

Case 1: A Boy with Lymphomatoid Papulosis or Lymphoma?

Dr. S. Y. Cheng

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CASE SUMMARY

History and physical examination

An eight-year old boy developed itchy erythematous urticarial plaques over both lower limbs and buttock in August 1995. There was no associated fever or joint pain. The condition totally subsided in two months after oral anti-histamine therapy.

In April 1996, the patient suddenly developed multiple asymptomatic discrete brownish papules, 2 to 3 mm in diameter, over both buttock and lower limbs (Figure 1). The patient defaulted follow up for one year during which the papular eruptions decreased in size but never completely subsided.

In November 1997 he developed sudden onset of intensely itchy nodules at both limbs, trunk and buttock. This time the lesions were larger and more erythematous than the previous ones, and some formed an arcuate shape (Figure 2). Over the course of a few months, the lesions wax and wane with some showing partial regression, leaving postinflammatory hyperpigmentation. There was no systemic upset nor extra-cutaneous involvement. His past health was good with no significant family history.

Investigations and diagnosis

Skin biopsy performed in August 1995 showed dense perivascular infiltrate of neutrophils in the dermis. The vessel wall was swollen and infiltrated by inflammatory cells. The epidermis was unremarkable. Immunofluorescence study showed C3 deposition in the dermal-epidermal junction and vessel walls in papillary dermis. The diagnosis was urticarial vasculitis.

Skin biopsy performed in April 1996 showed wedge shaped dermal infiltrate consisting of abundant atypical mononuclear cells with large and irregular



Figure 1: Multiple brownish papular eruptions at both buttock and lower limbs



Figure 2: Erythematous nodular eruptions with arcuate shape pattern

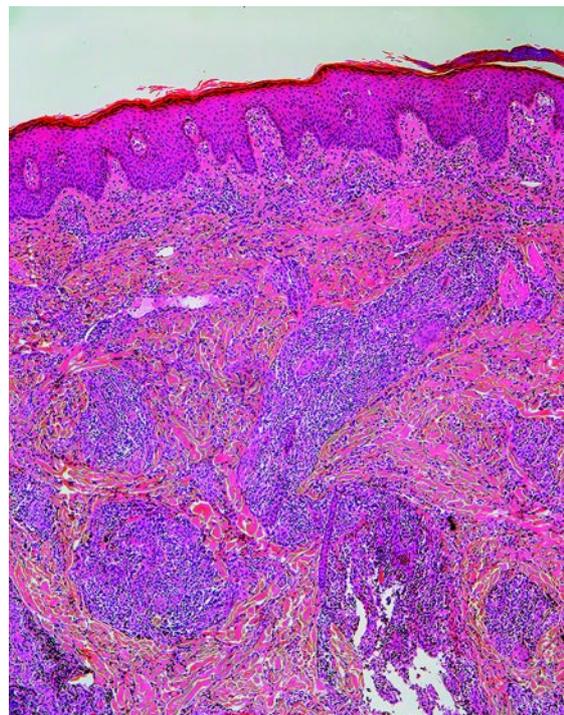


Figure 3: Low power view showing dense nodular polymorphous dermal infiltrate in a predominantly perivascular distribution

hyperchromatic nuclei and small to moderate amount of pinkish cytoplasm. Mitoses was infrequent and there was no Pautrier microabscess. Vasculitis was not found. The diagnosis was lymphomatoid papulosis.

In view of a change in the morphology of the cutaneous lesions, malignant lymphoid change was suspected. Thus a third skin biopsy was performed in November 1997. This showed similar features to the second biopsy except that mitoses were more frequent. The histological diagnosis was still lymphomatoid papulosis (Figure 3 and 4).

Investigations so far include complete blood picture, liver and renal function tests, autoimmune markers screening were normal.

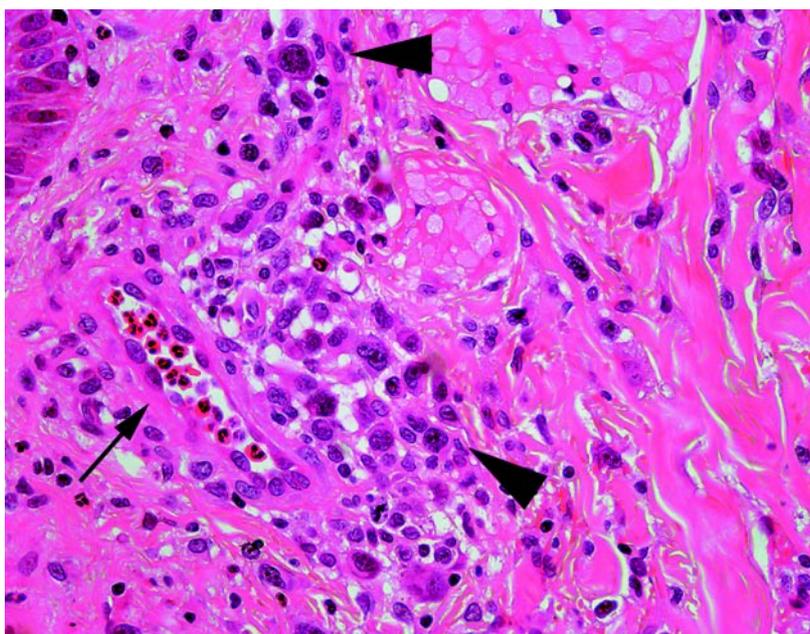


Figure 4: High power view with arrowhead pointing at atypical lymphoid cells and arrow pointing at eosinophils within a vessel

(Photographs kindly supplied by Dr. K. C. Lee of Princess Margaret Hospital)

Management and progress

The patient was given a course of oral erythromycin and topical 0.05% clobetasol butyrate. Fortunately, the lesions gradually regressed. It was not sure whether the remission was due to natural course or as a result of the treatments.

REVIEW ON LYMPHOMATOID PAPULOSIS

Lymphomatoid papulosis is defined as a chronic recurrent self-healing papulonecrotic or papulo-nodular skin eruption.¹ Despite an alarming histologic appearance suggestive of malignant lymphoma, it usually runs a benign course. Clonal T cell receptor gene rearrangement is often present but this clonality does not necessarily mean malignancy. However, 10 to 20% of these patients do develop malignant lymphoid change, most commonly mycosis fungoides (35%), secondary CD30 lymphoma (32%) and Hodgkin's disease (24%).²

Pathogenesis

The pathogenesis of lymphomatoid papulosis is uncertain. There had not been any reported association with urticarial vasculitis which is an immune complex mediated leucocytoclastic vasculitis. It is possible that a common antigen, for example a virus, triggers initially an immune complex reaction and later a lymphoproliferative reaction.

Histological types

Histologically there are two types: type A and type B. Type A consists of CD30+ve large atypical Reed Sternberg-like cells with numerous mitoses and inflammatory cells. Epidermotropism is not found. Type B consists of CD30-ve atypical cerebriform mononuclear cells similar to those seen in mycosis fungoides and epidermotropism is found.

CD 30 +ve lymphoproliferative diseases

Because of morphological and immunophenotypic similarities between large atypical cells in lymphomatoid papulosis and neoplastic cells in CD30+ve large cell lymphoma, these diseases are believed to represent a spectrum of CD30+ve lymphoproliferative diseases.^{3,4,5,6} The spectrum ranges

from the benign end of lymphomatoid papulosis, to the other end of malignant diseases such as mycosis fungoides, anaplastic large cell lymphoma and Hodgkin's disease.

CD30+ve large cell lymphoma usually presents with solitary or regionally distributed nodules with infrequent regression (20%) and extracutaneous involvement (25-30%).⁴ The CD30+ve cells form large cohesive sheets rather than wedge shape pattern and it may infiltrate into subcutis. The proportion of CD30+ve cells to inflammatory cells is high, usually >75%.⁴ On the other hand, lymphomatoid papulosis consists of papulonodules in regional or diffuse distribution with no extracutaneous involvement. It almost always shows regression. Histologically, wedge shape pattern of infiltration is characteristic with smaller percentage of CD30 positivity of 25-50% only.⁴ It does not infiltrate the subcutis. In practice borderline cases with clinical and histological features in between these two disorders exist. We may encounter patients with clinical picture of lymphomatoid papulosis but histological features of CD30+ve large cell lymphoma, or vice versa.³

It is sometimes difficult to determine whether a patient with lymphomatoid papulosis has undergone malignant lymphoid change. The morphology and size of the lesions or the presence of regression are not reliable signs.⁴ A change in the behaviour of eruption, presence of lymphadenopathy or B symptoms (weight loss, fever or chills) are more important. As in our patient, even though the histological diagnosis was still consistent with lymphomatoid papulosis, more frequent follow up with repeated biopsy at suspected sites are mandatory. He may belong to one of the borderline cases that has a higher chance of transforming into malignant lymphoma. The histological slides should be sent for immunophenotyping studies. The ratio of atypical cells to inflammatory cells (% of CD30+ve)³ and a change in the tumor cell phenotype with additional loss of T cell antigen (CD5 and 7)¹ are important clues to malignant transformation. Any infiltration into subcutis should also be taken seriously.

Management

Therapy should be tailored to individual patient; the severity of disease should be considered since no treatment alters risk of progression of the disease. In cases of lymphomatoid papulosis, therapy ranges from simple observation, topical steroid, oral antibiotic,

PUVA, topical mechlorethamine and carmustine, to low dose methotrexate and 13-cis retinoic acid. The use of acyclovir and interferon alpha are being investigated.^{1,3,7}

For borderline cases, since they have similar clinical behaviour as lymphomatoid papulosis with 80% showing regression, they should be treated more conservatively. Even for those with CD30+ve large cell lymphoma, observation for several months is advisable because a small proportion will show regression. Apart from therapies above, more aggressive approach can be adopted such as radiotherapy and systemic chemotherapy for generalized florid skin disease and extra-cutaneous involvement. However, paediatric patients may not tolerate aggressive chemotherapy or radiotherapy as well as adult patients. In such group, pulse super-potent topical steroid⁸ or alpha interferon combined with PUVA⁹ can be tried. Last but not the least, patient education about the need for long term regular follow up is mandatory.

Learning points:

Lymphomatoid papulosis needs close surveillance for malignant transformation. Histological proof of such transformation often needs repeated skin biopsy.

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