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CASE REPORT

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Intramuscular mixed tumour with clonal chromosomal changes

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Abstract A case of an entirely intramuscular mixed tumour occurred in an 82-year-old man, who presented with a large mass in the region of the right triceps muscle. A lobulated tumour was seen, with plump, round epithelioid cells embedded in a chondromyxoid stroma. Immunohistochemical examination showed strong S100 protein and pancytokeratin positivity in most of the tumour cells. Cytogenetic analysis revealed complex clonal chromosomal changes: 47, XY, +i (2) (q10), –15, der (17)t(15;17) (q11; p12), +r. Differential diagnosis against extraskeletal myxoid chondrosarcoma (EMC) may be problematic, particularly in an incisional biopsy. Chromosomal analysis can be very helpful in solving this problem, since EMC shows a specific reciprocal chromosome translocation characterised as t (9;22) (q22–31) (q11–12).

Key words Soft tissue · Neoplasm · Mixed tumour · Pleomorphic adenoma · Cytogenetics

Introduction

Mixed tumours in the salivary gland (pleomorphic adenoma) and the skin (chondroid syringoma) are well-defined entities, but similar counterparts in soft tissues remain rare [4]. Kilpatrick et al. recently described 19 mixed tumours/myoepitheliomas of soft tissues [5], which appeared as circumscribed and lobulated masses composed of nests of epithelioid to spindle cells in a chondromyxoid stroma, sometimes with focal ductular differentiation. As with their salivary gland counterparts, the morphologic spectrum is quite wide. Immunophenotypic findings are similar to those in comparable lesions arising in salivary glands. We describe an intramuscular mixed tumour with clonal chromosomal changes, the first such case to have been defined in karyotypic terms. The data support the distinct nature of mixed tumour when it arises in soft tissue.

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Case report

A 82-year-old man was admitted because of general deterioration after a cerebrovascular accident and worsening dementia. On physical examination a painless solid mass about 4×5×15 cm in size in the region of the right triceps muscle was discovered. Additional history revealed that the tumour had developed within the last few months and had produced few symptoms. The patinet had no specific neurological loss, nor did he show any functional impairment of the right arm as a result of the tumour. MRI scan (Philips gyroscan, 1.0 T) revealed a sharply defined, highly nonhomogeneous lesion located in the triceps muscle compartment on the gradient echo image (34/10, flip angle 50.0°) through the upper extremity; the tumour did not infiltrate the bone. An incisional biopsy was performed, followed by wide excision of the tumour (including the entire triceps muscle). The wound healed uneventfully and the patient had little functional loss attributable to this resection. There was no evidence of tumour elsewhere, and no possible primary source was seen in salivary gland or lung. However, his general neurological condition continued to deteriorate, and he succumbed to dementia 4 months postoperatively. Up to then, no signs of systemic dissemination or of local or locoregional recurrence were present.

Materials and methods

Parts of the incisional biopsy and the resection specimen were fixed in buffered formalin and processed in the usual way for paraffin embedding. Sections 4 μm thick were cut and stained with haematoxylin and eosin. Part of the tumour was snap frozen. A fresh sample from the incisional biopsy was processed for short-term culture (5 days), and cytogenetic analysis including fluorescence in situ hybridization (FISH) was performed according to

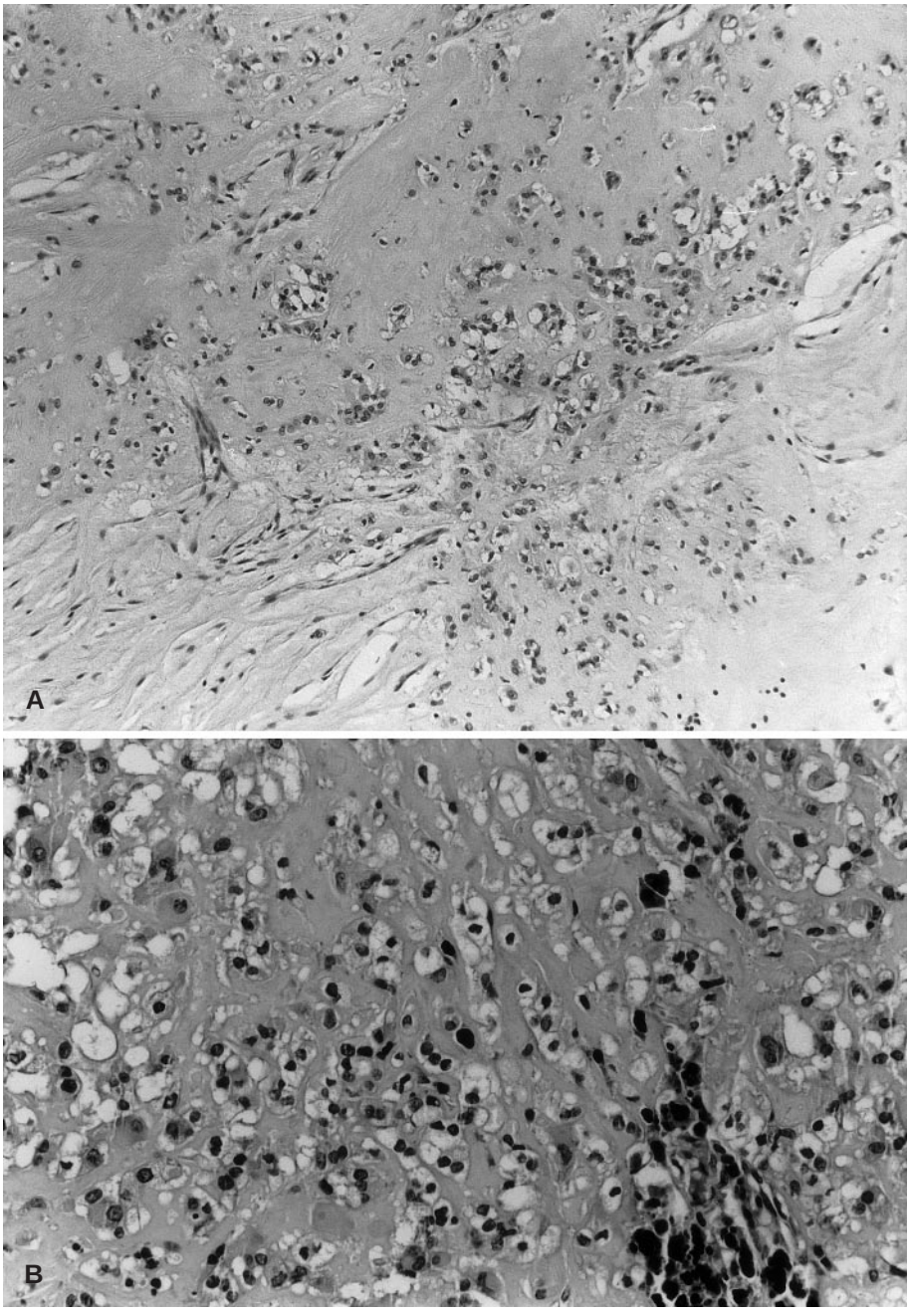

Fig. 1 **A** Strands and clusters of tumour cells set in a hyalinized to chondromyxoid stroma. There is considerable haemosiderin deposition. **B** Large, round cells with abundant pale cytoplasm, arranged in strands or clusters, set in a hyalinized stroma

standard procedures. Sections from frozen material and paraffin-embedded material were stained with a panel of antibodies using the avidin–biotin–peroxidase complex (ABC) technique. The antibodies included S-100 protein (1:740, Dako, Glostrup, Denmark), muscle specific actin (HHF-35 1:8000 Enzo, New York), pancytokeratin (Lu-5, 1:30, Biogenex, San Ramon, USA), epithelial membrane antigen (EMA; E29 1:50, Dako), desmin (D 33 1:50, Dako) CD 34 (anti-HPCA-1, Becton and Dickinson, San Jose USA), ulex (1:20, Vector, Burlingame, USA), smooth muscle actin (I A4 1:3000 Sigma, St. Louis) and glial fibrillary acidic protein (GFAP, 1:100 Biogenex San Ramon, USA).

Results

Macroscopically, the neoplasm appeared as a soft, ovoid multinodular mass, measuring 14 cm in greatest diameter and with a distinct fibrous capsule. It was located within the triceps muscle. On section, the surface was grey to tan-brown without necrosis. Microscopically, a fibrous pseudocapsule surrounded the lesion. A lobulated tumour was seen, dominated by a prominent chondromyxoid stroma. Large round cells with abundant pale cytoplasm were arranged in solid clusters, cords or strands (Fig. 1). A lacelike growth pattern was also present. The chondroid areas predominated, but in some foci the epi-

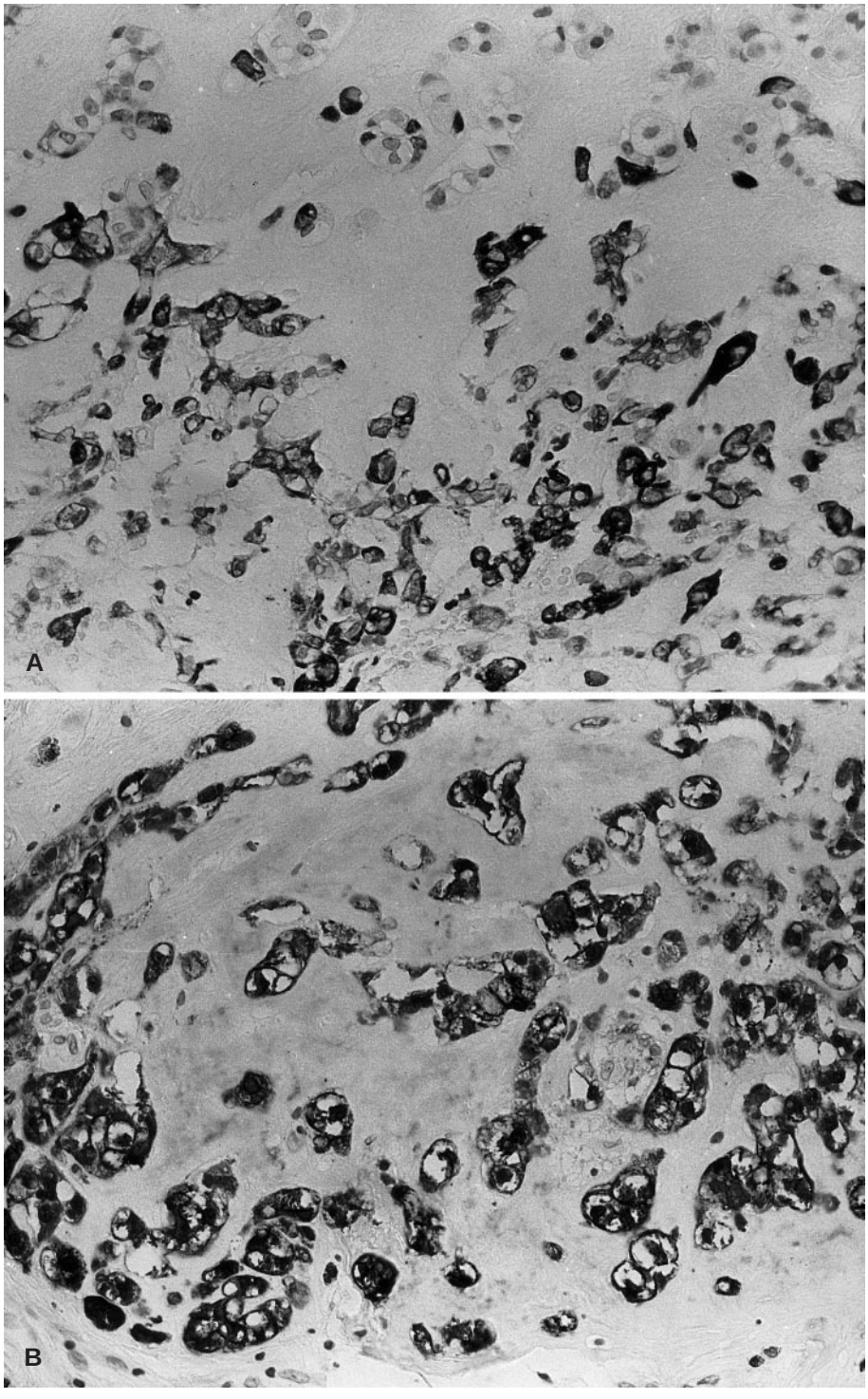

Fig. 2 Strong **A** pankeratin and **B** S100 positivity in the majority of tumour cells

thelial strands were embedded in a myxoid stroma. No duct-like stuctures were seen. Frank anaplasia was not present. Nuclear pleomorphism was mild. Mitoses were scarce (<1 per 10 high-power fields). Spindle cell areas were absent.

Immunohistochemical studies showed strong positivity of the tumour cells for S-100 protein and pancytokeratin (Fig. 2). The tumour cells also expressed EMA, but more focally. Tumour cells were negative for actin, desmin, CD 34, and GFAP. A final diagnosis of mixed tumour arising primarly in soft tissue was made.

Twenty G-banded metaphases were analyzed, five of which showed a normal male karyotype. Fifteen metaphases, however showed a clonal aberation characterized as 47, XY, +i (2) (q10), –15, der (17)t(15;17) (q11;p12), +r (Fig. 3). Whole chromosome 12 painting excluded the

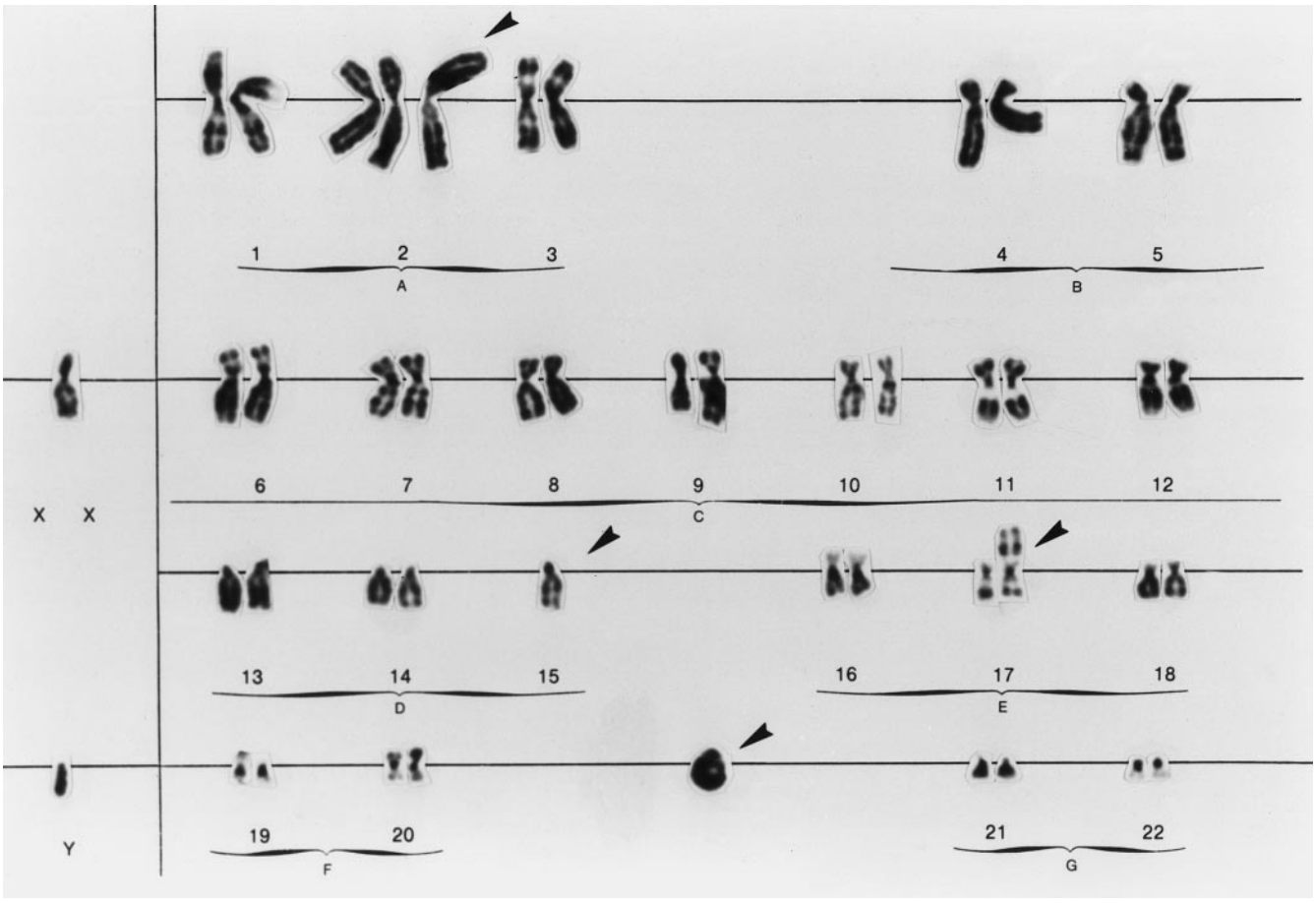

Fig. 3 G-banded karyotype of the intramuscular mixed tumour showing a 47, XY, +i(2)(q10), –15,der (17)t(15;17)(q11;p12), +r. *Arrowheads* indicate the abnormal chromosomes

presence of chromosome 12 material in the ring chromosome and in the presumed i (2q). Instead, a complex chromosome rearrangement was present, unrelated to previously reported chromosome changes in malignancy and quite unlike the changes usually seen in mixed tumour of salivary gland origin (see below).

Discussion

Mixed tumours and myoepitheliomas occuring primarily .in soft tissue are rare lesions. The largest series so far (19 cases) was published by Kilpatrick et al. [5]. Soft tissue mixed tumours appear as lobulated, relatively well-circumscribed tumours in the subcutis and less frequently in the subfascial soft tissue. In the series reported by Kilpatrick et al., 4 cases had arisen in the lower limbs or limb girdle, 2 in the foot and 1 in the ankle. The tumour in the present case was entirely intramuscular within the triceps and had a prominently chondroid appearance, as described by Kilpatrick et al. in 4 of their 19 cases.

The differential diagnosis should include extraskeletal myxoid chondrosarcoma (EMC) and parachordoma. With regard to parachordoma, this rare tumour appears to fit in the spectrum of myoepithelioma-mixed tumour and a distiction between parachordoma and other myoepithelial-mixed tumours has not hitherto been believed to be reproducible or meaningful [4].

However, some authors regard parachondroma as a separate entity. Only one cytogenetic study on parachondroma has been reported, and there were no clonal chromosomal abnormalities [6].

Differential diagnosis against EMC is more relevant, and however, we used both immunohistochemistry and cytogenetic investigation for that purpose. The presence of strong S-100 and cytokeratin expression in the present tumour does not support a diagnosis of EMC. EMC has been said by most authors to exhibit strong S-100 protein positivity, but this was based on old data. A recent study suggests that such positivity is seen in no more than 20% of cases [2]. In addition, expression of cytokeratin and EMA has only exceptionally been reported in EMC [3].

The cytogenetic results on our incisional biopsy ruled out an EMC, since no t (9;22)(q22–q31;q12) characteristic for this tumour was found [6]. FISH analysis also excluded involvement of 12q, which is a component of ring or marker chromosomes in other borderline and low-grade mesenchymal tumours, such as atypical lipoma, aggressive angiomyxoma and inflammatory myofibroblastic tumour.

With regard to chromosome investigation in mixed tumours no cytogenetic information on chondroid syringo-

ma of the skin is available, but pleomorphic adenomas of the salivary gland have been extensively investigated. Recurrent chromosome rearrangements, particularly reciprocal translocations, with breakpoints on 8q12, 3p21 and 12q14–15 have been described in these tumours [1]. It is interesting, therefore, that the present case has quite different aberrations from those previously reported in comparable salivary gland lesions.

Although this tumour was unusually large, conclusions regarding survival and tumour size in mixed tumours of soft tissue cannot be established with certainty owing to the small number of reported cases and short follow-up. In contrast, the clinical behaviour of EMC is well known: it is generally a relatively slow-growing tumour, with recurrence and eventual metastases in the majority of cases [3]. Further cases and a longer follow-up are needed to assess the biological behaviour of mixed tumours in soft tissue.

Although additional cases should be karyotyped, the clonal chromosomal changes in this case support the recognition of this type of mixed tumour as a separate entity. Mixed tumours should be considered in the differential diagnosis when an extraskeletal chondroid lesion is investigated. Immunohistochemistry and cytogenetics are very useful in establishing the final diagnosis.

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