CASE REPORT

Inflammatory myofibroblastic tumour of paranasal sinuses with fatal outcome: reactive lesion or tumour?

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Inflammatory myofibroblastic tumours (IMTs) are clinicopathologically distinctive but biologically controversial entities, which have been described in the lungs, abdomen, retroperitoneum, and extremities, but rarely affect the head and neck region. IMT usually follows a benign clinical course after radical excision, but invasive, locally recurrent, and metastatic forms of abdominal and mediastinal IMT have also been described. This report describes a case of IMT of the paranasal sinuses with a fatal outcome. A 22 year old woman was admitted to hospital as a result of epistaxis. Computed tomography scan and magnetic resonance imaging showed an expansive process in the paranasal sinuses, extending into the nasal cavity, orbita, and endocranium. The tumour progressed despite several surgical procedures. Radiotherapy, corticosteroids, and chemotherapy were unsuccessful, and the patient died four years after diagnosis, as a result of extensive intracranial spread of the tumour. This is the first known case of an IMT of the head and neck region with a fatal outcome. It shows that the aggressive behaviour of IMTs is not limited to abdominal and mediastinal locations, and supports recent observations that at least a subset of IMTs represents true neoplasia rather than reactive myofibroblastic proliferation.

An inflammatory myofibroblastic tumour (IMT) is a clinicopathologically distinctive but biologically controversial entity that was originally described as a non-neoplastic lesion in the lung and designated initially as an inflammatory pseudotumour.¹ Since then, similar lesions have been seen in diverse extrapulmonary sites, most commonly the abdomen, retroperitoneum, and extremities.^{1,2} In most cases, IMTs behave as benign lesions, but invasive, locally recurrent, and metastatic forms of abdominal and mediastinal IMT have also been reported.³

"An inflammatory myofibroblastic tumour is a clinicopathologically distinctive but biologically controversial entity that was originally described as a non-neoplastic lesion in the lung"

IMTs rarely affect the head and neck region. To date, 19 cases of IMT have been described in the nasal cavity and maxillary sinuses,⁴ nine have been described in the oral cavity (with the mandible as the site of predilection),⁵ and only a few well documented IMTs have been found in the larynx.⁶ In general, they have followed a benign clinical course, with favourable outcome after radical local excision.⁴⁻⁶

We report a case of IMT in a 22 year old woman, occurring in the paranasal sinuses, with a fatal outcome.

Figure 1 Magnetic resonance image of the tumour.

CASE REPORT

A 22 year old pregnant woman was admitted to hospital as a result of epistaxis in August 1996. A capillary haemangioma was diagnosed from a small biopsy taken from her left nasal cavity. One month later, a protrusion of her left eye appeared. The computed tomography (CT) scan and magnetic resonance imaging showed an expansive process in the paranasal sinuses, which was extending into the nasal cavity and septum, left orbit, and endocranium. After termination of pregnancy, the tumour was resected with a sublabial approach, but reappeared a month later. After a second operation, the patient was unsuccessfully treated with radiotherapy (total dose 30 Gy) and corticosteroids. The tumour progressed, despite several surgical procedures. In September 1999, a total maxillectomy and exenteration of the left orbit was performed as a result of massive tumour involvement. A nine week course of chemotherapy with Endoxan (500 mg/week) was started in March 2000. Subsequently, a combined ear, nose, and throat and neurosurgical team performed resection of a recidivant destructive tumour from the nasal cavity, paranasal sinuses, anterior, and middle cranial fossae. In November 2000, the tumour mass was rapidly growing again and filled all the surgical defects, with multifocal infiltration of the brain and massive intracranial and right orbital spread (fig 1; CT scan, frontal view). After more than seven operations, accompanied by corticosteroids and radio/chemotherapy, only palliative treatment was administered. The patient died four years after the initial diagnosis.

On histology, the tumour was composed of an admixture of spindle cells, forming both a fascicular and storiform growth

Abbreviations: CT, computed tomography; IMT, inflammatory myofibroblastic tumour

Figure 2 Inflammatory myofibroblastic tumour. Haematoxylin and eosin stain.

pattern, and inflammatory cells (fig 2). The nuclei of the spindle cells were elongated, slightly polymorphous, and contained one or more small nucleoli and pale eosinophilic cytoplasm. Occasional regular mitoses in the spindle cell component were seen. No necroses or ganglion-like cells were seen. Inflammatory cells were mainly lymphocytes and plasma cells, unevenly distributed within the lesion. Lymphocytes were polyclonal. Polymorphonuclear cells, predominantly eosinophils, were also admixed in the inflammatory infiltrate.

Immunohistochemically, the spindle cells were consistent with a myofibroblastic phenotype. They were vimentin and smooth muscle actin positive, but desmin and cytokeratin negative. In addition, the spindle cells were not reactive with antibodies specific for cyclin D1, p53, bcl-2, or ALK. Special stains for microorganisms, including mycobacteria and fungi, in addition to viruses (Epstein-Barr virus in situ hybridisation), were negative.

DISCUSSION

The most common clinical presentation of IMT is as an incidentally discovered mass, followed by specific symptoms related to the site of origin. Intraorally, these tumours present as a painless swelling of relative short duration, which is firm and indurated on physical examination.⁵ In the nasal cavity and paranasal sinuses, the initial presenting sign is usually a non-specific sinonasal mass, which had been growing over a period of months or years.⁴ The clinical or endoscopic findings may demonstrate a tumefaction covered by normal mucosa, a polyp, an oedematous mucosa, hypertrophic concha, or a haemorrhagic rhinorrhoea.⁴ IMTs located in the paranasal sinuses are usually associated with at least one sinus wall destruction.⁴

Although IMTs of the nasal cavity and maxillary sinuses have no age preference, patients with oral IMTs are usually children or young adults.^{4,5} Unlike their counterparts at other locations, IMTs of the nasal cavity, maxillary sinuses, and oral cavity are generally not associated with non-specific systemic symptoms, such as unexplained fever, weight loss, and laboratory abnormalities.^{1,3,4}

CT scan and/or magnetic resonance imaging of IMTs in the head and neck region often suggest infiltrative growth and aggressive malignant potential.³ Therefore, correct diagnosis is imperative to prevent unnecessary overtreatment.

Histologically, IMT is composed of myofibroblastic spindle cells, admixed with a prominent infiltrate of lymphocytes, plasma cells, and acute inflammatory cells. Three basic histological patterns, none of which appears to have a discernible

association with clinical behaviour, have been described, namely: (1) myxoid/vascular pattern, resembling inflammatory granulation tissue; (2) compact spindle cell pattern with fascicular and/or storiform areas and variation of cellular density; and (3) hypocellular pattern, densely collagenised and reminiscent of a fibrous scar.¹ The three patterns may well be equally represented within the tumour, often blending into one another, with one or two patterns predominating. Lymphocytes are polyclonal. Immunohistochemistry confirms the myofibroblastic phenotype of the spindle cells, which are typically reactive to vimentin (99%), smooth muscle actin (92%), and muscle specific actin (89%).¹ In addition, the spindle cells may also be positive for desmin (69%) and cytokeratin (36%).¹

"Our case is unique in its clinical course, because it is the first and only known case of inflammatory myofibroblastic tumour of the paranasal sinuses with a fatal outcome as a result of extensive intracranial spread of the tumour"

Treatment and clinical outcome are generally favourable. Most reports and series of extrapulmonary IMTs indicate that these tumours pursue an innocuous clinical course, with a frequency of local recurrence of approximately 25%.² Radical excision is therefore curative in more than 90% of extrapulmonary IMTs, including head and neck IMTs.² In the head and neck region, only one case of IMT of the maxillary sinus showed extension to pterygopalatine fossa after only corticosteroid treatment.⁷ Very large lesions, or those arising in areas difficult to excise completely, such as mesenteric, omental, peritoneal, pelvic, or retroperitoneal sites, and paranasal sinuses, tend to recur, with a potential for metastatic spread in rare instances.^{1,8} Indeed, a metastatic potential has been noted, although in only one series involving 38 patients with abdominal and mediastinal IMTs; two patients had lung and one had brain metastases.³ Reliable histological criteria for the prediction of the clinical outcome have not been firmly established so far. The combination of cellular atypia, the presence of ganglion-like cells, p53 expression, and DNA aneuploidy might help to identify IMTs that have the potential for aggressive clinical behaviour with recurrence or malignant transformation.⁹ Our case is unique in its clinical course, because it is the first and only known case of IMT of the paranasal sinuses with a fatal outcome as a result of extensive intracranial spread of the tumour, despite several surgical procedures and additional radiotherapy, corticosteroids, and chemotherapy.

The aetiology and pathogenesis of IMT still remain unknown. Cytogenetic and molecular studies point to the possibility that at least some subsets of IMT are in fact true neoplasms.¹⁰ Clonal rearrangements of the short arm of chromosome 2, involving the ALK receptor tyrosine kinase locus region, have been detected in up to 50% of soft tissue IMTs.^{8,11} However, a subset of IMTs is most probably infection associated. Namely, Epstein-Barr virus has been detected in some splenic and hepatic IMTs,¹² actinomycetes and nocardia in some hepatic and pulmonary IMTs, and mycoplasma in some pulmonary IMTs.¹³ In addition, the essential role of human herpesvirus 8 in triggering the development of seven IMTs (five in the lung, one in a limb, and one in the retroperitoneal lymph node) has also been suggested.¹⁴

The differential diagnosis of IMTs in the oral cavity and paranasal sinuses mainly includes lesions composed of myofibroblasts and fibroblasts, which may pose considerable challenges because of their morphological overlap with IMTs. When myofibroblasts are set in a loose or myxoid stroma, the histological pattern may be indistinguishable from nodular fasciitis.⁵ However, IMTs are generally larger than nodular fasciitis, tend to occur in younger age groups, and are composed of longer fascicles of spindle cells in an inflammatory

Take home messages

- We report the first known case of an inflammatory myofibroblastic tumour (IMT) of the head and neck region with a fatal outcome
- This shows that the aggressive behaviour of IMTs is not limited to abdominal and mediastinal locations
- Our case supports recent observations that at least a subset of IMTs represents true neoplasia rather than reactive myofibroblastic proliferation

background rich in plasma cells.^{5–15} In contrast, nodular fasciitis usually lacks the striking inflammatory infiltrate characteristically present in IMT.¹⁵ Fibromatosis of the oral cavity is characterised by broad interlacing fascicles of mature fibroblasts, with a variable degree of collagenisation, and by the absence of an inflammatory component.¹⁶ Follicular dendritic cell tumour, also described in the oral cavity, is composed of whorls or fascicles of plump spindle shaped to ovoid cells, showing morphological and phenotypical (CD21+, CD35+, CD23+) features of follicular dendritic cells, set in an inflammatory background of lymphocytes and histiocytes.¹⁷ When IMT contains enlarged histiocyte-like cells, inflammatory malignant fibrous histiocytoma has to be taken into consideration, characteristically containing a “sea” of neutrophils.¹⁵ Compact cellularity, a fascicular pattern, and nuclear atypia should also raise the suspicion of other neoplasms with a spindle cell appearance, such as sarcomatoid carcinoma, high grade angiosarcoma with spindle cell areas, leiomyosarcoma, and fibrosarcoma.¹⁸

In conclusion, IMT of the head and neck region is a distinct clinicopathological entity, characterised histologically by fascicles of spindle cells in an inflammatory background rich in plasma cells. Clinically and radiologically, it may simulate a malignant tumour. Although these tumours generally behave as benign lesions that are usually cured by radical excision, our case clearly demonstrates that IMT of the paranasal sinuses can grow aggressively. The patient eventually died at 26 years of age as a result of extensive intracranial spread of the tumour. Our case supports recent observations that at least a subset of IMTs represents true neoplasia.

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