur DK, Sinh G, Pandya SK: Melanotic tumor of the acoustic nerve: case report. **J Neurosurg 27:**166–170, 1967
20. De Cerchio L, Contratti F, Fraioli MF: Dorsal dumb-bell melanotic schwannoma operated on by posterior and anterior approach: case report and a review of the literature. **Eur Spine J 15 (17 Suppl):**664–669, 2006
21. Di Bella C, Declich P, Assi A, Cenacchi G, Sironi M, Cozzi L, et al: Melanotic schwannoma of the sympathetic ganglia: a histologic, immunohistochemical and ultrastructural study. **J Neurooncol 35:**149–152, 1997
22. Di Gregorio C, Fano RA, Criscuolo M: Melanotic schwannoma: a case report. **Appl Pathol 2:**110–115, 1984
23. Ducastelle T, Ducastelle C, Hemet J, Lefort J, Borde J: Melanotic schwannoma (pigmented neurilemmoma). A light and electron microscopic study of a case with double tumoral localization and periosteal implantation. **Ann Pathol 1:**205–212, 1981
24. Erlandson RA: Melanotic schwannoma of spinal nerve origin. **Ultrastruct Pathol 9:**123–129, 1985
25. Font RL, Truong LD: Melanotic schwannoma of the soft tissues. Electron-microscopic observations and review of the literature. **Am J Surg Pathol 8:**129–138, 1984
26. Gelfand ET, Taylor RF, Hendin D, Akabutu J, Callaghan JC: Melanotic malignant schwannoma of the right atrium. **J Thorac Cardiovasc Surg 74:**808–812, 1977
27. Ghadially FN: Diagnosis of human tumors. Case 15: Melanotic schwannoma. **Ultrastruct Pathol 5:**369–374, 1983
28. Goasguen O, Boucher E, Pouit B, Soulard R, Le Charpentier M, Pernot P: [Melanotic schwannoma, a tumor with an unpredictable prognosis: case report and review of the literature.] **Neurochirurgie 49:**31–38, 2003 (Fr)
29. Gratz KW, Makek M, Sailer HF: Malignant melanotic schwannoma of the oral cavity. **Int J Oral Maxillofac Surg 20:**236–238, 1991
30. Grayson W, Hale MJ: Epithelioid psammomatous melanotic schwannoma with osseous metaplasia. **Arch Pathol Lab Med 122:**285–287, 1998
31. Graziani N, Gambarelli D, Bartoli JM, Dechambenoit G, Bellard S, Grisoli F: [Extra medullary intradural melanotic tumor: apropos of a case of dorsal pigmented neurinoma. Review of the literature.] **Neurochirurgie 34:**210–217, 1988 (Fr)
32. Gregorios JB, Chou SM, Bay J: Melanotic schwannoma of the spinal cord. **Neurosurgery 11:**57–60, 1982
33. Hisaoka M, Ohta H, Haratake J, Horie A: Melanocytic schwannoma in the spinal canal. **Acta Pathol Jpn 41:**685–688, 1991
34. Hodson JJ: An intra-osseous tumor combination of biological importance—invasion of a melanotic schwannoma by an adamantinoma. **J Pathol Bacteriol 82:**257–266, 1961
35. Hollinger P, Godoy N, Sturzenegger M: Magnetic resonance imaging findings in isolated spinal psammomatous melanotic schwannoma. **J Neurol 246:**1100–1102, 1999
36. Iizuka H, Nakamura T, Kadoya S: [Spinal melanotic schwannoma: report of a case.] **No Shinkei Geka 16:**1199–1205, 1988 (Jpn)
37. Jaffer S, Woodruff JM: Cytology of melanotic schwannoma in a fine needle aspirate and pleural fluid. A case report. **Acta Cytol 44:**1095–1100, 2000
38. Janzer RC, Makek M: Intraoral malignant melanotic schwannoma. Ultrasctructural evidence for melanogenesis by Schwann's cells. **Arch Pathol Lab Med 107:**298–301, 1983
39. Katati MJ, Martin JM, Massare E, Arjona V: [Melanocytic schwannoma. A case report and review of the literature.] **Rev Neurol 31:**427–430, 2000 (Fr)

40. Katenkamp D, Filippowa N, Raikhlin NT: [Melanocytic schwannoma. Light and electron microscopic findings on the morphology, diagnosis and differential diagnosis.] **Zentralbl Allg Pathol 131:**107–118, 1986 (Ger)
41. Killeen RM, Davy CL, Bauserman SC: Melanocytic schwannoma. **Cancer 62:**174–183, 1988
42. Krichen H, Daghfous MS, Mrabet A, Douik M, Slimane N, Forest M: [Extended melanocytic tumor of the cervical spine. A propos of a case of melanotic schwannoma.] **Ann Pathol 13:**184–187, 1993 (Fr)
43. Kuchelmeister K, Lotz C, Schonmayr R, Schachenmayr W: April 2004: woman in her early fifties with a cervical intraspinal and extraspinal mass lesion. **Brain Pathol 14:**453–454, 458–459, 2004
44. Le Cam-Savin C, Gontier MF, Martin A, Sevestre H, Cordonnier C, Smadja A: [Spinal melanocytic schwannoma with malignant course. Microscopic and ultrastructural study of a case.] **Arch Anat Cytol Pathol 43:**160–163, 1995 (Fr)
45. Liessi G, Barbazza R, Sartori F, Sabbadin P, Scapinello A: CT and MR imaging of melanocytic schwannomas; report of three cases. **Eur J Radiol 11:**138–142, 1990
46. Lowman RM, Livolsi VA: Pigmented (melanotic) schwannomas of the spinal canal. **Cancer 46:**391–397, 1980
47. Ludvikova M, Michal M, Marek J, Syrucek M: Psammomatous melanotic schwannoma. **Cesk Patol 33:**141–145, 1997 (Abstract)
48. Mandybur TI: Melanotic nerve sheath tumors. **J Neurosurg 41:** 187–192, 1974
49. Marchese MJ, McDonald JV: Intramedullary melanotic schwannoma of the cervical spinal cord: report of a case. **Surg Neurol 33:**353–355, 1990
50. Marco V, Sirvent J, Alvarez Moro J, Clavel M, Muntal MT, Bauza A: Malignant melanotic schwannomas fine-needle aspiration biopsy findings. **Diagn Cytopathol 18:**284–286, 1998
51. McGavran WL III, Sypert GW, Ballinger WE: Melanotic schwannoma. **Neurosurgery 2:**47–51, 1978
52. Mennemeyer RP, Hallman KO, Hammar SP, Raisis JE, Tytus JS, Bockus D: Melanotic schwannoma. Clinical and ultrastructural studies of three cases with evidence of intracellular melanin synthesis. **Am J Surg Pathol 3:**3–10, 1979
53. Millar WG: Malignant melanotic tumor of ganglion cells arising from the thoracic sympathetic ganglion. **J Pathol 35:**351–357, 1932
54. Miller RT, Sarikaya H, Sos A: Melanotic schwannoma of the acoustic nerve. **Arch Pathol Lab Med 110:**153–154, 1986
55. Nakai T, Rappaport H: A study of the histogenesis of experimental melanotic tumors resembling cellular blue nevi: the evidence in support of their neurogenic origin. **Am J Pathol 43:**175–199, 1963
56. Napoli P, De Domenico P: Primary melanotic schwannoma of the spinal canal. **Appl Pathol 5:**253–260, 1987
57. Ngaage DL, Khan ZA, Cale AR: Esophageal melanotic schwannoma presenting with superior vena caval obstruction. **Thorac Cardiovasc Surg 50:**103–104, 2002
58. Noubari BA, Chiaramonte I, Magro G, Tropea R, Mancuso P: Spinal malignant melanotic schwannoma. Case report. **J Neurosurg Sci 42:**245–249, 1998
59. Parent M, Beyls-Noel I, Lecomte-Houcke M, Fontane C, Dupont A: [Melanotic schwannoma. Anatomo-clinical study of a case and review of the literature.] **Arch Anat Cytol Pathol 35:**76–81, 1987 (Fr)
60. Paris F, Cabanes J, Munoz C, Tamarit L: Melanotic spinothoracic schwannoma. **Thorax 34:**243–246, 1979
61. Parker JB, Marcus PB, Martin JH: Spinal melanotic clear-cell sarcoma: a light and electron microscopic study. **Cancer 46:** 718–724, 1980
62. Peltier J, Page C, Toussaint P, Bruniau A, Desenclos C, Le Gars D: Melanocytic schwannomas. Report of three cases. **Neurochirurgie 51:**183–189, 2005
63. Prieto-Rodriguez M, Camanas-Sanz A, Bas T, Cortes B, Vera-Sempere FJ: Psammomatous melanotic schwannoma localized in the mediastinum: diagnosis by fine-needle aspiration cytology. **Diagn Cytopathol 19:**298–302, 1998
64. Ranjan A, Chacko G, Chandi SM: Intracerebellar melanotic schwannoma: a case report. **Br J Neurosurg 9:**687–689, 1995
65. Robertson I, Cook MG, Wilson DF, Henderson DW: Malignant schwannoma of cranial nerves. **Pathology 15:**421–429, 1983
66. Santaguida C, Sabbagh AJ, Guiot MC, Del Maestro RF: Aggressive intramedullary melanotic schwannoma: case report. **Neurosurgery 55:**1430, 2004
67. Schmitz KJ, Unkel C, Grabellus F, Baba HA, Dirsch O, Neumann A: Melanotic schwannoma of the neck mimicking a malignant melanoma. **Eur Arch Otorhinolaryngol 262:**182–185, 2005
68. Schulz H, Haneke A, Caleff N: [Benign melanotic neurinoma of the oral mucous membrane.] **Dtsch Zahn Mund Kieferheilkd Zentralbl Gesamte 44:**369–373, 1965 (Ger)
69. Shields JA, Font RL, Eagle RC Jr, Shields CL, Gass JD: Melanotic schwannoma of the choroid. Immunohistochemistry and electron microscopic observations. **Ophthalmology 101:**843–849, 1994
70. Shillitoe AJ: Melanotic schwannoma. **J Pathol Bacteriol 90:** 667–668, 1965
71. Simansky DA, Aviel-Ronen S, Reder I, Paley M, Refaely Y, Yellin A: Psammomatous melanotic schwannoma: presentation of a rare primary lung tumor. **Ann Thorac Surg 70:**671–672, 2000
72. Sola-Perez J, Perez-Guillermo M, Bas-Bernal A, Gimenez-Bascunana A, Montes-Clavero C: Melanocytic schwannoma. The cytologic aspect in fine-needle aspiration cytology (FNAC): report of a case located in the spinal cord. **Diagn Cytopathol 11:** 291–296, 1994
73. Solomon RA, Handler MS, Sedelli RV, Stein BM: Intramedullary melanotic schwannoma of the cervicomedullary junction. **Neurosurgery 20:**36–38, 1987
74. Stein ME, Loberant N, Kessel I, Kuten A: Melanocytic schwannoma of the spinal cord: a case report. **East Afr Med J 70:**597–599, 1993
75. Tawk RG, Tan D, Mechtler L, Fenstermaker RA: Melanotic schwannoma with drop metastases to the caudal spine and high expression of CD117 (c-kit). **J Neurooncol 71:**151–156, 2005
76. Theodossiou A, Segditsas T: [Intra-abdominally situated melanotic schwannoma.] **Zentralbl Allg Pathol 114:**168–172, 1971 (Ger)
77. Thewes M, Jungfer-Weber B, Wiebecke B, Engst R, Ring J: Malignant epithelioid schwannoma with melanocytic differentiation: a rare tumor with an unusual feature. **Acta Derm Venereol 77:**493–494, 1997
78. Vallat-Decouvelaere AV, Wassef M, Lot G, Catala M, Moussalam M, Caruel N, et al: Spinal melanotic schwannoma: a tumor with poor prognosis. **Histopathology 35:**558–566, 1999
79. Webb JN: The ultra-structure of a melanotic schwannoma of the skin. **J Pathol 137:**25–36, 1982
80. Zhang HY, Yang GH, Chen HJ, Wei B, Ke Q, Guo H, et al: Clinicopathological, immunohistochemical, and ultrastructural study of 13 cases of melanotic schwannoma. **Chin Med J 118:**1451–1461, 2005

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