Atypical fibroxanthoma is an uncommon, cutaneous mesenchymal tumour. It usually appears as a solitary nodule or ulcerous nodule on sun-damaged skin of the elderly people. Histologically, an anaplastic activity with marked cytological atypia, increased number of mitotic figures and presence of multinucleated giant cells belies its usually benign clinical course and excellent prognosis. Atypical fibroxanthoma is regarded as a superficial, less aggressive counterpart of malignant fibrous histiocytoma. These 2 tumours are histologically indistinguishable but their clinical presentation differs. Atypical fibroxanthoma arises superficially; it is usually confined in the dermis of the head and neck of the elderly, whereas malignant fibrous histiocytoma arises in deep soft tissues of the extremities and in the retro-peritoneum of younger people. Moreover, atypical fibroxanthoma has almost always a benign clinical course, unlike malignant fibrous histiocytoma, which is characterized by a high incidence of metastasis and a high recurrence rate.

The treatment of choice of atypical fibroxanthoma is wide surgical excision, since the possibility of recurrence is highly correlated to positive tumour margins. We report a case of atypical fibroxanthoma in a female patient suffering from scleroderma. Despite the aggressive treatment, the tumour recurred several times. This is the first documented case of atypical fibroxanthoma occurring a patient with a collagen disorder.

Case Report

A 57-year-old Caucasian woman presented to our department of Oral and Maxillofacial Surgery with an 8-month history of a painless ulcerative pre-auricular tumour measuring 3x3cm. She reported the appearance of a small nodule 8 months ago which had grown rapidly and become ulcerated. The lesion was fragile and asymptomatic, but due to its cosmetic appearance the patient had to cover it with a piece of gauze. The rest of the examination was unremarkable with no palpable cervical adenopathy. The chest film was free of metastatic lesions, although there was an extended pulmonary fibrosis due to scleroderma. The patient had a smaller lesion resected from the same area one year ago. The histological examination of this tumour revealed a keratoacanthoma.

The patient suffered from scleroderma diagnosed 10 years ago, being controlled with Prezolon 5 mg (1x3) and Cyclophosphamide 50 mg (1x3). Despite the aggressive immunosuppressive therapy, she had developed pulmonary hypertension due to the disease, but she had no gastrointestinal symptoms. Her medical history also revealed moderate hypertension and coronal disease.

A punch biopsy of the pre-auricular tumour was performed and the patient was initially treated with radiotherapy due to her compromised medical status. The radiotherapy started immediately because the tumour was
growing fast and was clinically diagnosed as a squamous cell carcinoma.

The biopsy showed an atypical spindle cell neoplasm, which did not stain with cytokeratin, S-100 protein, HMB-45, MelanA and SMA. The tumour was histologically characterized as sarcoma. Radiotherapy was subsequently abandoned. Under general anesthesia a wide excision of the tumour was performed. Part of the superficial temporal fascia and part of the zygomatic arch were also excised (Figs. 1 and 2). The defect was covered with free skin grafts because the duration of the surgery should be kept to a minimum due to compromised medical status of the patient.

The biopsy specimen demonstrated a well-circumscribed, non-encapsulated tumour localized in the dermis, contiguous with the ulcerated epidermis. The cells were large, pleomorphic, longitudinal and spindle-shaped with an abundant eosinophilic cytoplasm and frequent mitotic figures (Fig. 3). The margins of the specimen were not infiltrated and the nearest distance from the margins of the tumour was 1cm. Immunohistochemical staining of proliferative cells was strongly positive for vimentin, S-100 (Fig. 4) and CD68, but much more weakly positive for cytokeratin 8/18 and smooth muscle actin (SMA). Tumour cells did not show any reactivity with HMB 45, MelanA, KerAE1/AE3, Ker LMW, KerHMW, Ker7, Ker20, EMA and CD34. The diagnosis of atypical fibroxanthoma was established.

2 months later the patient presented to our department with 2 nodules located at the margins of the skin graft. Excision of one nodule under local anesthesia was performed. The histological examination of the specimen revealed a recurrence of the primary tumour. The next month the patient underwent a wide excision of the nodules under general anesthesia and the defect was again reconstructed with free skin grafts (Figs. 5 and 6). Once again biopsy was indicative of an atypical fibroxanthoma. The patient has been closely followed for 18 months and she has shown no evidence of a recurrence or distant metastasis. The patient eventually died from the systemic disease.
Discussion

Atypical fibroxanthoma was first reported by Helwig in 1963\(^6\). He described a solitary spindle cell neoplasm arising on the sun damaged skin of an elderly patient.

Atypical fibroxanthoma begins as a small, firm and solitary nodule, which may be ulcerated (36%) or bleeding (26%)\(^7\). It usually grows rapidly, but remains asymptomatic. Some nodules have a pigmented appearance due to hemosiderin deposits. In this case, differential diagnosis from melanomas may be difficult. Atypical fibroxanthoma usually appears on the head and neck of elderly people with a mean age of 71-86 years\(^5\), and less often on the trunk and extremities of younger people. Very rarely it can affect the eye\(^8\). Our patient was 57 years old and presented with a large painless ulcer on the pre-auricular region.

The pathogenesis of atypical fibroxanthoma is still unknown, although many predisposing factors have been reported. Ultraviolet radiation seems to play a major role by inducing p53 mutations at dipyrimidine sites\(^9\). Other predisposing factors include trauma, burns, radiotherapy, post-cardiac and post-renal transplantation and immunosuppressive therapy\(^10,11\).

A high incidence of cutaneous malignancies has been reported in transplant recipients, which is attributed to the need of lifelong maintenance immunosuppressive therapy\(^12\). Immunosuppressive therapy impairs the tumour surveillance mechanism of lymphocytes, disrupting the balance between tumourigenesis and tumourilysis\(^13\). Immunosuppressive therapy and perhaps the initial radiation therapy may have contributed to the presence of multiple recurrences in our patient despite wide surgical excision.

The diagnosis of atypical fibroxanthoma is based on histological examination and immunohistochemistry, since its clinical course and appearance leads to a variety of preoperative diagnosis, such as squamous cell carcinoma, basal cell carcinoma, pyogenic granuloma, melanoma, dermatosarcoma, cutaneous lymphoma and malignant fibrous histiocytoma\(^5,10\).

Immunohistochemical studies are helpful in establishing the diagnosis and in differentiating atypical fibroxanthoma from other cutaneous malignancies. Atypical fibroxanthoma stains positively with vimentin only, and shows variable reaction with a1-antitrypsin, factor XII and smooth muscle actin (SMA)\(^13,14\). Squamous and spindle cell carcinoma stain positively with cytokeratin and epithelial membrane antigen, whereas atypical fibroxanthoma does not stain with these markers\(^15\). Moreover, atypical fibroxanthoma does not stain with S-100 protein and HMB-45, which are usually positive in melanomas\(^16\). However, the absence of positive reaction with these markers can not confirm the diagnosis of atypical fibroxanthoma, because in some cases spindle cell carcinomas may not stain with cytokeratin and melanomas may not stain with S-100 protein\(^5\). In our case, the tumour stained with vimentin and there was a mild reactivity with SMA, which has been reported before\(^5\). Interestingly, in our case, there was a strong reaction with S-100 protein, which has not been reported before. It seems that reactivity with S-100 protein cannot exclude the diagnosis of atypical fibroxanthoma.

Immunohistochemical studies are also used in order to differentiate atypical fibroxanthoma from its malignant counterpart, namely malignant fibrous histiocytoma. LN-2 is a 35kDa protein mainly expressed on the nuclear membrane of B-lymphocytes. This protein has been consistently identified in malignant fibrous histiocytomas but not in atypical fibroxanthomas\(^11\). It seems that LN-2 is a reliable marker in distinguishing between the 2 lesions.
The treatment of choice is wide surgical excision with at least 1 cm margin\textsuperscript{18}. We absolutely agree with Gonzalez-Garcia et al\textsuperscript{7} that curettage and cryosurgery are never indicated since they can lead to a remarkably higher recurrence rate. Mohs microsurgery is a conservative approach that should only be reserved for tumours adjacent to important anatomic structures. Radiotherapy is advocated by some authors, but some others suggest that following radiotherapy the tumour may show a more aggressive clinical course\textsuperscript{7,19}. We chose to treat our patient with wide surgical excision despite her compromised medical status.

Atypical fibroxanthomas are known to recur in about 12\% of cases\textsuperscript{20}, with a mean time of 2 years between surgery and recurrence. Recurrences are usually a consequence of inadequate surgical margins\textsuperscript{7,21}. However, multiple recurrences occurred in our patient despite the wide excision of the primary tumour, suggesting that immunosuppressive therapy and radiotherapy might also play an important role in clinical course of the tumour. The existence of occasional recurrences advocates for a close follow-up of the patient, at least for the first 2 years following surgery.

Although extremely uncommon, metastatic spread has been described by some authors\textsuperscript{6,22}. Metastasis is usually associated with large tumours with deep vascular invasion and with immunocompromised hosts. According to Helwig\textsuperscript{6}, metastasis usually occurs within 12 to 18 months. Metastasis from atypical fibroxanthoma is not always fatal, since surgical control or even cure may also happen.

References


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