level as preoperatively. Plasma gonadotrophins were persistently suppressed. A dexamethasone suppression test was repeated (2 mg daily for 5 days) (Table 1). During this test, urinary free cortisol levels were fully suppressed, but plasma testosterone remained elevated above the normal adult levels. Urinary pregnanetriol was normal basally, and remained normal throughout.

Twelve months postoperatively plasma testosterone levels had fallen to within the normal adult range and now remain there (Figure 2).

Discussion

Initially this boy had been thought to have idiopathic precocious puberty, and earlier clinical examination elsewhere had not shown an enlarged testis. This had been the rationale for the cyproterone therapy, which was ineffective. We are not sure at what age the right testis became enlarged.

The biochemical investigations at age 9 were consistent with excess testicular androgen production. The slightly raised urinary pregnanetriol excretion was not high enough to indicate an adrenal source, and there was no suppression with dexamethasone. The low (prepubertal) gonadotrophin values were against idiopathic or other forms of hypothalamic precocious puberty.

The unusual feature in this case is the evidence for nodular hyperplasia in the testicular tissue surrounding the main tumour nodule. This feature has not been reported in humans, but Bonser & Robson (1940) described both interstitial cell hyperplasia and real interstitial cell tumour growth in rodents following oestrogen stimulation. In these studies a gradual transition was found between hyperplasia and benign and even malignant tumour growth. Dalgaard & Hesselberg (1957) discussed the distinction between hyperplasia and tumour of the interstitial cells, and pointed out that a clear distinction is not always practicable.

In the present case it was also surprising that the other testis continued to produce levels of androgen above that of the normal adult male for some months postoperatively, in spite of transient fall on the day of operation. We were concerned that there could also be a hyperplastic change in the left testis, but the gradual fall to the normal adult range suggests that the left testis is essentially normal.

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Lymphomatoid papulosis and primary cutaneous Hodgkin's disease[1]

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A case is described of a man who had lymphomatoid papulosis for 20 years and in whom a focus of Hodgkin's disease occurred in a persistent plaque in the skin. There was later involvement of the regional lymph nodes. This association does not appear to have been described previously.

Case report

A 69-year-old man presented to St Bartholomew's Hospital in March 1978. For 20 years he had had recurrent papules on the limbs and trunk, on average about 4 lesions each year, the largest lesion being 1.0 cm in diameter. Individual lesions caused itching, became necrotic and ulcerated, but healed spontaneously over the course of one to two months to leave depigmented varioliform scars. A diagnosis of cutaneous 'vasculitis' had been made but no biopsy was taken.

In December 1977 he had developed a new lesion in the left antecubital fossa. This resembled previous lesions, but it healed only partially with scarring, became indurated and ulcerated and was unaffected by local therapy and a course of prednisolone 15 mg orally daily. In June 1978 a biopsy was taken which showed mild acanthosis, spongiosis and patchy infiltration of the epidermis by lymphoid cells. The upper dermis was oedematous and contained focal aggregates of lymphocytes, macrophages, eosinophils,

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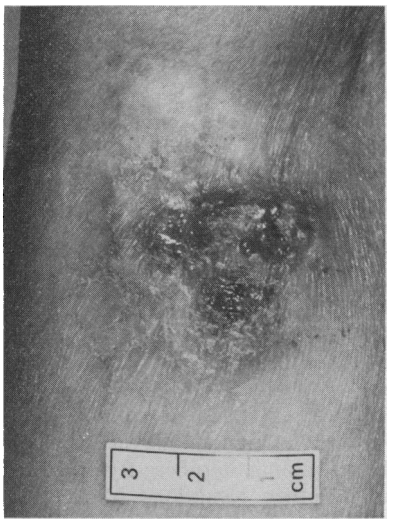

Figure 1. Persistent plaque in left antecubital fossa

neutrophils, plasma cells and several cells with large, hyperchromatic, irregularly-shaped nuclei. Much of the infiltrate was related to vessels and many mitoses were present. Lymphomatoid papulosis was considered to be the most likely diagnosis.

In August 1978 he developed a further papule on the dorsum of the hand. Histology showed a sharply localized lesion with a heavy, lymphocytic infiltrate in the upper dermis extending into the epidermis which showed partial necrosis at the centre of the lesion. Large, atypical lymphoid cells, often in mitosis, were present in addition to the perivascular infiltrate of small lymphocytes. Extravasation of red cells into the dermis was present at the centre of the lesion. A diagnosis of lymphomatoid papulosis was made.

By March 1979 the lesion in the antecubital fossa had enlarged to 3×2.5 cm and remained ulcerated (Figure 1). It was excised and the defect closed by a distally-placed transposition flap. In May 1979 a solitary, firm, mobile lymph node became palpable in the left axilla and this too was excised.

The patient also suffered from chronic bronchitis and asthma and one of his sisters had died aged 56 years from a 'lymphoma'.

Histology: The specimen from the March 1979 operation showed an ulcerated piece of skin with a pleomorphic cellular infiltrate in the base of the ulcer extending below non-ulcerated epidermis and deeply into subcutaneous adipose tissue (Figure 2). The infiltrate was similar to that of the previous biopsy (June 1978) but included larger numbers of mononuclear cells with atypical,

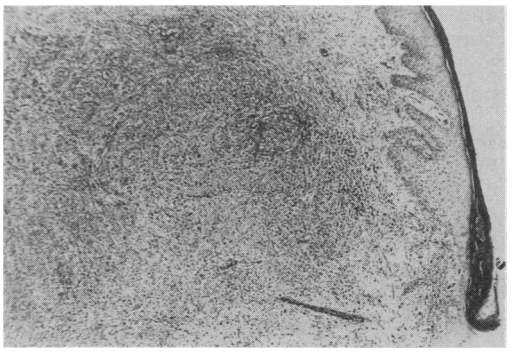

Figure 2. Margin of ulcerated plaque in left antecubital fossa. ($\times 35$)

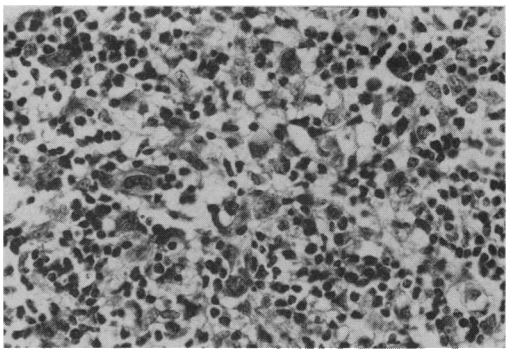

Figure 3. Subcutaneous nodular infiltrate with Sternberg-Reed cells. ($\times 320$)

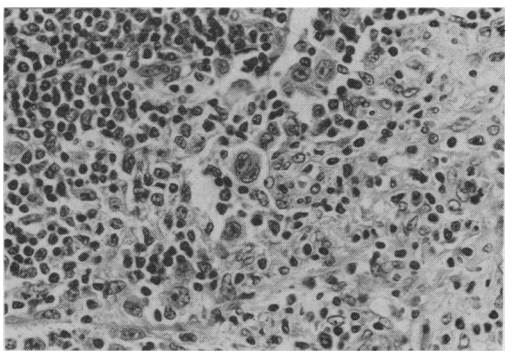

Figure 4. Lymph node biopsy showing Sternberg-Reed cells in lymph node sinuses. ($\times 320$)

hyperchromatic, pleomorphic nuclei, frequent mitotic figures and multinucleate cells with prominent eosinophilic nucleoli characteristic of Sternberg-Reed cells (Figure 3).

Sections of the lymph node excised from the left axilla showed a most unusual appearance, with most of the node enlargement due to reactive hyperplasia with prominent active germinal centres but with infiltration of the peripheral sinus

and some of the deeper sinuses with hyperchromatic pleomorphic nuclei and mitoses. Numerous Sternberg-Reed cells and eosinophil polymorphs (Figure 4) were also present.

Investigations: Peripheral blood counts, plasma urea and electrolytes, and liver function tests were normal. The ESR never exceeded 15 mm/hour. Direct immunofluorescence of the lesion from the left arm revealed the presence of the C_3 component of complement in the walls of blood vessels accompanied by smaller amounts of IgM and IgA; ANF was positive at a titre of 1:100. Computerized axial tomography revealed no abnormality of the para-aortic nodes, spleen or hepatic parenchyma. No hilar or mediastinal node enlargement was detectable on chest radiography and the lung fields were clear. Respiratory function tests revealed airflow obstruction. Examination of the bone marrow in August 1979 was normal.

Management and progress: In view of the history, physical and histological findings, a diagnosis of lymphomatoid papulosis was initially made. However, the persistence of the lesion and its histological appearance raised the possibility of Hodgkin's disease. Although the pattern of lymph node involvement was most unusual for primary lymph node Hodgkin's disease, the presence of typical Sternberg-Reed cells in the sinuses suggested lymphatic spread of Hodgkin's disease from a primary extranodal source and was compatible with a focus of primary Hodgkin's disease that had spread from the skin to the lymph nodes.

A second enlarged node, found in the left axilla, was treated by irradiation: 4000 rad in 23 fractions was given to the left cervico-axillary canal. The patient has since remained symptomless and disease free.

Discussion

Nonspecific cutaneous lesions often occur in Hodgkin's disease. The most common of these are pruritus, herpes zoster and acquired xeroderma (Amblard *et al.* 1973). Specific lesions, i.e. those in which there is an infiltrate of Hodgkin's disease in the skin, are rare and occur in advanced or aggressive disease (Amblard *et al.* 1973, Epstein & MacEachern 1937, Van der Meiren 1948, Benninghoff *et al.* 1970, Kaplan 1972) by haematogenous spread in the later stages of the disease, by direct spread from involved bones (usually ribs), or retrograde lymphatic spread of tumour tissue from involved lymph nodes.

The first description of specific Hodgkin's infiltrate in the skin is attributed to Grosz (1906). Many cases where cutaneous involvement has been the first presentation have since been recorded, the majority having advanced or locally aggressive disease in nodes and internal organs.

Hodgkin's disease can present in the skin and remain localized to the skin for a long period. Seven such cases have been recorded (Hövelborn 1932, Van der Meiren 1946, Szur *et al.* 1970). One patient is known to have died from the disease, widespread lymph node involvement being present at post-mortem examination (Van der Meiren 1946). In all these cases the diagnosis was made on histological criteria, in particular the presence of a heavy infiltrate of Sternberg-Reed cells in the corium, despite the fact that in one case (Van der Meiren 1946) the clinical picture and course of the disease were typical of mycosis fungoides. Sternberg-Reed cells by themselves are no longer considered to be pathognomonic of Hodgkin's disease. Cells resembling Sternberg-Reed cells can also appear in other conditions (Allen 1948, Hartsock 1968, Lukes *et al.* 1969, Strum *et al.* 1970, Tindle *et al.* 1972, Wright 1970) and bizarre giant cells, some of which are difficult or impossible to distinguish from Sternberg-Reed cells (Brehmer-Andersson 1976) may be found in the skin lesions of mycosis fungoides. Brehmer-Andersson (1976) doubts the validity of the diagnosis of the recorded cases of primary cutanous Hodgkin's disease and also states that some of the previously published cases of lymphomatoid papulosis ought to be regarded as mycosis fungoides. She concludes that the presence of cells which are 'difficult or impossible' to distinguish from Sternberg-Reed cells is not in itself sufficient reason to make a diagnosis of Hodgkin's disease; and that the seven previously documented cases of primary cutaneous Hodgkin's disease, in view of their histological picture together with the primary localization of disease in the skin and the protracted course of the disease, can be better diagnosed as mycosis fungoides, thus questioning the concept of primary cutaneous Hodgkin's disease. In our opinion the 3 cases of Szur *et al.* (1970) would probably be better regarded as lymphomatoid papulosis than as mycosis fungoides.

However, in Hodgkin's disease it is the setting in which Sternberg-Reed cells occur that is of more importance than the presence of the cells themselves. In our patient the histological features of the persistent plaque, which showed a deeply situated nodular infiltrate with polymorphic cytological features and typical Sternberg-Reed cells with mitoses, are regarded as evidence of Hodgkin's disease occurring primarily in the skin and possibly representing true malignant transformation in a plaque of lymphomatoid papulosis. The cellular infiltrate in the axillary node was equally typical of Hodgkin's disease, despite its unusual situation in the node. The

unusual situation of this infiltrate is compatible with subsequent spread of disease from a primary focus in the skin.

Since 1968, when MacAuley first coined the name lymphomatoid papulosis to describe a clinically benign but histologically malignant condition, over 80 cases have been recorded (for review *see* Doutre *et al.* 1977). Three of the cases developed systemic malignancy: one developed an undifferentiated lymphoma, another an anaplastic sarcoma, and the third a reticulum cell sarcoma. They had had lymphomatoid papulosis for 40, 18, and 8 years respectively. None of the other reported patients have had lymphadenopathy with the exception of Doutre's patient. In that patient axillary lymphadenopathy was present but no lymph node biopsy was performed. There is no recorded instance of lymphadenopathy with histological findings in association with lymphomatoid papulosis.

The patient reported here had lymphomatoid papulosis for 20 years with a typical clinical and histological presentation, and Hodgkin's disease developed in a persistent plaque in the skin and spread to involve the regional nodes. Unfortunately no biopsy prior to 1978 is available to give histological support to the retrospective diagnosis of lymphomatoid papulosis.

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Poliomyelitis-type illness associated with severe asthma in a child[1]

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If a child develops an acute paralytic illness shortly after an attack of asthma, this might appear to be a complete coincidence. However, in the last six years 18 such cases have been described which are clinically so similar that there would seem to be a direct relationship between the asthma and the paralysis. The nature of this relationship is not at all clear but it may have an important bearing on the fundamental aetiology of both conditions. The case described here illustrates many of the features of this syndrome.

Case report

S B was born on 8.1.1965. He developed eczema at five months of age and asthma at one year. Because of his asthma and eczema he received no immunization of any kind but his siblings had been given Sabin polio immunization.

He was admitted to hospital in 1967 when two years old with a history of being unwell for two weeks. Initially, he had developed a croupy cough and an associated asthmatic attack. His condition had improved on antibiotics over the course of a week, then three days before admission he complained of pain in his left arm and for two days had been unable to move it. At this time he was afebrile, fully conscious and without meningeal signs. He had a flaccid paralysis of his left arm. There was no sensory loss and the rest of the nervous system was normal.

Blood examination showed a haemoglobin of 11.0 g/dl and a total white cell count of 10.0×10^9/l. Cerebrospinal fluid examination showed a protein of 210 mg/l, glucose 4.5 mmol/l; globulin positive, Lange 0111 0000, and contained 1–2 lymphocytes/ml. Neutralizing polio antibody titres were as follows: Type 1 – 1:16, Type 2 – 1:1024, Type 3 – 1:1024. Repeat values measured two weeks and two months later were identical. Faeces cultures were negative for viruses on four occasions. In 1980, serum immunoglobulins were measured and showed IgG 86 iu/ml, IgA 96 iu/ml, IgM 175 iu/ml.

There has been no significant recovery in the muscles of the left arm. Wasting and secondary growth failure have become marked. His asthma has remained severe and he has required numerous hospital admissions. Systemic and inhalation steroids have had to be used for long periods.

[1]Case presented to Clinical Section, 6 June 1980. Accepted 13 October 1980

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