

## Malignant ectomesenchymoma of the paranasal sinuses with proptosis

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**Key-words.** Malignant ectomesenchymoma; soft tissue tumour; neuroectodermal elements; mesenchymal neoplastic elements

**Abstract.** *Malignant ectomesenchymoma of the paranasal sinuses with proptosis.* *Problem:* A 36-year-old woman presented with a feeling of pressure in the right orbit and proptosis of the right eye after a “common cold”.

*Methodology:* Computed tomography (CT) of the maxillofacial region revealed, and endoscopy confirmed, a mass in the right ethmoid sinus, eroding the lamina papyracea and extending into the orbit. Pathology of multiple biopsies revealed a nasal neoplasm composed of neuroectodermal and mesenchymal neoplastic elements, suggestive of a malignant ectomesenchymoma (MEM). Magnetic resonance imaging was used for MEM staging. Computed tomography of the chest and abdomen show no evidence of distant metastases.

*Results:* Due to the intracranial and intraorbital extension of the tumour, radical surgery was not an option. Appropriate chemotherapy (6 cycles of vincristine/ifosfamide/adriamycin and 2 cycles of vincristine/ifosfamide/cisplatin) and intensity-modulated radiation therapy were administered.

*Conclusion:* Twenty-eight months after treatment, there was no evidence of residual or metastatic disease.

### Introduction

According to the histological classification of the World Health Organization, malignant ectomesenchymoma (MEM) belongs to the soft tissue tumour group. The most widely accepted theory suggests that MEM arise from the ectomesenchyme, which gives rise to pluripotent migratory neural crest cells that can differentiate into neuroectodermal and mesenchymal tissues. Because these pluripotent cells are widely distributed throughout the body, MEMs may arise in diverse sites within the soft tissue or in the central nervous system. Neuroectodermal elements are mainly represented by ganglion cells or neuroma-like structures (such as neuroblastoma) and mesenchymal components usually consist of rhabdomyoblastoma.<sup>1</sup> This highly

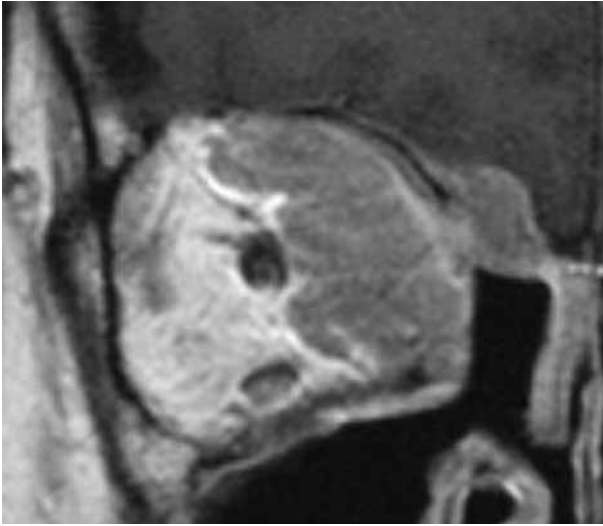
malignant tumour predominantly affects children and young adults, and spreads by direct extension and hematogenous and lymphatic dissemination. MEMs are predominantly located in the central nervous system, abdominal organs, extremities, middle ear, nasopharynx, and neck. Location in the nasal cavity is rare.<sup>1</sup> To our knowledge, this case is only the third published case describing a MEM of the nose.

### Case report

A 36-year-old woman with no relevant medical history, presented to the otolaryngology department in September 2007 with a feeling of pressure in the right orbit and proptosis of the right eye. One week earlier, she had an upper respiratory tract infection with symptoms of nasal conges-

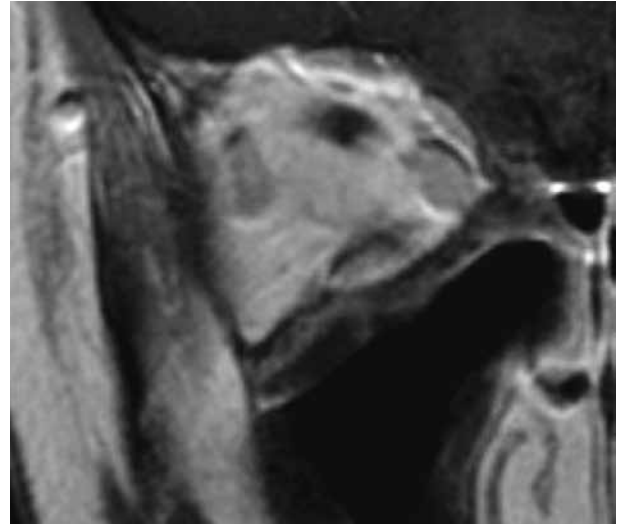
tion, cough, and postnasal drip. Despite antibiotic therapy with amoxicillin clavulanic acid the symptoms worsened. However, blood analysis was normal.

Computed tomography (CT) of the maxillofacial region, performed in another hospital, revealed a mass in the right ethmoid sinus that was eroding the lamina papyracea and extending into the superomedial part of the orbit. Although some erosion of the cribriform plate and fovea ethmoidalis was also visible, there was no evidence for extension into the anterior cranial fossa. Because the differential diagnosis between a tumour and an atypical peri-orbital abscess was made, an urgent functional endoscopic sinus inspection was undertaken. During this procedure, hyperplastic mucosa without purulence was seen in the anterior ethmoid sinus



*Figure 1*

Coronal gadolinium-enhanced T1-weighted image, showing intra-orbital and intracranial tumour extension on initial presentation (21-09-2007).



*Figure 2*

Coronal gadolinium-enhanced T1-weighted image after chemoradiotherapy, showing regression of tumour mass (10-09-2008).

and a soft tissue mass was revealed that extended from the right ethmoid sinus into the orbit. Multiple biopsies were taken from this soft tissue mass. Pathology showed a positive staining for desmin and myogenin, suggesting rhabdomyosarcoma. However, there was also a positive staining for chromogranin and neurofilament, which are elements of a neuroblastoma. The composition of this primitive neuroectodermal tumour with elements of both rhabdomyosarcoma and neuroblastoma is pathognomonic for an MEM.

Because of this unexpected pathology, staging included a magnetic resonance imaging (MRI) study of the maxillofacial region to evaluate regional extension and a CT study of the chest and abdomen to exclude dissemination and distant metastasis. On MRI, the tumour showed intra-orbital extension, involving the superior and medial rectus muscle, as well as some intracra-

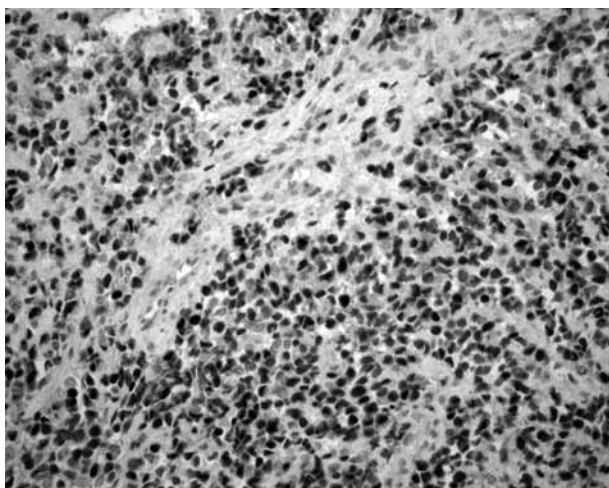
nial extension with thickening and enhancement of the dura (Figure 1). CT study of the chest and abdomen did not show evidence for distant metastases. Because it was locally advanced, with intra-orbital and intracranial extension, the tumour was considered inoperable.

The patient was treated with a combination of chemotherapy and radiation therapy. Chemotherapy consisted of 6 cycles of vincristine 1.2 mg/m<sup>2</sup>, ifosfamide 3 g/m<sup>2</sup> and adriamycin 20 mg/m<sup>2</sup> (VIA) and 2 cycles of vincristine 100 mg/m<sup>2</sup>, ifosfamide 2 g/m<sup>2</sup> and platinol 30 mg/m<sup>2</sup> (VIP). Afterwards, intensity-modulated radiation therapy was delivered to the residual tumour at a total dose of 66 Gy. An MRI study 12 months after chemoradiotherapy showed a significant reduction in tumour volume (Figure 2). At 28 months after therapy, clinical examination, endoscopy, CT and MRI revealed no evidence of loco-regional recurrence or metastases.

## Pathology

Because it was the sole determinant for the diagnosis of MEM, the pathologic characteristics of this tumour type will be emphasized hereafter. As mentioned above, MEM is composed of two main components: a mesenchymal element (most often rhabdomyosarcoma) and a neuroectodermal element (often neuroblastoma).

The tumour in this patient had intermixed primitive mesenchymal and neuroectodermal components, as demonstrated by immunocytochemistry. One tumour component included cells that were positive for markers of skeletal muscle differentiation, including desmin and myogenin (Figure 3). The other tumour component was composed of cells that were positive for markers of neuroectodermal differentiation, including chromogranin (Figure 4a) and neurofilament (Figure 4b). The occurrence of two elements of



*Figure 3*

Positive nuclear myogenin staining, indicating skeletal muscle differentiation.

primitive neuroectodermal origin, a mesenchymal element and a neuroectodermal element, is pathognomonic for MEM.

### Discussion

MEM is an uncommon neoplasm composed of neuroectodermal and mesenchymal neoplastic elements. While MEM appears to have a predilection for the genital organs, this tumour type may affect any region of the body, including the central nervous system, abdominal organs, extremities, middle ear, nasopharynx, and neck.<sup>1</sup> However, location of MEM in the nasal cavity is very rare. The pathologist has a crucial role in the detection of the biphasic aspect of the tumour on pathologic examination. Difficulties with the pathological examination, diagnosis, differential diagnosis, staging, treatment and prognosis will be discussed.

#### *Rarity of the diagnosis*

To our knowledge this case is only the third published case describ-

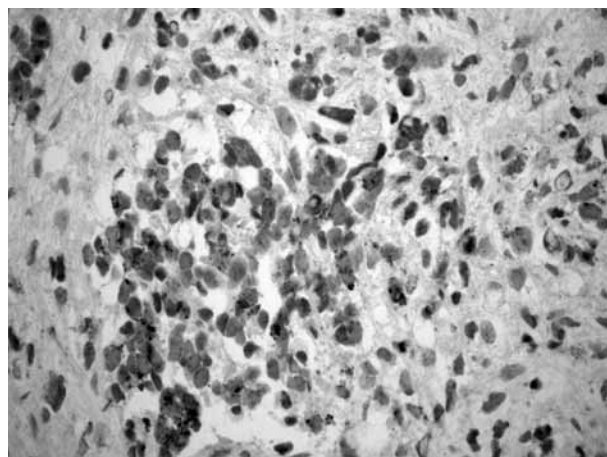
ing a (para)nasal MEM. The first case was a 62-year-old man who was treated with surgery (in toto resection via endoscopic surgery) and adjuvant radiation therapy to the nasal cavity (59,4 Gy).<sup>1</sup> After 36 months, there was no recurrence noted. The only other case, a 62-year-old male, was treated with trimodal therapy: surgical resection, chemotherapy (weekly cisplatin 45 mg total), and radiotherapy (50 Gy total),<sup>2</sup> and was without recurrence after a follow-up of 17 months. These two previous cases presented with symp-

oms of nasal obstruction. Our patient complained of proptosis without nasal obstruction.

#### *Difficulty of the diagnosis*

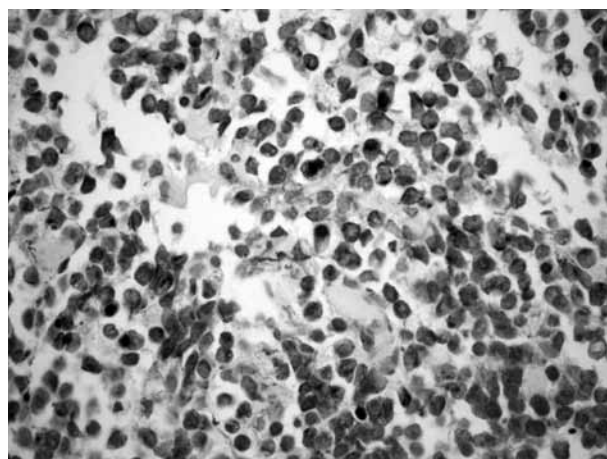
As mentioned above, the sole determinant for the diagnosis of MEM is the typical biphasic aspect of the tumour, revealed by pathologic examination.<sup>3</sup>

First, the pathologic diagnosis of MEM can pose problems when only small specimens of the tumour are available. Because the neural components are easily



*Figure 4a*

Positive chromogranin staining, indicating neuroectodermal differentiation.



*Figure 4b*

Positive neurofilament staining, indicating neuroectodermal differentiation.

overlooked, ectomesenchymomas (as MEM) are frequently confused with rhabdomyosarcomas.<sup>3</sup> For this reason multiple biopsies have to be taken.

Second, the pathological diagnosis depends on how strictly both components are defined. MEM is defined as the combination of neuroblasts and/or ganglion cells and malignant mesenchymal tissues of various types, usually rhabdomyosarcoma.<sup>4</sup> The jury is still out regarding whether ganglion cells are essential in the neuroectodermal component. In the present case, ganglion cells were absent, possibly due to sampling error.

#### *Differential diagnosis*

In the present case, a peri-orbital abscess was initially suspected due to the recent history of an upper respiratory tract infection and proptosis. The worsening of symptoms despite antibiotic therapy with amoxicillin clavulanic acid and normal blood analysis rendered a tumour of the nasal cavity more plausible. Owing to the predominance of epithelial differentiation, the differential diagnostic consideration should include a poorly differentiated neuroendocrine carcinoma, olfactory esthesioneuroblastoma and rhabdomyosarcoma.<sup>1</sup>

#### *Further investigation & staging*

MEM spreads by direct extension, as well as haematogenous and lymphatic dissemination.<sup>1</sup> Staging was performed with an MRI study of the maxillofacial region to evaluate regional extension, as well as a CT scan of the chest and abdomen to exclude dissemination and distant metastasis.

#### *Treatment and prognosis*

Due to its rarity, the different sites where it can arise, and the difference in age of patients who present with this tumour, there is no solid consensus on the optimal therapy for MEM.<sup>2</sup> In the present case, treatment was focused on the most common malignant component of MEM, which is rhabdomyosarcoma. Due to the local advancement in the present case, radical surgery was not an option and we therefore opted for chemotherapy combined with external radiation therapy as for rhabdomyosarcoma. In the literature, the best therapeutic approach for ectomesenchymoma seems to be a combination of surgery, radiation therapy and chemotherapy.<sup>2</sup>

The present case was the first case of nasal MEM where surgery was not part of the treatment. Nevertheless, after 28 months of follow-up, no evidence of residual or metastatic disease was observed. Because the present case showed excellent radiosensitivity, the necessity of surgery in the treatment of MEM can be discussed.

The prognosis associated with MEM depends on the resectability of the tumour and its stage at diagnosis. A survival rate of 60% over a follow-up interval of 15 months to 12 years has been reported in the literature.<sup>5</sup>

#### **Conclusion**

MEM is a rare soft tissue tumour composed of both neuroectodermal and mesenchymal neoplastic elements, and its proper identification is clinically critical. MEM can be identified only by careful morphological examination and broad-spectrum immunostaining.

The diagnosis is made on the typical biphasic aspect of this tumour and cannot be identified using small pathological specimens. According to the literature, the best therapeutic approach for ectomesenchymoma seems to be a combination of surgery, radiotherapy, and chemotherapy. Due to local tumour advancement, radical surgery was not an option in the present case and appropriate chemoradiation therapy was administered as for rhabdomyosarcoma. A 28-month follow-up examination revealed no evidence of residual or metastatic disease.

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