



# Malignant peripheral nerve sheath tumor (MPNST) arising from angiosarcoma: a rare case report

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## Abstract

**Purpose** An extremely rare case of divergent differentiation of a cutaneous angiosarcoma to a malignant peripheral nerve sheath tumor (MPNST) is presented.

**Methods** A 62-year-old male patient presented with an angiosarcoma of the left buccal region, which was excised with wide surgical margins. Four months after the operation, the tumor recurred locally as a MPNST. The recurrent tumor was treated with surgical excision followed by postoperative radiotherapy. Four years later, the patient presented with solitary lung metastasis. The patient underwent upper right lobectomy.

**Results** The patient is alive and disease-free 2 years after the lobectomy and 6 years after initial presentation.

**Conclusions** Divergent differentiation of an angiosarcoma to a neurosarcoma supports the theory that cells of the neural crest capable of differentiating both to neuroectoderm and to mesenchyme give origin to these tumors.

**Keywords** Malignant peripheral nerve sheath tumor · Head and neck sarcoma · Angiosarcoma · Divergent differentiation

## Introduction

Malignant peripheral nerve sheath tumors (MPNSTs) arise from peripheral nerve sheaths *de novo* or in association with plexiform neurofibromas and have an extremely high predilection for patients with neurofibromatosis type 1 (NF-1) [1]. Angiosarcoma is a rare endothelial-derived tumor with a very poor prognosis. The head and neck variety of the tumor

mainly affects the scalp and the face and most commonly presents itself as an exophytic, enlarging mass [2]. Angiosarcoma arising as a transformation of a preexisting MPNST tumor is an extremely rare occurrence [3]. A MPNST (sarcoma) arising as a transformation of an angiosarcoma has not been reported in the literature. We present a case of a facial cutaneous angiosarcoma, which recurred locally and distally as a metastatic MPNST.

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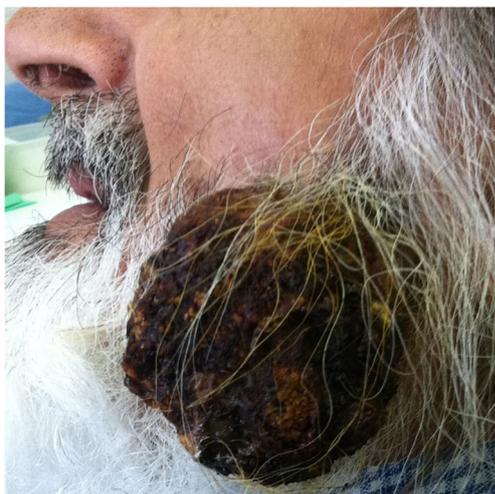
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## Case report

A 62-year old male presented at the Maxillofacial Surgery Department (Anticancer Hospital Theagenio, Thessaloniki, Greece) with a painless, large (7.5 × 6 cm) exophytic cutaneous mass of the left buccal region (Fig. 1). The patient suffered from diabetes type 2 which was adequately controlled with metformin. The patient reported that the mass appeared 30 years ago but had progressively and rapidly enlarged during the last 3 months. A computed tomography (CT) was performed to determine the extent of the lesion. The lesion appeared solid, non-homogenous, with an obvious thickening of the surrounding skin without invading deeper structures



**Fig. 1** Photograph showing the exophytic tumor of the left buccal region at the initial presentation

(Fig. 2). The initial biopsy was indicative of a high-grade sarcoma.

In the first operation, wide excision of the tumor along with 1.5–2 cm of surrounding skin was performed with simultaneous en bloc superficial parotidectomy, excision of a part of the masseter muscle, malar fat pad, and buccinator muscle, and simultaneous removal of the contents of submandibular triangle. The mandibular branch of the facial nerve was sacrificed as it could not safely be separated from the tumor mass without compromising tumor integrity. The defect was covered with a bilobed cervical-deltpectoral rotational flap. Split-thickness skin graft from the thigh was used to cover the skin defect that remained in the deltoid region. Postoperatively, limited partial flap necrosis occurred, which

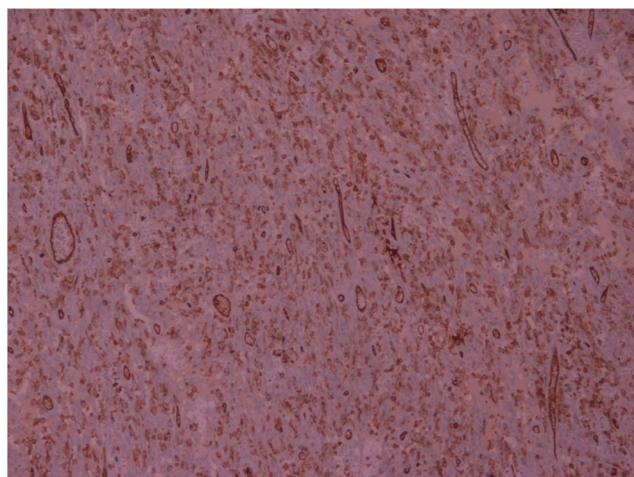


**Fig. 2** CT image showing a large mass deriving from the skin with non-homogenous contrast enhancement

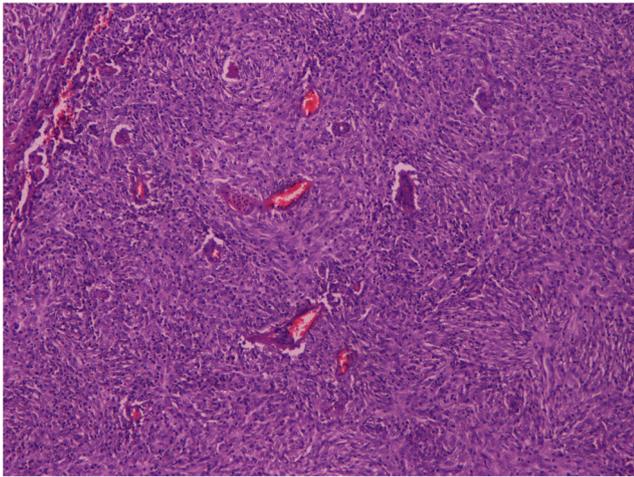
was adequately treated with conservative local measures. The pathologic examination of the specimen was reported as an angiosarcoma with components of a basal cell carcinoma of the skin. On hematoxylin-eosin (H-E) stained sections, focal areas of irregularly anastomosed vessels were present together with fascicles of neoplastic cells. Throughout the tumor, there were numerous mitotic figures as well as areas of necrosis. Some areas showed typical features of basal cell carcinomas. All the peripheral and deep margins were free of tumor invasion. The tumor infiltrated the dermis but did not extend to the underlying adipose or salivary gland tissue. The tumor stained positive to vimentin, CD 31 (Fig. 3), and SMA (smooth muscle actin) and negative to S-100, desmin, MelanA, CD 34, factor VIII, HHV8, keratin AE1/AE3, keratin 5/6, keratin HMW, and to HMB 45. Five lymph nodes were isolated from the submandibular triangle, which were all negative for tumor invasion.

The patient did not receive adjuvant therapy at that time and remained under regular follow-up.

Four months later, the patient presented with local recurrence located at the region of the zygomatic arch. The second operation included removal of the exophytic mass with 1–1.5 cm of the surrounding skin to the level of periosteum with simultaneous en bloc removal of the zygomatic arch and bone and the remaining parotid gland and sacrifice of the temporal branch of the facial nerve. The defect was covered with a split-thickness skin graft taken from the thigh. The histopathology report was different than that of the previous operation. It revealed the presence of a high-grade peripheral nerve sheath tumor (MPNST) with a high level of mitotic activity (16/10 HPF) and sparse necrotic areas. The tumor was mainly composed of spindle-shaped cells arranged in bundles (Fig. 4). The tumor tested positive to vimentin and focally to protein S-100 (Fig. 5). The peripheral and deep surgical margins were free of tumor invasion, but the “barrier” of normal tissue was



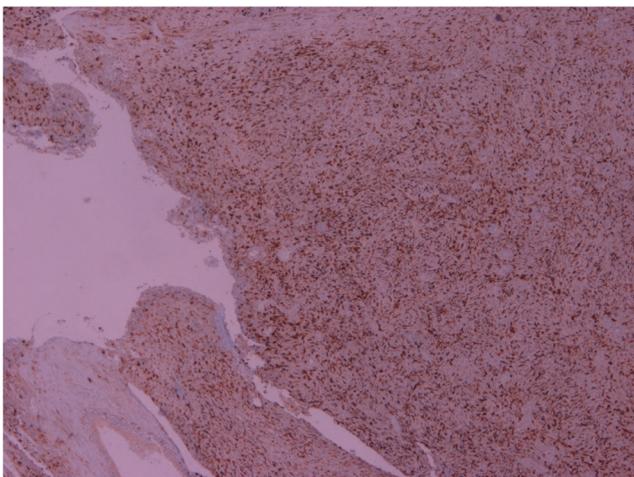
**Fig. 3** Immunohistochemical analysis of angiosarcoma showing positive staining to CD 31 protein (CD 31 X4)



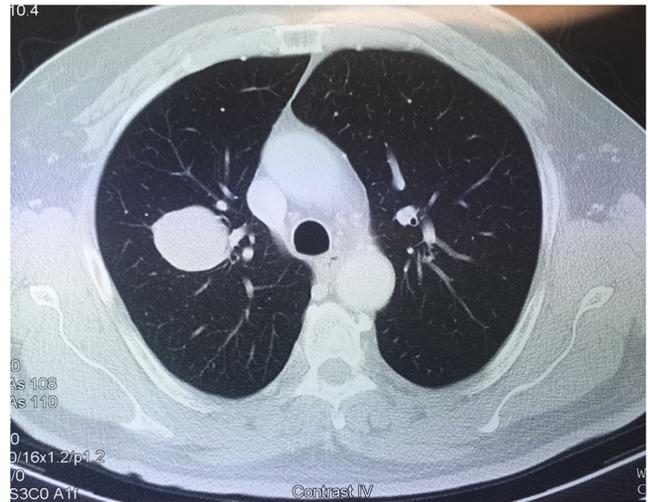
**Fig. 4** Histological section of MPNST (HEX4)

thin. The patient received adjuvant locoregional radiotherapy (6000 cGy).

Four years later, the patient started to smoke again. In the routine chest radiograph and in the CT scan that followed, a mass of 4.3 cm of maximum diameter revealed itself, located at the upper lobe of the right lung (Fig. 6). A CT-guided core biopsy was subsequently performed, which revealed the presence of metastatic sarcoma. Due to the absence of other metastatic foci, an upper right lobectomy was performed. The final histology report confirmed the presence of MPNST (sarcoma). The tumor cells resembled the features of the primary site cells. The tumor composed mainly of spindle-shaped cells with marked mitotic activity. Cartilage elements could also be identified. The tumor cells tested positive to S-100 protein, to CEA, and to the CD 56 marker. The surgical margins were negative. The patient has been systematically followed up with regular multispecialty clinical and radiological control and did not reveal any local or distant metastasis 24 months following the lobectomy.



**Fig. 5** Immunohistochemical analysis of MPNST showing positivity to S-100 protein (S-100 X4)



**Fig. 6** CT image showing a single metastatic lesion of the right lung

## Discussion

Cutaneous angiosarcomas of the face are extremely rare tumors arising from capillary and lymphatic endothelial cells. These tumors may be sporadic or may be associated with preexisting lymphedema or previous radiotherapy [4]. They have a very poor prognosis and a very high propensity for local recurrence even after optimal local and regional treatment [5]. Patel et al. [6] found in their series an overall 5-year survival of 38%, with younger patients (< 70 years) exhibiting a significantly better prognosis than older counterparts. It is generally accepted that multimodality combined treatment offers a significantly better chance for survival, and most authors recommend wide surgical excision combined with postoperative radiotherapy and sometimes adjuvant chemotherapy [6–8]. It has been reported, however, that status of surgical margins (positive or negative) did not significantly alter survival rates, but combined treatment did [8]. This patient presented with a cutaneous angiosarcoma of the face with focal areas of typical basal cell carcinoma. The clinical course of the tumor suggests that an angiosarcoma developed on the basis of a basal cell carcinoma. This is the first case, to our knowledge, in which an angiosarcoma developed on the basis of a long-term pre-existing basal cell carcinoma. The tumor was excised in wide surgical margins. However, no adjuvant therapy was performed at that time. The tumor rapidly recurred locally, no longer as an angiosarcoma but as a MPNST.

MPNSTs arise from the elements that comprise the nerve sheaths, namely, the Schwann cells and the perineural fibroblasts. Occasionally, the patient suffers from neuropathic symptoms, such as pain, paresthesia, or motor weakness depending on the involved nerve. The majority of these tumors are high-grade tumors with marked mitotic activity. Surgery followed by radiotherapy is the best treatment option. Adjuvant chemotherapy has not shown any additional benefits

[9]. Five-year survival ranges from 16 to 60%. Wide excisions and adjuvant high-dose radiotherapy have shown survival benefits [9, 10].

Angiosarcomas that arise from pre-existing MPNSTs have been reported in the literature, although they are exceptionally rare [11]. Few cases of simultaneous existence of focuses of MPNST and angiosarcoma in the same tumor have also been reported [3]. Rhabdomyosarcomas and even squamous cell carcinomas have also been reported to arise on the basis of MPNSTs. In our case, a MPNST arose as a local recurrence from a pre-existing angiosarcoma. Apart from a distinct change to the histologic structure of the recurrent tumor, there was also an immunohistochemical confirmation of divergent differentiation of the tumor cells. The primary tumor stained positive to CD 31, a platelet-endothelial cell adhesion molecule, and SMA, which are markers identified in angiosarcomas. The recurrent tumor lost positivity to CD 31 and stained positive to S-100 protein, which tested negative to primary tumor. The metastatic site to the lungs had the same histologic and immunohistopathologic features of the recurrent tumor. To our knowledge, this reverse differentiation of a vascular sarcoma to a neurosarcoma has never been reported before in the published literature.

This capacity of divergent differentiation of neuroectodermic tumors has been attributed to the marked ability of neoplastic neuroectoderm to differentiate into heterogeneous tissues such as muscular tissue giving rise to rhabdomyoblastomas or vascular tissue giving rise to angiosarcomas. Bone and cartilage have also been described in MPNSTs due to this pluripotent differentiation [12]. Cartilage has also been found in our case in the metastatic site, which was located inside the lungs. This theory does not satisfactorily explain the reverse differentiation from an angiosarcoma to a neurosarcoma that occurred in our case. Another theory supports that cells of the neural crest capable of differentiating both to neuroectoderm and to mesenchyme give origin to these tumors [13]. This theory gives a better explanation to this case, as the same neoplastic cell is capable of differentiating into different types of sarcomas. However, both theories cannot satisfactorily explain the epithelium-derived tumors that rarely arise from MPNSTs.

In this case, a long-standing basal cell carcinoma became a high-grade angiosarcoma probably due to genetic defects that predisposed the patient to malignancies. Despite the wide local excision, the angiosarcoma quickly recurred, which highlights the need for adjuvant radiotherapy that, according to the literature, may have locally controlled the disease. The tumor recurred as a MPNST, suggesting that the neoplastic cell was capable of differentiating into both neuroectoderm and into mesenchyme. Adjuvant radiation succeeded in locally controlling the disease, but a distant sole lung metastasis appeared 4 years following surgical excision. The patient underwent

upper right lobectomy and 20 months after surgery, the patient is alive and disease-free.

## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** This article does not contain any studies with human participants or animals performed by any of the authors.

**Informed consent** This article does not contain any studies with human participants or animals performed by any of the authors.

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