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Case report

Synovial metaplasia of the skin

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Abstract. We present two female patients, aged 15 and 45 years, with synovial metaplasia of the skin. Both lesions, localized in the knee and hand respectively, arose after preceding local trauma. Case 1 had intradermal irregular cystic spaces in the adjacent myxoid stroma of which large polygonal eosinophilic cells were found. In contrast, case 2 was characterized by a longitudinal space within the lower dermis and subcutis which was lined by a membrane similar to hyperplastic synovium. The cells of the membrane showed an eosinophilic spindle shaped cytoplasm with processes towards the lumen. In both cases the eosinophilic cells, strongly suggestive of fibroblasts, showed staining for vimentin only, whereas no reactivity could be obtained with antibodies to actin, desmin, S-100 protein, Factor VIII related antigen, cytokeratin, epithelial membrane antigen, carcinoembryonic antigen and CD 68. The absence of CD 68 positivity differs from that seen in normal and hyperplastic synovium. Delayed wound healing around a nidus seems the most likely cause of the change.

Key words: Skin – Cyst – Synovial metaplasia – Immunohistochemistry

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Introduction

Synovial metaplasia of the skin is a recently recognised rare, benign tumour-like lesion (Gonzalez et al. 1987) which nearly always arises after trauma. It is characterized by intradermal cystic cavities which are often lined by a membrane similar to hyperplastic synovium.

Table 1. Clinical details in 11 cases of synovial metaplasia of the skin

Authors	Sex	Age	Location	Previous trauma
Gonzalez et al. 1987				
Case 1	F	82	Anterior chest	Surgery (implant. of a myocardial pacemaker)
Case 2	F	27	Abdomen	Surgery (appendectomy)
Case 3	M	77	Abdomen	Surgery (small-bowel obstruction)
Stern and Sexton 1988				
Case 4	F	7	Scalp	Surgery (implant. of sialastic expanders)
Gomez Dorronsoro et al. 1988				
Case 5	M	28	Upper arm	Surgery (removal of a rheumatoid nodule)
Bhawan et al. 1990				
Case 6	M	40	Index	None
Case 7	F	40	Palm	Wound by splinter
Case 8	M	20	Abdomen	Surgery (laparotomy, reason not stated)
Case 9	M	67	Face	None (associated with basal cell carcinoma)
Present study				
Case 10	F	45	Dorsum of hand	Burn
Case 11	F	15	Knee	Inclusion of a foreign body

In addition, characteristic eosinophilic cells of epithelioid appearance can be found. At present nine such cases have been reported in the literature (see Table 1).

In order to highlight the spectrum of histological appearances not stressed by previous reports, we present two further cases.

Case reports

Case 1. In a 45-year-old woman a nodular skin lesion, 8 mm in diameter, was removed from the dorsum of the right hand. The tumour had been present for 18 months and arose in a scar after burn 3 months previously. The healing of the resulting wound was delayed. No recurrence was seen within a follow-up period of 17 months.

Case 2. A 15-year-old girl presented with a lesion in the deeper dermis of the knee. The lesion appeared after preceding trauma to the respective knee-joint several months before. At excision a hard foreign body suggestive of a small stone was removed from the cystic cavity of the specimen. A follow-up of 12 months revealed no recurrence.

Materials and methods

The formalin-fixed specimens were paraffin-embedded, cut at 4 μm and stained with haematoxylin-eosin, alcian blue (pH 2.5) and a Masson's trichrome stain. Further sections from each lesion were studied immunohistochemically by the avidin-biotin-peroxidase (ABP) method using the following primary antibodies: (1) anti-alpha-1 smooth muscle actin (IA 4, monoclonal, Sigma, 1:16000); (2) anti-muscle actin (HHF 35, monoclonal, Enzo Diagnostics, 1:25000); (3) anti-S–100 protein (polyclonal, Dako, 1:2000); (4) anti-vimentin (polyclonal, Eurodiagnostic, 1:20); (5) anti-Factor VIII related antigen (anti-F VIII RAG, polyclonal, Dako, 1:500); (6) anti-cytokeratin (Lu5, monoclonal, Boehringer Mannheim, 1:50); (7) anti-epithelial membrane antigen (EMA, monoclonal, Dako, 1:50); (8) anti-carcinoembryonic antigen (CEA, monoclonal, Dako, 1:300); (9) anti CD 68 (monoclonal, Dako, 1:50). The specifity of the immunostaining was verified by staining known positive control tissue sections (positive controls) as well as replacement of the primary antibody by phosphate buffered saline (negative controls).

Results

In case 1 the lesion was located within the dermis and consisted of cystic spaces of varying size, which communicated with each other (Fig. 1a). From the wall of the largest cyst, plump villous-like projections protruded into the lumen. The lumina of the cysts were focally filled with fibrin. All spaces were lined either by flattened or large "bizarre" cells of polygonal shape (Fig. 1b). The latter were characterized by an eosinophilic cytoplasm in which one or multiple rounded or ovoid, hypochromatic nuclei with distinct nucleoli could be found. A few of these cells displayed regular mitotic figures. The stromal tissue surrounding the spaces was often myxoid and also showed these eosinophilic cells sometimes forming solid, more cellular sheets (Fig. 1c). Among those cells lymphocytes and granulocytes were interspersed. The overlying epidermis was characterized by a hyper- and parakeratosis.

In case 2 the lesion was situated within the lower dermis and superficial subcutis and was an extended

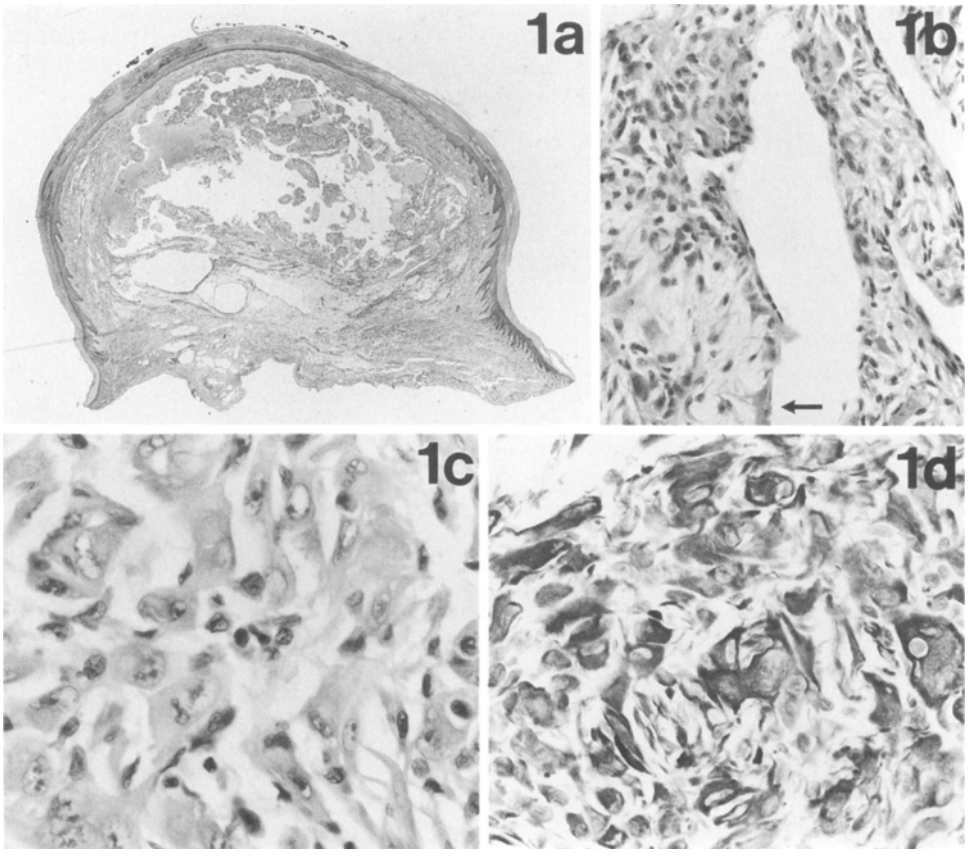

Fig. 1a. Intradermal lesion consisting of multiple cystic spaces some of which are filled with fibrin. H & E, × 12. **b.** The spaces are lined either by flattened or by large cells (arrow). Note the adjacent myxoid stroma. H & E, × 200. **c.** The typical cells of the lesion display eosinophilic, polygonal cytoplasm and single or multiple, hypochromatic nuclei with distinct nucleoli. H & E, × 480. **d.** Immunohistochemistry of the typical cells shows strong intracytoplasmic reactivity for vimentin. ABP-method, × 450

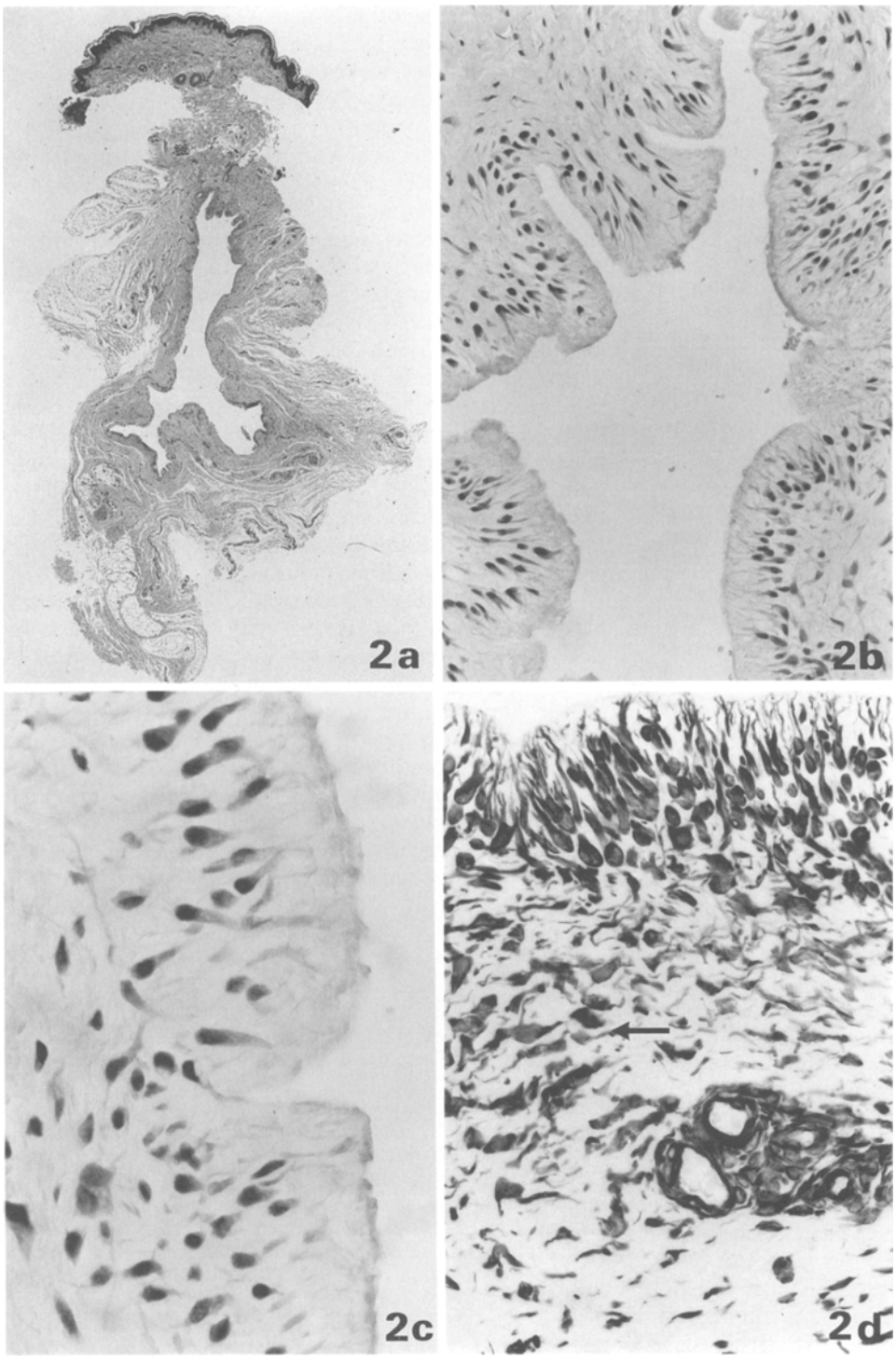

Fig. 2a. Longitudinal cystic space within the lower dermis and predominantly superficial subcutis. H & E, × 12. **b.** The space is lined by a membrane with villous projections towards the lumen similar to hyperplastic synovium. H & E, × 200. **c.** The membrane shows more spindled cells with basally located nuclei and cytoplasmic processes extending to the luminal surface. H & E, × 480. **d.** Immunohistochemistry reveals strong intracytoplasmic vimentin-reactivity of the membrane-cells and a pronounced outlining of their cytoplasmic processes. In more hypocellular areas, beneath the membrane, the cells show a more polygonal shape *(arrow)* as indicated by their immunoreactivity. ABP-method, × 450

cystic space (Fig. 2a). The cyst was lined by a synovium-like membrane with small villous projections into the lumen (Fig. 2b). The cells of the membrane were of spindle shape, showed basally located, hyperchromatic nuclei and an eosinophilic cytoplasm with processes directed to the lumen (Fig. 2c) revealing a perpendicular orientation with regard to the plane of the luminal surface. Beneath the membrane there was a hypocellular fibrous tissue with some polygonal eosinophilic cells, typical fibroblasts and fibrocytes and many capillaries. In neither cases could a trans-epidermal fistula be found. Histochemical studies revealed abundant alcian blue-positive material within the stromal component of case 1, and within the membrane and surrounding tissue of case 2. These findings were highly suggestive of the deposition of acid mucosubstances including hyaluronic acid.

Immunohistochemically in case 1 the polygonal eosinophilic cells were found to exhibit a pronounced cytoplasmic immunoreaction with the antibody to vimentin (Fig. 1d). In case 2 the cytoplasm of the membrane-lining cells was also strongly positive for vimentin; moreover, this was demonstrated within their cytoplasmic processes which reached to the inner surface of the cavity (Fig. 2d).

The polygonal and lining cells mentioned above were non-reactive to the other antibodies used.

Discussion

Synovial metaplasia of the skin is a reactive intradermal lesion which has been reported to arise mostly after surgical trauma (Gonzalez et al. 1987; Stern and Sexton 1988; Gomez Dorronsoro et al. 1988; Bhawan et al. 1990). The occurrence after burn and in the vicinity of a foreign body, as in our cases, is not unexpected but has not been previously described. This also demonstrates that the mode of trauma probably is not a significant factor in the origin of these lesions.

At present it is generally believed that a "nidus" is necessary as a starting point for the development of cutaneous synovial metaplasia. Thus, it parallels the occurrence of synovium-like structures in deeper soft tissues which can be found after air injection (Edwards et al. 1981), implantation of silastic rods (Hunter et al. 1983) and at the bone-cement interface in hip replacements (Goldring et al. 1983). In our study, fibrin (in the first case) and a stone (in the second one) can be regarded as the niduli.

Since traumatic injuries of the skin are very frequent and, by contrast, cutaneous synovial metaplasia is a very rare lesion, additional factors must be of pathogenetic relevance. However, when reviewing all published cases including the two reported herein, no typical additional variables are evident. The lesions were found to arise at any age (range from 7 to 82 years), showed no sex preponderance, affecting 5 males and 6 females, and were localized in different anatomical sites. Thus, at the moment only a prolonged failure of healing around a nidus is known to be aetiologically relevant.

The histological pattern of cutaneous synovial metaplasia is characterized by the presence of a cyst-lining membrane similar to hyperplastic synovium as in our case 2 (Gonzalez et al. 1987). The features of our case 1, however, displayed a different pattern which was dominated by irregular cystic spaces, myxoid stromal areas and polygonal eosinophilic cells of epithelioid appearance. A membrane-like structure was not demonstrable. By reviewing the illustrations of all cases published so far it seems likely that our two cases represent each end of the spectrum of possible histological appearances. Therefore, case 1 may be considered as a more immature form of cutaneous synovial metaplasia, whereas case 2 corresponds to the classical or mature form. This is of practical importance since in non-classical cases, devoid of a synovium-like membrane, the correct diagnosis may be missed.

The typical cells of the lesion are eosinophilic and of polygonal shape or more spindled, with cytoplasmic processes in areas of membrane-formation. Independent of their configuration, the cells are exclusively positive for vimentin in those cases which have been examined immunohistochemically (Gonzalez et al. 1987; Stern and Sexton 1988; Gomez Dorronsoro et al. 1988; Bhawan et al. 1990). In addition, by their CD 68-negativity a monocytic-macrophagic origin for these cells has been largely excluded by our study. The absence of immunoreaction to actin-antibodies makes a myofibroblastic origin unlikely. In comparing the given immunohistochemical profile with that of normal and hyperplastic synovium, it is apparently identical with regard to vimentin-positivity and cytokeratin-negativity (Miettinen and Virtanen 1984; Apte and Athanasou 1992), but contrasts with the staining for macrophage-associated antigens, like CD 68, which are usually seen in synovium (Athanasou et al. 1988). The descriptive name "synovial metaplasia", therefore, is based only on histological similarities. It may be justified in classical cases but is questionable in more immature lesions and is by no means evidence for true synoviocytic differentiation. It seems most likely that the cells under discussion are proliferating fibroblasts; a curious cell shape for fibroblasts is not uncommon and can be found in other reactive lesions (proliferative fasciitis and fibroepithelial stromal polyps) in skin and visceral locations. Preceding trauma may sometimes play a role in those conditions.

Differential diagnoses may vary. Where there is membrane formation the diagnosis may be established more easily because there is no similar lesion from which to discriminate. If, however, some of the features described in our first case are present the differential diagnosis includes all kinds of post-inflammatory degenerate true cutaneous cysts and cystic tumours (Bhawan et al. 1990) as well as mucous cysts when located in the finger. All these lesions, however, can be excluded by the occurrence of distinctive large eosinophilic cells which are present in the cyst-lining of synovial metaplasia.

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