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LETTERS TO THE EDITOR

Multicentric Reticulohistiocytosis Indicating Metastasis of an Unknown Primary Tumour

Sir,

Multicentric reticulohistiocytosis (MR) is a rare disease and belongs to the group of class II or non-Langerhans' histiocytoses (1, 2). These histiocytoses are characterized by local proliferation of resident mononuclear phagocytes other than Langerhans' cells. In MR aggregates of histiocytes are localized in the skin, mucosa and synovia, resulting in destructive arthritis. As approximately one third of MR cases are associated with malignancy (3), this disease has now been accepted as a facultative neoplasia. Here, we report on a patient presenting with the diagnosis of MR, which led to the discovery of a metastazing carcinoma with an unknown primary tumour.

CASE REPORT

A 39-year-old woman had had erythematous nodules since August 1994, affecting her fingers, hands (Fig. 1) and knees. In addition, arthritic pain and decreased mobility were reported in the affected joints. In 1995 reddish pruritic papules appeared in her face and on her forearms and chest. Physical examination revealed a subcutaneous tumour of 5 cm in diameter in the left axilla. However, palpation of the breasts was normal. Laboratory findings, including erythrocyte sedimentation rate, RBC, WBC and chemistry, were within normal limits. X-rays of both hands showed numerous periarticular erosions of the proximal phalangeal joints. Histological examination of lesional skin demonstrated rather diffuse dermal aggregates of histiocytes, composed of large, round to oval cells with eosinophil ground-glass cytoplasm and of multinucleate giant cells. The overlying epidermis was slightly acanthotic. Immunophenotyping revealed that the histiocytic infiltrates were CD1a- and S100-negative, and Mac 387- and CD68-positive (Fig. 2). Histology from a biopsy of the tumour in the left axilla showed infiltrates of medium-sized carcinoma cells, with low expression of estrogen receptors and high expression of progesteron receptors by immunhistochemistry. The tumour cells were also positive for epithelial and cytokeratin antigens (CK-MNF, KL-1, BER-EP 4 and HEA 135) but negative for CD45, vimentin, HMB45, S-100, CD68 and CD15. This phenotype indicates that the origin of the tumour cells is derived from breast epithelium. However, all other examinations, including computer tomography of the chest and abdomen, ultrasound of the abdomen, panendoscopy, skeletal scintigraphy, mammography, magnetic resonance tomography and ultrasound of the breasts, failed to show infiltration by either a carcinoma or reticulohistiocytosis. Since the patient refused surgery or radiotherapy she was put on tamoxifen (30 mg/day), based on the immunohistochemically detected hormone receptor status of the metastatic cells. Three months later the tumour size in the left axilla has shrunk down to 1.5 cm in diameter and other clinical parameters were within normal limits, indicating a response to tamoxifen and partial remission of the tumour disease. However, this beneficial effect was not coupled with regression of the MR.

DISCUSSION

Our patient presented with the typical clinical features of MR, namely erythematous and pruritic nodules on the skin of the fingers, hands and knees, painful arthritis of the fingers and erosions of the joints, as evidenced by X-ray findings. The diagnosis was confirmed by histological and immunochemical analysis of the cutaneous nodules. To differentiate Langerhans' cell or class I histiocytoses from non-Langerhans' cell histiocytoses, immunophenotypical characterization of the tumour cells is neccessary. Similar to other non-Langerhans' cell histiocytoses, MR is CD68-positive and CD1a-negative (2). CD68 seems to be the most reliable monocyte-macrophage marker in the diagnosis of MR. It has been reported positive in 12 out of 12 cases of RM (3). However, anti-CD68 mAb are only available for cryostat sections and snap-frozen material is needed for immunhistochemistry. By contrast, anti-CD1a antibodies became recently available for paraffin-embedded specimens, thus offering an easily accessible and reliable diagnostic marker for immunhistochemical differentiation of histiocytosis in routine material.

Until to date approximately 135 cases of MR have been reported in the literature, and in 42 cases an associated malignancy was found. Haematological neoplasia ($n=5$), breast cancer ($n=5$) and stomach cancer ($n=4$) were the most often reported underlying diseases (3). Malignancy was determined for the first time in approximately 50% of cases presenting initially with the clinical picture of MR (3). In our patient, MR led to the detection of previously not known lymph node metastases of a carcinoma expressing the immunhistological phenotype of breast cancer cells. However,

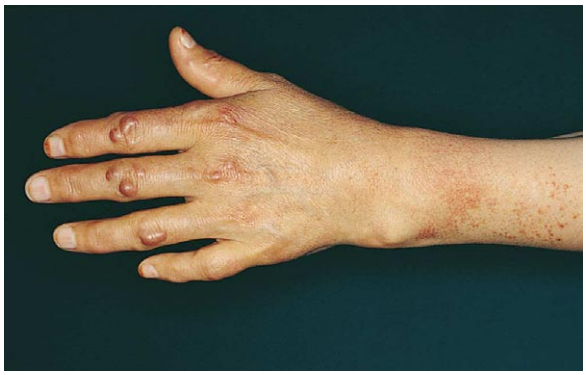

Fig. 1. Clinical feature of erythematous nodules.

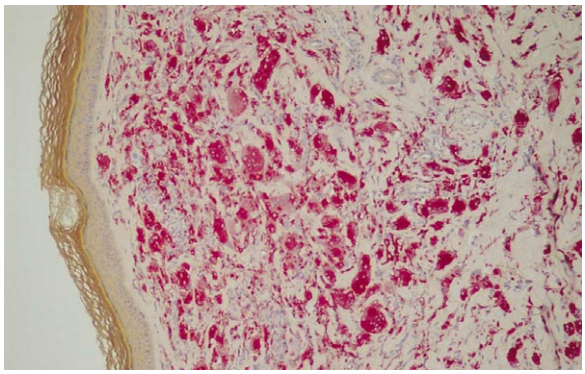

Fig. 2. CD68-positive cells in lesional skin.

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we were not able to find the primary tumour. Remarkably, no primary tumour is found in about 5% of the patients with breast cancer metastasis (4). Some of these women may suffer from a carcinoma of dystopic breast glands, seen in 1–5% of the female population (5).

In conclusion, our case report demonstrates that MR is not only a marker for manifest or occult malignancy, but also for metastasis from an unknown primary tumour. The disease fulfils all the criteria of a paraneoplastic syndrome, indicating that all patients with MR should be evaluated and monitored carefully.

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Agminated Xanthogranuloma: An Unusual Presentation of Juvenile Xanthogranuloma

Sir,

Juvenile xanthogranuloma is a benign histiocytic lesion, which most commonly occurs in children as small yellowish papules generally less than 1 cm in size (1). A macronodular variant has been reported in infants, with lesions measuring as large as 10 cm (2–4). We here report on 2 adults with asymptomatic agminated papules, which coalesced to form multinodular plaques on the extremities.

CASE REPORTS

Case 1

An 18-year-old Russian immigrant complained of an asymptomatic skin lesion of the forearm, which had been present for approximately 1 month. His general health was excellent and he took no medications. He was a student and had been in the United States for one and a half years. There was no history of trauma to the site.

On physical examination there was a plaque on the left forearm, composed of numerous coalescing papules (Fig. 1). The area was indurated, devoid of hair, and measured approximately 4.0×3.0 cm. The most superficial papule was yellow brown in color, whereas the deeper seated component was flesh-colored. A few satellite lesions were palpable along the ulnar aspect of the forearm. There was no regional adenopathy, and no café au lait spots or other stigmata of neurofibromatosis were present.

Laboratory results, including complete blood count, chemistry panel, cholesterol and triglycerides, were unremarkable. Radiographs of the left forearm and chest were normal. A skin biopsy demonstrated a proliferation of foamy histiocytes, which were admixed with numerous eosinophils. Tissue cultures (including aerobic, fungal and mycobacterial cultures) were negative. Electron microscopy showed a sheet-like infiltrate of mononuclear cells with abundant cytoplasm and numerous organelles. The cells demonstrated in-folded reniform nuclei and numerous primary lysosomes and phagolysosomes characteristic of histiocytes. Additionally, cytoplasmic lipid vacuoles typical of early foam cell formation were noted. Birbeck granules were not identified, and the lesion was classified as a non-Langerhans' cell histiocytosis.

Case 2

A 42-year-old woman complained of a lesion of the left inner thigh, which had been present for approximately 1 year. It reportedly began as a "red sore" and subsequently became firm and nodular. The patient was in good health and her only medication was aspirin. She had a history of shaving the bikini line in that area.

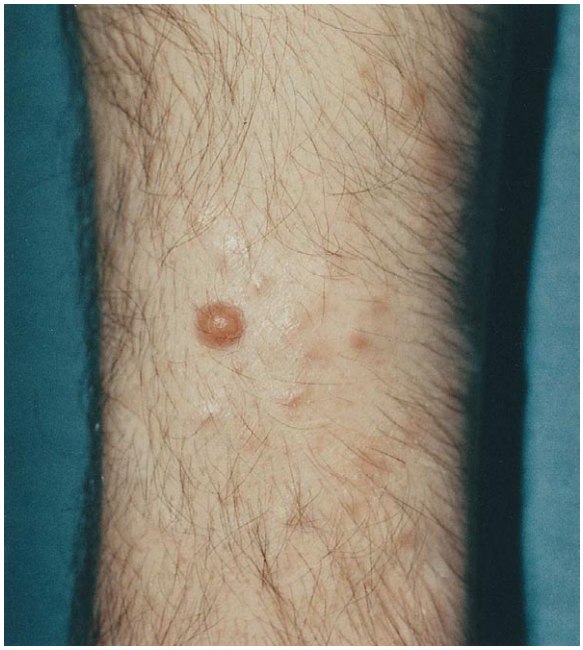

Fig. 1. A plaque on the left forearm is composed of numerous coalescing papules. Note satellite lesions and alopecia.

On examination, there was a 6.0×4.0 cm indurated plaque, with reddish-brown papules within it (Fig. 2). Laboratory results were unremarkable (complete blood count, chemistry panel and triglycerides). Her cholesterol was slightly elevated at 204. A skin biopsy showed a nodular dermal infiltrate of bland appearing histiocytes, some of which were multinucleated. Touton-type giant cells were not observed. Tissue cultures (aerobic, fungal, mycobacterial) showed no growth. A skin biopsy was interpreted as a xanthogranuloma.