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Malignant schwannoma of the parapharyngeal space in von Recklinghausen's disease: a case report and review of the literature

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Abstract
Neurofibromatosis (NF) or von Recklinghausen's disease is frequently accompanied by malignant tumours, which can occur at any site in the body. These malignancies are mainly of soft tissue origin. Of all head and neck malignancies, the number of soft tissue sarcomas is limited and in combination with NF this type of tumour is a rare event. In this report we describe the clinical course of a young female patient with NF, who presented with a massive malignant schwannoma in the parapharyngeal space, and review the pertinent literature.

Key words: Neurofibromatosis; Head and neck neoplasms, malignant schwannoma

Introduction

Von Recklinghausen's disease or neurofibromatosis (NF) is an autosomal dominant disorder with a frequency of 1 in 3000. Approximately half of those affected, have inherited the mutation and the other half harbour a new mutation. NF is a progressive disease and shows a marked variation in expression in affected individuals (Riccardi, 1981).

Characteristically the patients present with café-au-lait spots, neurofibromas of the peripheral and central nervous systems, as well as skeletal abnormalities which develop during infancy and childhood (Preston *et al.*, 1952; Riccardi, 1981). NF is known to be complicated by malignancies. These malignancies are mainly of soft tissue origin and can arise at any site in the body (D'Agostino *et al.*, 1963; Riccardi, 1981). In general, 10 to 25 per cent of the soft tissue sarcomas are found in the head and neck area (Barnes, 1985).

In this report we describe the history of a young female patient with NF who developed a rapidly growing tumour in the parapharyngeal space, classified as a malignant schwannoma (MS), and review the pertinent literature.

Case history

An 18-year-old girl was referred to our hospital for treatment of a rapidly growing tumour in the right tonsillar fossa. She presented elsewhere with a two-week history of pain in the throat accompanied by referred ear pain. Furthermore, there was dysphagia and a mild fever. Intra-oral examination revealed a swelling in the right tonsillar fossa and peritonsillar region with displacement of the uvula to the left. With a presumptive diagnosis of a peritonsillar abscess the mass was incised. A small amount of purulent material was released and antibiotics were given, without clinical improvement. After two days a tonsillectomy was performed. During the operation abundant bleeding precluded total removal of the mass. Only part of the tumour could be excised. At microscopic examination a malignant tumour was seen and the patient was referred to our institute for further treatment.

At examination we saw a healthy looking girl in a good nutritional state. She was the only member of her family known with von Recklinghausen's disease (NF). At examination under general anaesthesia a tumour mass with a greatest diameter of 7 cm was found in the right tonsillar fossa with a deep elongated central ulcer, extending parapharyngeally to the base of the skull. The tumour was mobile in relation to the prevertebral fascia but fixed to the base of the skull and to the right ascending ramus of the mandible. The tumour tissue was vulnerable and bled easily. In the right submandibular/subdigastric region, a firm mass was palpated in continuity with the parapharyngeal tumour (Figure 1). On further physical examination we found six café-au-lait spots on her trunk and a few scars of previous oper-

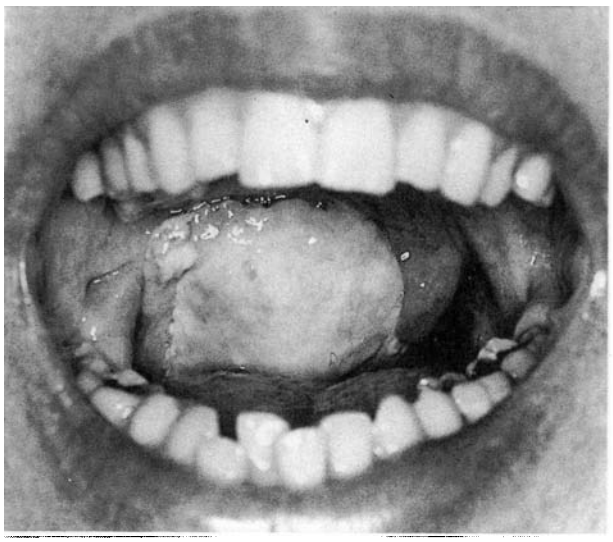

FIG. 1
A parapharyngeal swelling with grey-white appearance. Note the displacement of the uvula to the left.

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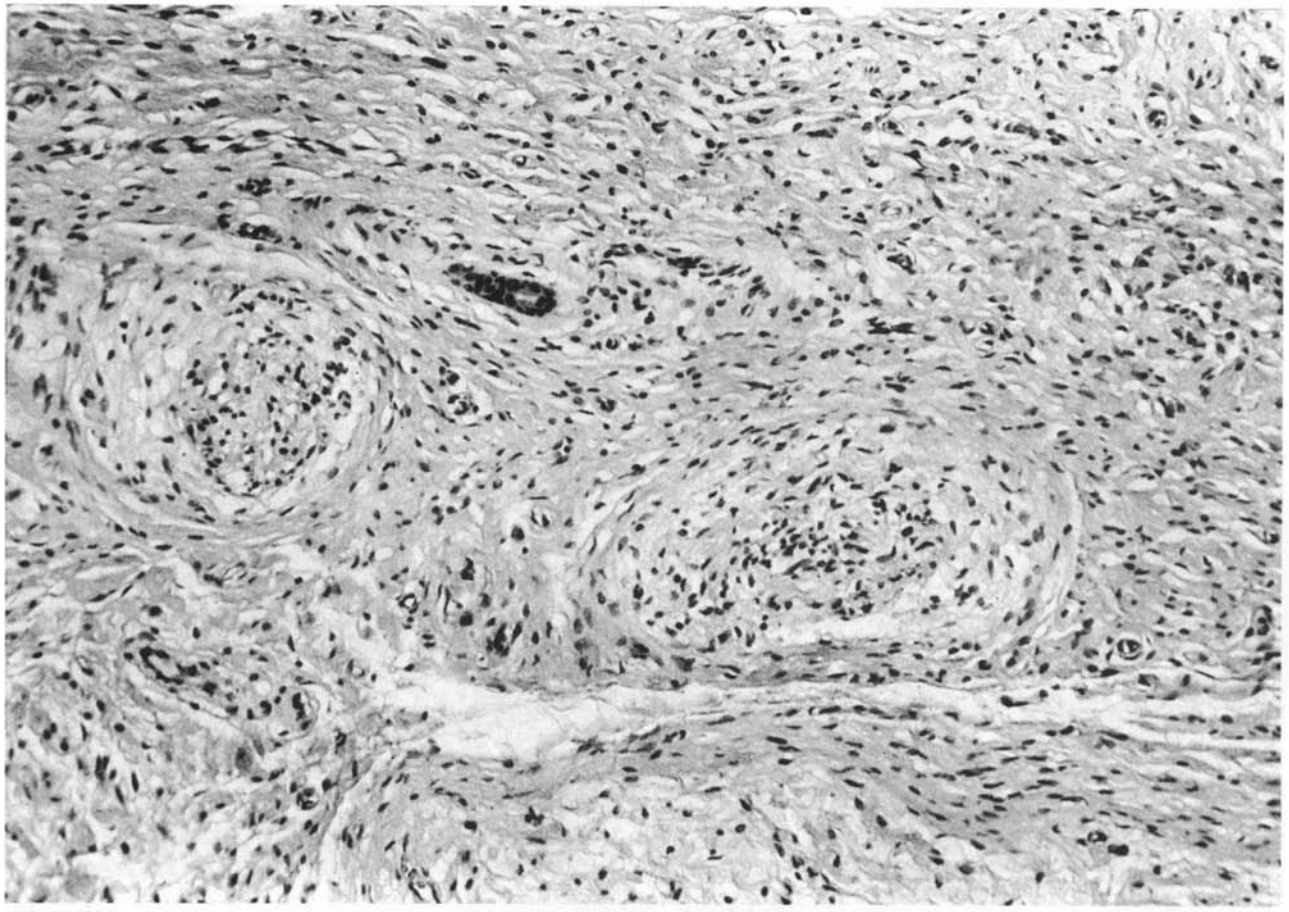

FIG. 2

Microscopy of a diffuse benign neurofibroma, removed from the left breast. (H&E; ×100).

ative removals of neurofibromas of the left breast and thoracic wall. The histology of these lesions is shown in Figure 2.

A CT scan revealed a large parapharyngeal tumour which extended from the base of the skull to the caudal end of the mandibular angle with destruction of the lateral laminae of the pterygoid process and the ascending ramus of the mandible (Figure 3).

Biopsies of the tumour showed a spindle-cell tumour. The cells were arranged in short fascicles and solid cellular areas. There was a moderate degree of cellular pleomorphism, necrosis was absent, mitoses were frequent. There was a rich vascular pattern reminiscent of haemangiopericytoma. Immunopathologically, the tumour showed vimentin positivity. Epithelial markers were negative, as were the desmin, S-100, melanin and Factor (F)-XIIIa markers. The tumour was classified as a sarcoma, probably a malignant schwannoma (Figure 4).

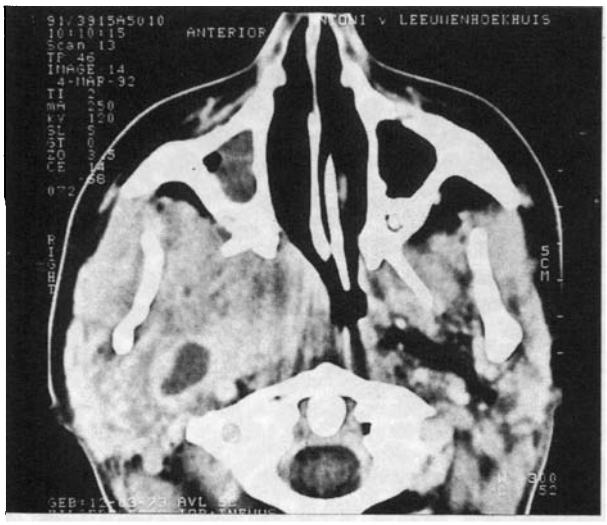

FIG. 3

CT scan image of the parapharyngeal tumour mass. Note the central necrosis and the destruction of the lateral laminae of the pterygoid process.

Because the patient's tumour was fixed to the base of the skull, radical surgical excision was impossible. A chemotherapeutic regimen of adriamycin (75 mg/m^2) and ifosfamide (59 mg/m^2) with two-week intervals (and G-CSF, 300 μg daily, on days 2 to 10, to hasten haematological recovery) was started. The tumour did not respond well and, because of progressive disease, the second chemotherapy course was discontinued. Because of impending airway obstruction a tracheotomy was performed. Immediately thereafter radiotherapy was started. The tumour continued to progress rapidly and the radiation had to be stopped prematurely, after 22 Gy, as well. The local and general condition deteriorated rapidly with complete blockage of the oropharynx for passage of food due to massive tumour growth after two weeks. Further palliative treatment consisted of analgesia (morphine 175 mg daily, naproxen 500 mg twice daily) and nasogastric tube feeding was necessary.

Six weeks later, however, the patient showed an unexpected improvement in her condition. After the spontaneous release of a substantial piece of necrotic tissue, it was possible for her to speak again and to swallow. This phenomenon was explained as a late effect of the radiotherapy and additional radiotherapy was initiated. During the following six weeks, she received a total dose of 66 Gy in 33 fractions. The tumour regression continued and after two months she was decannulated and discharged from the hospital in a relatively good condition. Good palliation was

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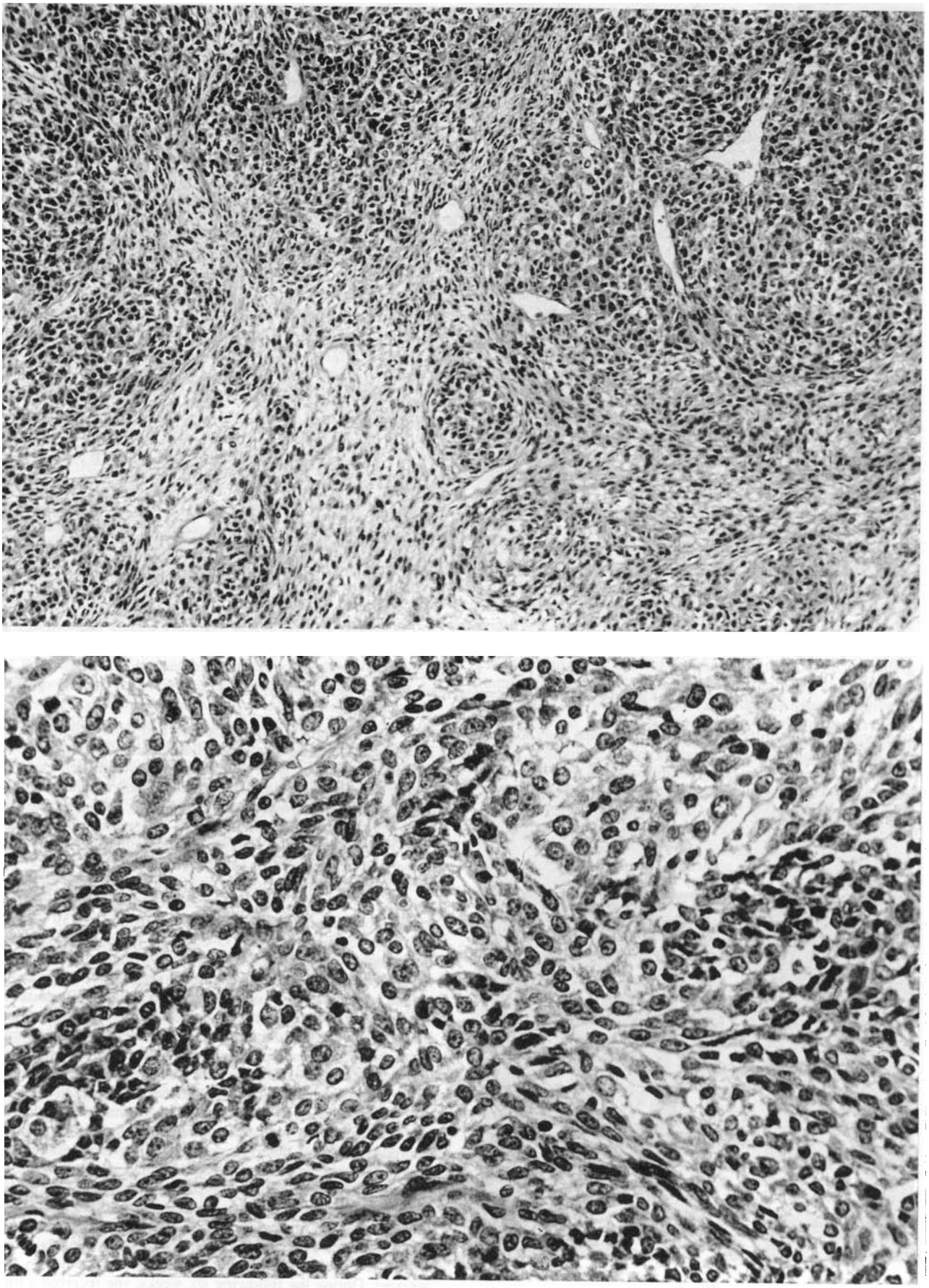

FIG. 4

Microscopy of the biopsy from the parapharyngeal tumour mass. (A) Overview of the malignant schwannoma with a haemangiopericytoma-like vascular pattern (H&E; ×100). (B) Note the spindle cells in fascicular arrangement (H&E; ×250).

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TABLE I
LITERATURE REVIEW OF THE LAST 30 YEARS OF HEAD AND NECK SOFT TISSUE SARCOMA IN NEUROFIBROMATOSIS

References	Sex/age in years	Histology	Site	Treatment	Survival in years
D'Agostino *et al.*, 1963	F/22	Lipos	Temporal	Surg + RT	5, 5D(L)
	F/18	Unclass	Neck	Surg	1, 5D(M)
	M/19	MS	Neck	Surg	0, 5D(L)
Oberman and Sullenger, 1967	M/??	MS	Neck	Surg	5 (L)
	M/31	MS	Neck	Surg	2D (L)
	F/61	MS	Neck	Surg	7D (L)
Gosh *et al.*, 1973	5 Pat	MS	?	?	?
Knight *et al.*, 1973	F/34	MS	Neck	?	D
Chaudhuri *et al.* 1980	M/14	Angios	Neck	Surg	?
Martin and Kleinsasser, 1981	F/14	MS	Neck	Surg + CT	1D (M)
	F/10	MS	Submand	Surg	5 NED
	M/40	MS	Neck	Surg	0, 5NED*
Ducatman and Scheithauer 1983	F/23	MS	Zygoma	Surg + RT	5, 5D (L)
	F/23	MS	Neck	Surg + RT	3, 2D (L)
Brooks *et al.*, 1985	F/12	MS	Neck	Surg + RT + CT	13 NED
	M/25	MS	Neck	Surg + RT	0, 3D
Aduana *et al.*, 1988	F/71	HPC	Buccal	Surg	?
Greager *et al.*, 1992	1 Pat	MS	?	Surg	26 NED
	5 Pat	MS	?	?	2 D
Al-Ghami *et al.*, 1992	2 Pat	MS	?	Surg + RT	1 D

Pat = patient; lipos = liposarcoma; unclass = unclassified sarcoma; MS = malignant schwannoma; angios = angiosarcoma; HPC = haemangiopericytoma; surg = surgery; RT = radiotherapy; CT = chemotherapy; D = dead of disease, NED = no evidence of disease; L = local recurrence; M = metastatic disease; ? = unknown. *This patient also had a follicular thyroid carcinoma.

obtained. The disease stabilized with a mass still present, as shown by repeated CT scans, compatible with residual disease. Six months later, the locally residual tumour showed rapid progression and a cerebellar metastasis occurred. No further treatment was given and patient died 12 months after onset of the disease.

Discussion

To our knowledge, this is the only report in the last 30 years of a parapharyngeal localized soft tissue malignancy accompanying NF. A tumour of the parapharyngeal space (malignant or benign) is uncommon by itself and accounts for 0.5 per cent of all head and neck tumours (Allison *et al.*, 1989).

Malignant tumours arise in a small percentage of the patients exhibiting manifestations of NF. The majority of these neoplasms are soft tissue sarcomas. In 25 to 70 per cent of patients with malignant schwannomas NF is present (Preston *et al.*, 1952; D'Agostino *et al.*, 1963; Chaudhuri *et al.*, 1980; Riccardi, 1981; Riccardi *et al.*, 1984; Barnes, 1985; Schneider *et al.*, 1986). In some instances, a pre-existing benign neurofibroma can be demonstrated in contiguity with the malignant tumour (Oberman and Sullenger, 1967; Gosh *et al.*, 1973; Storm *et al.*, 1980). Other soft tissue tumour types found in NF are rhabdomyosarcoma, angiosarcoma, liposarcoma, haemangiopericytoma and unclassifiable sarcomas (Knight *et al.*, 1973; Chaudhuri *etal.*, 1980). Less frequently reported malignancies in relation to NF include squamous cell carcinoma, melanoma and several types of leukaemia (Knight *et al.*, 1973; Riccardi, 1981).

Reviewing the literature of the last 30 years we found eleven well-documented reports on head and neck soft tissue sarcomas in 29 patients with NF as shown in Table I (D'Agostino *et al.*, 1963; Oberman and Sullenger, 1967; Gosh *et al.*, 1973; Knight *et al.*, 1973; Chaudhuri *et al.*, 1980; Martin and Kleinsasser, 1981; Ducatman and Scheithauer, 1983; Brooks *et al.*, 1985; Aduana *et al.*, 1988; Al-Ghami *et al.*, 1992; Greager *et al.*, 1992). From these series 25 cases were described as malignant schwannomas (MS), of which ten were located in the neck.

Aduana *et al.* (1988) reported a case of a haemangiopericytoma (HPC) arising in a plexiform neurofibroma of the buccal region. Ducatman and Scheithauer (1983) reported MS in two patients with NF, who had received radiotherapy for an optic glioma and a soft tissue tumour in the zygomatic area, respectively 10 and 17 years before. These authors concluded that caution should be taken in subjecting patients with known NF to radiotherapy.

It is not known whether all the reported patients fulfil the criteria of NF (Riccardi, 1981). Our patient however showed the characteristics of von Recklinghausen's disease: histological review of the material removed from her left breast and thoracic wall showed plexiform neurofibromas, and at physical examination six café-au-lait spots were found with a diameter of more than 1.5 cm.

It is known that parapharyngeal tumours can remain quiescent for a long period of time and that not infrequently a surprisingly large tumour is diagnosed on incidental examination (Allison *et al.*, 1989). This probably also happened to our patient. Odynophagia and throat discomfort are the most common signs. Pain and neurological deficit are ominous signs, suggestive of malignancy. Because the surrounding walls are bony, enlargement of a parapharyngeal tumour is often seen as a distortion of the soft palate or the tonsillar fossa, mimicking a peritonsillar abscess. This can cause difficulties in making the correct diagnosis, as in our case.

The most likely histological diagnosis was a malignant schwannoma (MS), based on the presence of spindle-shaped cells surrounded by reticulum fibres. The prominent vascular pattern causes the haemangiopericytoma (HPC)-like appearance of this malignancy. Immunochemistry may be helpful in the differential diagnosis of soft tissue sarcomas. Nemes (1992) recently found positivity for Factor (F)-XIIIa in all cases tested of his series of 15 HPC. Other tumours with a HPC-like pattern (like synovial sarcoma, MS) were F-XIIIa negative. In our case the tumour cells were F-XIIIa negative, supporting the notion that the tumour was not a HPC.

Patients with von Recklinghausen's disease have a propensity to develop malignant tumours of the nerve sheath, such as malignant schwannomas (Hutcherson *et al.*, 1979; Riccardi, 1981; Ducatman and Scheithauer, 1983; Barnes, 1985; Schneider *et al.*, 1986). These tumours are uncommon and account for only five per cent of all soft tissue sarcomas (Storm *et al.*, 1980; Bailet *et al.*, 1991), affecting all ages with a preference for the extremities. Only 9 to 14 per cent are found in the head and neck area (Gosh *et al.*, 1973; Storm *et al.*, 1980; Barnes, 1985). They frequently arise in the deep soft tissues and present as a painful growing mass, grey-white in colour, well-circumscribed and sometimes encapsulated (D'Agostino *et al.*, 1963). In cases of nerve involvement, paresis or paralysis can occur. The duration of the symptoms is variable.

The five-year survival for MS is reported to range from 40 to 66 per cent. In up to 33 per cent of patients with MS, haematogenous metastases have been reported to develop in the lungs and bone (Bailet *et al.*, 1991). When the patient has stigmata of NF, cellular pleomorphism and mitotic activity are more prominent and a poorer prognosis is suggested (D'Agostino *et al.*, 1963; Gosh *et al.*, 1973; Hutcherson *et al.*, 1979; Storm *et al.*, 1980; Bailet *et al.*, 1991; Greager *et al.*, 1992).

The highly malignant forms of MS are best treated by wide local excision followed by radiotherapy (Storm *et al.*, 1980). In MS various chemotherapeutic agents have also been applied, singly or in combination. Responses to methotrexate and adriamycin have been reported, but the overall results are poor (Hutcherson *et al.*, 1979; Storm *et al.*, 1980). In our patient, the tumour was not resectable because of its wide fixation to the base of the skull. Chemotherapy (adriamycin + ifosfamide) did not show any effect and was discontinued after two courses. Only a late effect of radiotherapy was observed in our patient, probably due to damage of the vascular structures. This phenomenon has previously been described in the literature of HPC (Backwinkel and Diddams, 1970; Mira *et al.*, 1977). In these reports, a tumourous mass which was often still present after completion of radiotherapy, continued to shrink and sometimes disappeared after a few months (Mira *et al.*, 1977).

Conclusion

Our case presents (to our knowledge) the first report in the last 30 years of a patient with neurofibromatosis who developed a malignant schwannoma in the parapharyngeal space. When radical excision of a soft tissue sarcoma is not possible, radiotherapy may provide useful palliation. It should be noted that a markedly late (partial) response to radiotherapy can occur.

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