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View from Beneath: Pathology in Focus

Granulomatous cutaneous T-cell lymphoma of the neck

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Abstract
A case of cutaneous T-cell lymphoma is presented in which the diagnosis was obscured by a concomitant granulomatous infiltrate. A working diagnosis of tuberculosis delayed appropriate treatment for several months over which time rapid progression of the disease was seen. Inclusion of overlying skin in the repeat biopsies yielded the histological information to establish the correct diagnosis and there was rapid regression on completion of a course of radiotherapy.

Introduction

Mycosis fungoides is a specific disease first described in 1806 which is now encompassed within the overall classification of cutaneous T-cell lymphoma. Grouped with Sezary Syndrome it constitutes one third of all cases of cutaneous T-cell lymphoma (Edelson, 1980a). The incidence of cutaneous T-cell lymphoma nearly equals that of Hodgkin's disease (Edelson *et al.*, 1979a) but the former has a poorer prognosis with a mean survival of five years from diagnosis (Epstein *et al.*, 1972). Cell marker studies provide strong evidence that cutaneous T-cell lymphoma represents the expansion of a single malignant clone of T-cells (Edelson *et al.*, 1979b) which in over half the cases are helper T-cells (Berger *et al.*, 1979). Occasional clustering of Cutaneous T-cell lymphoma in families suggests there may be a genetic diathesis (Sandbank and Katzenellenbogen, 1968).

Histologically a granulomatous reaction is seen in some forms of cutaneous T-cell lymphoma but rarely presents a diagnostic problem. In *Mycosis fungoides* a granulomatous reaction is seen rarely but has on several occasions misled the histopathologist to suspect a chronic granulomatous infection or sarcoidosis (LeBoit *et al.*, 1988). We present a patient in whom the granulomatous reaction extended into the adjacent lymph nodes and muscles of the neck in a malignant fashion. The true nature of the disease was obscured for several months.

Case report

An 87-year-old lady presented with a painless swelling in the right side of the neck which had been noticed by her sister with whom she lived; she was otherwise well with normal appetite and stable weight. In the past multiple actinic keratoses on the face had been excised and three months earlier, a well differentiated squamous cell carcinoma had been excised from the upper lip.

On examination, the swelling was 6 × 7 cm, firm in texture and matted to the sternocleidomastoid muscle although the overlying skin appeared normal. Clinically it was malignant. In addition, there were three small mobile supraclavicular nodes and an axillary node all on the right side. Examination of the upper aerodigestive tract including an excision biopsy of the right tonsil and fine needle aspiration cytology of the largest mass was unhelpful. Open biopsy of the mass was performed. Histologically this showed an extensive granulomatous inflammatory reaction involving both muscle and subcutaneous tissues with areas of focal necrosis (Fig. 1). After discussion, although no organisms were identifiable, a diagnosis of tuberculosis was made and antituberculous therapy commenced. At six weeks cultures of the biopsy specimen and sputum for tubercle bacillus were negative.

Over the ensuing seven months, despite continuous therapy there was progressive enlargement of the right-sided mass accompanied now by a recurrent laryngeal nerve palsy, increasing discomfort and the appearance of some small left sided lymph nodes. A CT scan showed the mass to be abutting but not involving the thyroid gland and now extending from the temporo-mandibular joint to the sternoclavicular level. Further open biopsy of an adjacent node to the right neck mass was undertaken. Histology of this showed appearances thought to be of TB undergoing treatment. In view of the inconsistent clinical picture and difficult histological appearances, the slides were sent for review by a regional panel. The question of lymphoma was specifically put to the panel but there appeared to be no evidence to support this. A suggestion of Weber Christian panniculitis was made in view of the failure of the chronic granulomatous process to respond to antituberculous treatment. However, the addition of steroids to the therapy was of no benefit.

There was now early skin involvement overlying the right neck mass, massive enlargement on the left side of the neck, right axillary region and diffuse enlargement of the right breast. There was no lymphadenopathy elsewhere and no palpable liver or spleen. Clearly the histological diagnosis was in doubt. For the third time therefore an open biopsy of the right neck mass with an ellipse of the involved skin and trucut biopsies of the other involved regions, including the breast were taken. These specimens were reviewed by the Royal College of Surgeons' histopathology unit. The same granulomatous infiltrate was present in all sites; however, the overlying skin showed the histological features of *Mycosis fungoides* with atypical lymphocytes involving the epidermis (Fig. 2). An histological diagnosis of a granulomatous variant of cutaneous T-cell lymphoma was made. Immunohistochemistry confirmed the T-cell nature of the infiltrate. A facial nerve palsy that developed after biopsy required a lateral tarsorrhaphy.

Initial treatment was with chemotherapy. With no visible response in two weeks, radiotherapy was given as 3000 cGy to the neck in opposed fields and 3000 cGy to the supraclavicular fossae in ten fractions. There was immediate response, in two

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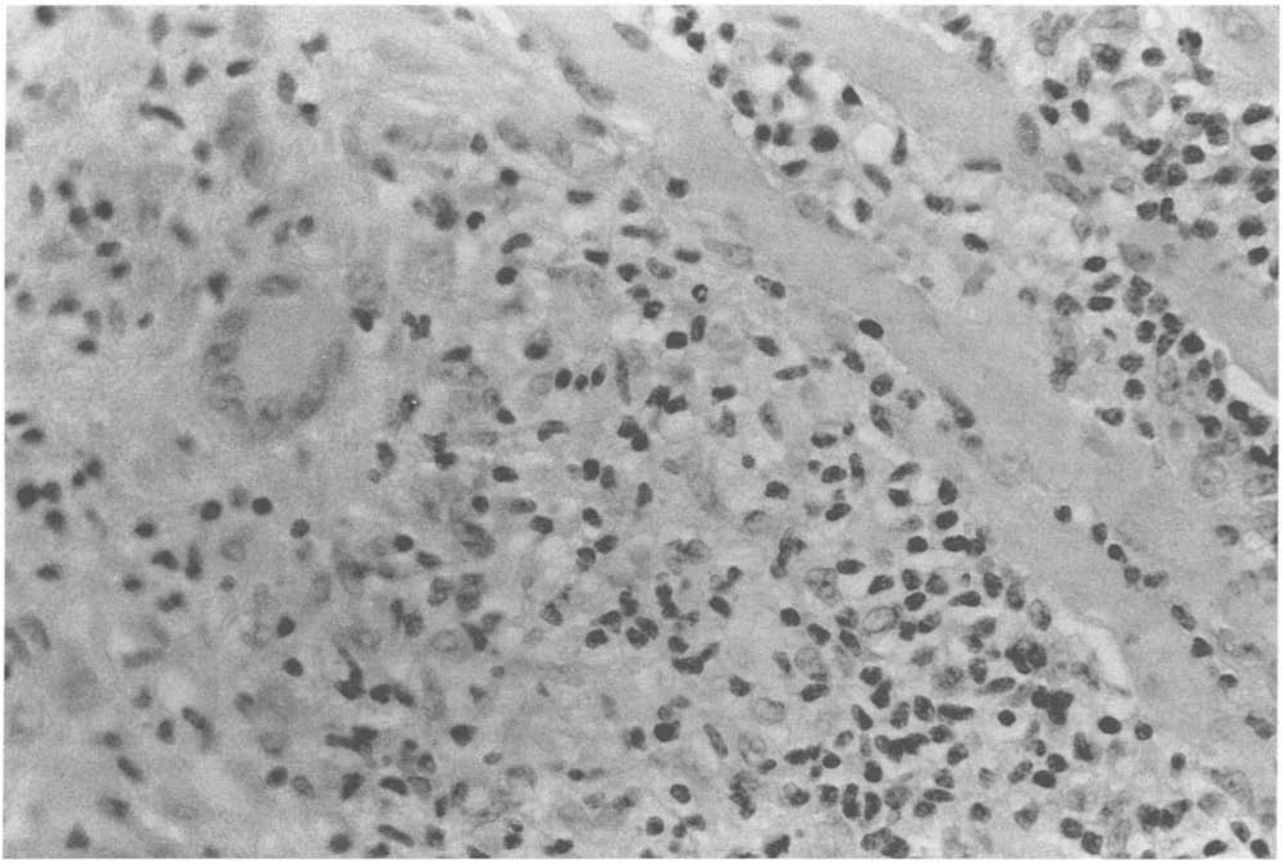

Fig. 1
Granulomatous inflammatory infiltrate including giant cells within muscle (×120).

months the skin involvement resolved, the facial palsy improved and the tumour bulk greatly diminished. Six months later some residual swelling on the right side of the neck was treated with a further 800 cGy as a palliative dose. The patient remains alive and well now one year after treatment.

Discussion

There are reports of difficulties and delay in reaching an histological diagnosis of the granulomatous variant of malignant lymphoma. In all cases the true nature of the disease has been obscured by the granulomatous infiltrate which has directed investigations to exclude chronic granulomatous conditions (Braylan *et al.*, 1977; Randle *et al.*, 1980). In *Mycosis fungoides* the granulomatous infiltrate has rarely obscured the typical histological pattern though there have been instances where non-granulomatous specimens have been required for an unequivocal diagnosis (LeBoit *et al.*, 1988). In the case presented here, repeated biopsies of the apparent tumour in the neck yielded only evidence of an extensive granulomatous infiltrate which was interpreted to be tuberculosis. Only when the overlying skin was included were the typical features of *Mycosis fungoides* seen of lymphocytic atypia and epidermotropism.

In *Mycosis fungoides* there is often a natural progression from patches to plaques to nodules with or without ulceration (Flaxman *et al.*, 1983). This progression may be slow with skin lesions present for up to 10 years before an histological diagnosis of *Mycosis fungoides* is made. Tumours may however arise without this orderly progression. Spread to extracutaneous tissues is recorded in 23 per cent of patients during subsequent follow-up (Fuks *et al.*, 1973) and carries a poorer prognosis. Lymph node involvement specifically decreases longevity from 34 to 18 months from the time of diagnosis (Epstein *et al.*, 1972). Histologically the more advanced or aggressive disease is often reflected in a change from epidermotropism to non-epidermotropism which may be reversible by treatment (Edelson, 1980b).

The significance of a granulomatous infiltrate is uncertain. It is seen in 9 per cent to 18.7 per cent of patients with Hodgkin's disease (O'Connell *et al.*, 1975) and may obscure the diagnosis despite widespread awareness (Braylan *et al.*, 1977; Randle et al., 1980). It is rare in Cutaneous T-cell Lymphoma but is being increasingly recognized (Flaxman *et al.*, 1983; Dabski and Stoll, 1987). It has been postulated that it may represent a protective hypersensitivity likening it to the more benign tuberculoid leprosy (Flaxman *et al.*, 1983). This report followed a patient for more than 30 years witnessing in the early years spontaneous healing of nodules suggesting an inherent resistance. This is disputed in a report of four cases of unremarkable survival of whom three developed CNS involvement soon after diagnosis. In all cases a granulomatous infiltrate was demonstrated which did not seem to improve the outlook for systemic involvement, disease control or the survival period (Dabski and Stoll, 1987). It seems likely that the only circumstances in which the granulomatous reaction is favourable is when it is extensive and lymphophagocytic giant cells are seen as in granulomatous slack skin (LeBoit *et al.*, 1988).

Both topical treatments and electron beam therapy have been used on *Mycosis fungoides* with similar success (Hoppe *et al.*, 1979; Vonderheid *et al.*, 1979). The development of more specific anti T-cell antibodies in heterologous antithymocyte globulin promises a more accurately targeted treatment (Edelson *et al.*, 1979b).

The histological difficulties of establishing the diagnosis of cutaneous T-cell lymphoma are unavoidable. This report and the experience of others indicate the importance of including the skin overlying a neck node when the diagnosis is in doubt. When a marked granulomatous reaction is present further biopsies from an area in which the reaction is less intense may help to

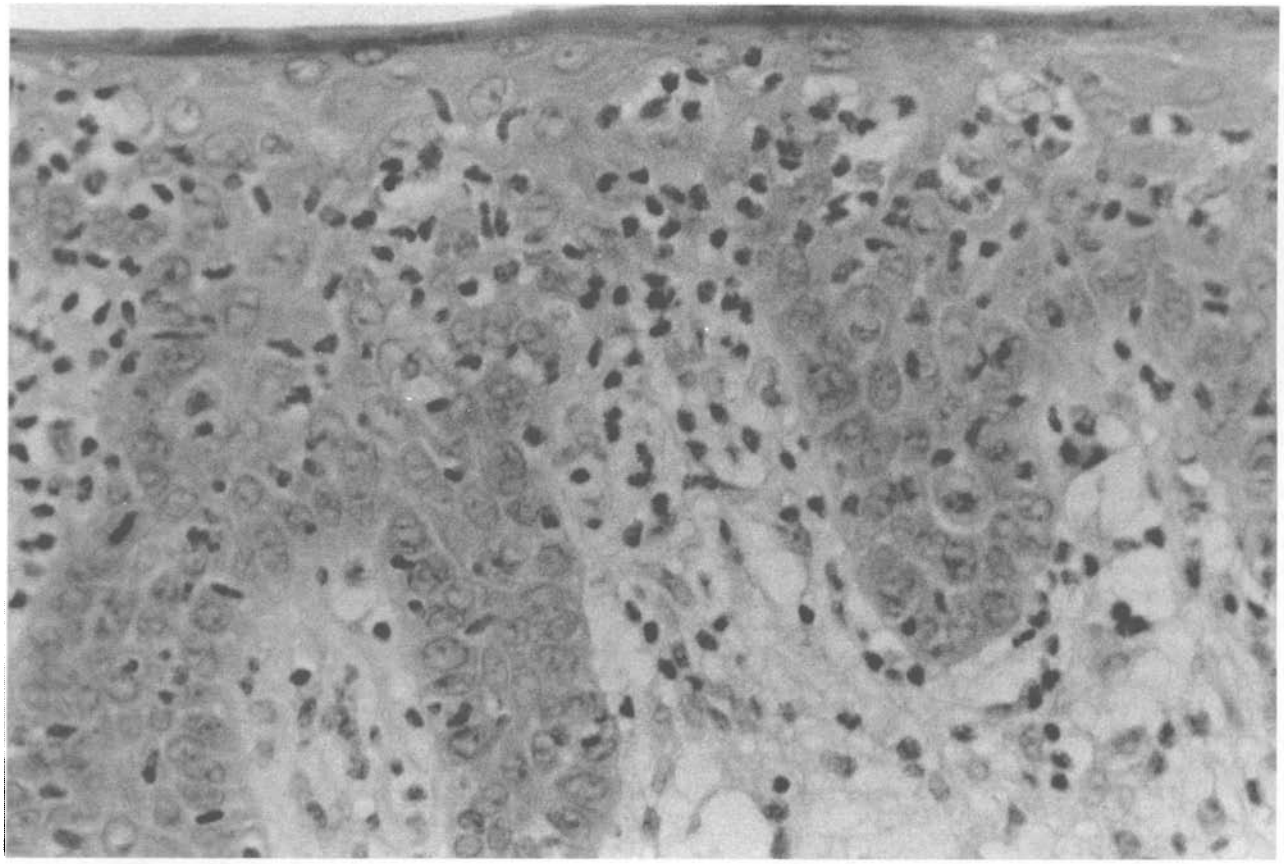

Fig. 2
Features of cutaneous T-cell lymphoma with atypical lymphocytes in papillary dermis and epidermis (×120).

focus attention on the characteristic pattern of cutaneous T-cell lymphoma.

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