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CLINICAL STUDY

Recurrent malignant epitheloid schwannoma of the lower lip

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Abstract: The authors describe a case of recurrent malignant epitheloid schwannoma of the lower lip. Histologically, the tumor was composed of fibroblast-like spindle cells in compact fascicles and areas of epitheloid growth, combined with demonstration of S-100, GFAP and NF positivity, which is characteristic for this type of tumor. The therapy consisted of a combination of surgery and radiotherapy and the patient was followed-up since the disease was diagnosed. A local re-operation had to follow the first surgical intervention consisting of a radical excision of tumor in the lower lip together with suprahyoid neck dissection six months later.
After the first operation, the patient received a radiation therapy with a total dosage of 12 Gy in seven fractions to the tumor area of the lower lip. After the second operation, an external radiotherapy with total dosage of 50 Gy was applied.
Despite the complex intensive therapy, the patient died of metastases into lungs, liver and spine 37 months after the initiation of the therapy *(Fig. 2, Ref. 17)*. Full Text (Free, PDF) *www.bmj.sk.*
Key words: malignant epitheloid schwannoma, malignant neurilemmoma, neurogenic sarcoma, lower lip.

Malignant epitheloid schwannomas (malignant neurilemmomas, neurogenic sarcomas) are rare tumors that account approximately for 5 % of all head and neck sarcomas (Hamza et al, 1997). They are encapsulated, firm, slow-growing solitary tumors that arise from the Schwann cells covering the axons. Clinically, they can present a neck mass, usually in parapharyngeal space (16). They rarely appear as a non-pigmented nodule of the skin. They may behave locally aggressive and have also a high risk for distant metastases. An early and correct histological diagnosis is necessary for the appropriate complete oncological treatment. The presented case report describes the course of a recurrent lesion affecting the lower lip.

Case report

The patient, a 72-year-old male, experienced a non-healing defect of the lower lip.

He first visited a local hospital where an excision biopsy was taken and the sample evaluated as an anaplastic carcinoma of the inferior lip. Although being referred immediately, the patient came to the oncological outpatient department 6 months later with a recurrent tumour of the lower lip. The oncologist recommended radiotherapy. The next day, the patient was admitted to the Department of Dermatology and radiotherapy was initiated. The radiotherapy consisted of a total dosage of 12 Gy in seven fractions to the tumour area of the lower lip. During the patient's hospital stay, an oral surgeon was consulted and recommended examination at the Department of Oral and Maxillofacial Surgery, University Hospital in Bratislava.

One month later, the patient was admitted to this department. At that time he was in a generally good physical condition, with history of diabetes mellitus treated with diet and oral antidiabetics including glipizide and buformine hydrochloride; he admitted to have been smoking 20 cigarettes a day for 30 years, denied alcohol abuse and reported no other health problems.

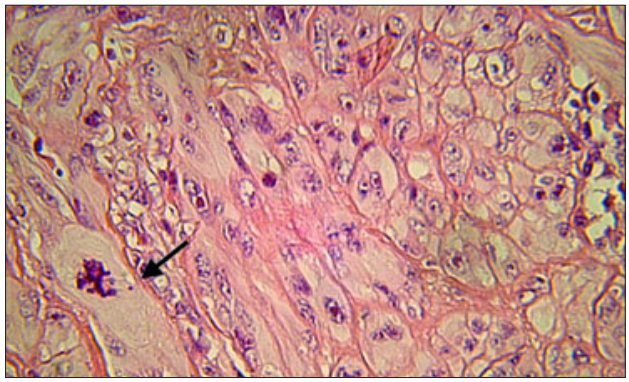

Fig. 1. Epithelioid schwannoma. The histological picture of the tumor mass comprises large epitheloid cells with marked cell borders. The presence of atypical bizarre cells with mitoses (arrow) suggests the malignant nature of the tumor. Haematoxylin and eosin, x400.

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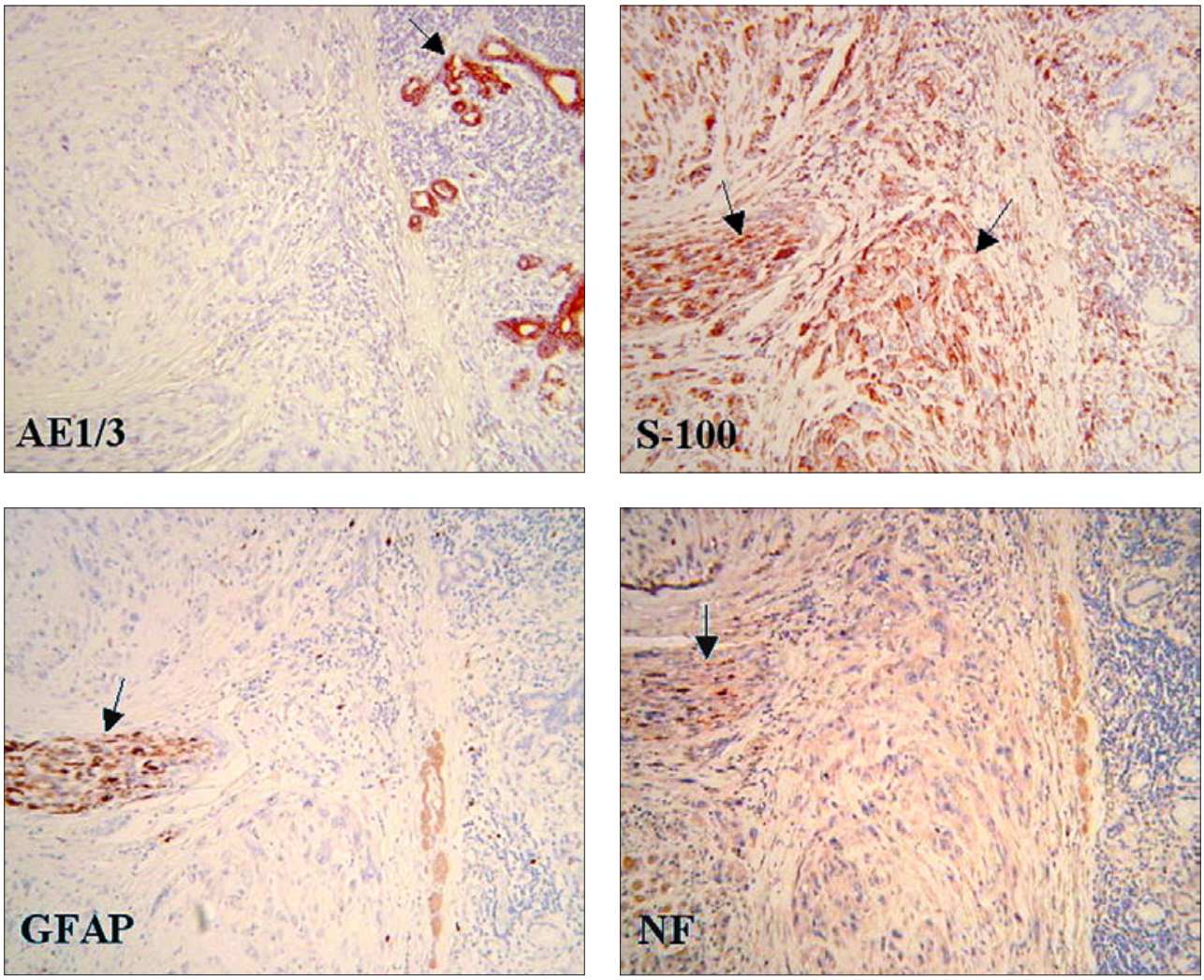

Fig. 2. Immunohistochemical analysis of the tumor mass adjacent to a salivary gland (right). Cytokeratins (AE1/3) are present only in ductal epithelial cells (arrow); S-100 protein is diffusely distributed in the tumor cells with a marked expression in nerve-like structures (arrow); neurophilaments (NF) are present in the cytoplasm of all tumour cells, best identifiable in the nerve-like structure (arrow). Avidin-biotin-peroxidase complex, diaminobenzidine, x250.

At the examination, a firm infiltrate was found in the lower lip on the right side, 15x25 mm in size, with a scar in the centre after the primary tumour excision with a superficial ulceration of 8 mm in diameter. The tumor was palpable, attached to the underlying tissue in the right submandibular area, along with a lymph node, 40x30 mm in size, clinically considered to be a regional metastasis. Based on the clinical examination, it was decided to perform a radical surgery to remove the tumour of the lower lip with subsequent plastic reconstruction using flaps from the adjacent tissue. At the same time, supraomohyoid neck dissection was performed with the removal of the lymph node metastasis. A histological examination proved it to be a metastasis in the submandibular lymph node. There were no signs of metastasis spread in the jugulo-digastric lymph nodes.

Five weeks after surgery, the patient continued to receive radiotherapy. A total dosage of 50 Gy was administered to the right region of the neck.

The patient was followed up at regular intervals. 6 months later, another local recurrence of the tumour was identified, at the primary site at the lower lip. At the same time a firm infiltrate was found below the level of the newly formed vermilion of the lower lip in the area of the alveolo-buccal groove, 30x20 mm in size. The tumour did not infiltrate the adjacent skin or mucosa. No pathology other than postoperative alterations could be found upon the examination of the neck (including ultrasound).

It was decided to remove the recurrent tumour surgically. Histopathology, a recurrence of the primary tumor was confirmed. Since there was no recurrence in the neck, an external radiotherapy TD 50 Gy was applied only to the area of the removed recurrence of the lower lip. During and after the radiotherapy,

the patient was checked at regular intervals by an oncologist and a maxillofacial surgeon.

One year later, the patient visited this Department for the follow up and a metastasis was suspected in the right clavicle area. CT and X-ray examinations were recommended. These revealed metastases also in lungs and liver. The patient died of an advanced metastatic malignancy one month later.

A pathological examination was performed at the Department of Pathology, Comenius University, Bratislava.

Histopathology

Tissue specimens were routinely fixed in 4 % formaldehyde, membedded in paraffin and 5 μm thick slices were stained with haematoxylin and eosin, mounted in plastic resin and evaluated munder the light microscope. Then 5 more m thick slices were deparaffinised, incubated for 5 minutes with 1 % H_2O_2 in ethanol for endogenous peroxidases exhaustion, boiled in citrate buffer, pH 6.0 for 10 minutes for antigen retrieval, transferred into phosphate buffered saline (pH 7.4), and processed in an automated stainer with primary antibodies against S-100 protein, cytokeratin cocktail (AE1/3), glial fibrillar acidic protein (GFAP) and neurofilaments (NF). The antibodies were obtained from DAKO, Glostrup, Denmark. A color reaction was developed with diaminobenzidine (DAKO); the slides were counterstained with haematoxylin. The first biopsy specimen was from the radical resection of the recurrence with the submandibular lymph node. The first biopsy – which included the two metastases in the lymph nodes – was diagnosed as low-differentiated carcinoma with focally sarcomatous appearance. One and half year after the first operation, the local recurrence was removed. That specimen was thoroughly analyzed at this institution. The histomorphological picture revealed fibroblast-like spindle cells in compact fascicles and areas of epitheloid growth (Fig. 1), combined with S-100, GFAP and NF positivity (Fig. 2). Therefore the tumour was reclassified to the malignant epitheloid schwannoma.

Discussion

Growth pattern: Superficial malignant schwannoma is a dermal/subcutaneous lesion that is usually circumscribed, consisting of spindle or epitheloid cells in short interdigitating fascicles, moulded together in nevoid clusters or in sheets and clumps separated by fibromyxoid stroma. It may contain spindle cell areas that blend into more epitheloid areas, particularly in recurrent tumors. It shows no evidence of melanocytic functional activity in the overlying epidermis. Secondary features may include ulceration of the overlying epidermis, haemorrhage and necrosis of the inflammatory infiltrate.

Cell morphology: The epitheloid cells are medium-sized or large, rounded or polygonal, mimicking melanoma or carcinoma cells. They have abundant cytoplasm and oval or irregular nuclei containing prominent nucleoli. A few mono- or multinucleated giant cells may be seen. Occasionally, the cells are small with little cytoplasm and arranged in cords reminiscent of lobular carcinoma of the breast. Some cells have signet ring morphology due to the accumulation of intracellular lipid droplets. Sometimes, the tumor cells appear clear or rhabdoid. Mitotic figures are frequent. Malignant schwannomas are a subgroup of soft tissue sarcomas; they may be associated with von Recklinghausen's disease but also occur isolated. The majority of these tumors express S-100 protein and NSE; they lack melanoma-associated antigens and cytokeratins. The cells are vimentin positive (1, 2).

The following guidelines are recommended by Gupta for the adequate management of malignant schwannomas in general:

1) Wide excision of not only the tumour itself but also of the surrounding neurovascular, subcutaneous and bony tissue remains the mainstay of an adequate treatment (7). The high rate of local recurrences described in the literature points at the problem of an insufficient tumor removal, as demonstrated in this article.

2) According to several studies, lymphatic metastases are rare in malignant schwannomas (1, 2, 4). Routine lymphadenotomy is therefore not recommended for patients with malignant schwannoma (5, 6). In this case, the patient came to the department with a local recurrence and metastases to local regional submandibular lymph nodes, which was an indication for a neck dissection.

3. The use of adjuvant radiation or chemotherapy after surgical excision of the tumour is frequently recommended in literature for T2 and T3 soft tissue sarcomas, whereas excision alone is adequate for T1 tumours (2, 4, 6). In the case described, there were recurrences and lymph node metastases. Thus, radiotherapy was indicated postoperatively and administered in full therapeutical dose.

Grevers described in their case report a patient with similar recurrent malignant epitheloid schwannoma, who had to undergo repeated surgeries due to local recurrences (8). That patient was followed up for a shorter period of time than ours and unfortunately the data about the patient's metastatic diseases and his survival are not available.

Hamza described fourteen patients with neurilemomas of the parapharyngeal space (9). The authors recommended that computed tomography and/or magnetic resonance studies should be routinely done to evaluate tumors of the parapharyngeal space.

Henkel reported a case of a similar tumour as described herein but in a different, though anatomically close location (10). It was a recurrent malignant epitheloid schwannoma of the inferior alveolar nerve. Submandibular lymph node metastases were detected already upon the primary surgery, thus, supraomohyoid neck dissection was carried out along with tumor removal (hemimandibulectomy with subsequent reconstruction) during the first surgery. Despite a thorough removal and exploration of margins of the removed tissue, which appeared negative, the patient's tumour recurred locally after eight months. Subsequent removal and histopathological examination showed a complete removal again. The tumour had recurred despite of a comprehensive anti-tumor therapy. Radicality is usually not effective for recurrences (15, 16).

Martinez Devasa reported a case of a low-grade epithelioid-type malignant peripheral nerve sheath tumor (MPNST) of the lower lip, with no recurrence after surgery and radiotherapy (14).

Colmenero reported 7 cases of MPNSTs. One included the lower lip – this was treated with wide local excision and radiotherapy (3). A recurrence one month later was treated by a resection of the whole lower lip and segmental mandibulectomy with no evidence of the disease after 9 months.

Laskin et al specifically described the epithelioid variant of MPNST – although none of their 26 cases involved head and neck (12). Discussion in this paper might be helpful to compare clinical behavior and management of this variant in different anatomical regions.

In addition, Lodding reported a light and electron microscopic, immunohistochemical, clinical and prognostic study of 14 patients with epithelioid malignant schwannoma (13). Honma reported a case of epithelioid malignant schwannoma involving the axillary fossa (11). Sestan described an intraosseous epithelioid malignant schwannoma of the tibial shaft (17). Recurrent malignant epithelioid schwannoma of the head and neck regions is a rare condition. Considering its severity and poor prognosis, it should be managed at institutions able to take the best care and to administer a comprehensive anti-tumour treatment. Due to tendency to recur and form metastases in lymph nodes and also in distant organs, the surgery requires to be appropriately radical, followed by a thorough follow-up. This should reveal the recurrence – if any – as soon as possible and allow a subsequent adequate intervention.

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