

# Sézary-type Cutaneous T-cell Leukaemia

## Response to Winkelmann Regimen

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**A 37-year-old woman presented with an aggressive leukaemic form of small T-cell Sézary syndrome. Despite this unusually malignant variant of the disease, there was a dramatic response to a modified Winkelmann regimen of chlorambucil and prednisolone, and a useful, sustained remission of 7 months. The Winkelmann regimen remains an important and relatively non-toxic chemotherapeutic option for palliation of advanced Sézary syndrome.**

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Sézary syndrome is an erythrodermic variant of mycosis fungoides with circulating malignant cerebriform T-cells and both belong to the general category of cutaneous T-cell lymphoma (CTCL). Mortality rates differ, but poor-risk patients with visceral involvement have a median survival of 2.5 years (1). Patients die as a result of florid progression of widely

disseminated disease, infection, or complications of treatment. Indeed, aggressive treatment of advanced disease is associated with high morbidity and mortality (2).

A patient who presented with advanced leukaemic phase of Sézary syndrome was treated with a modified version of the Winkelmann regimen (3). Her social circumstances precluded multiple, toxic chemotherapeutic regimens which might entail prolonged hospital admission and concomitant risk of complications.

### CASE REPORT

A 37-year-old woman developed a generalized and intensely pruritic eruption over 4 months. She was divorced and unemployed and had three children. On presentation the patient was ill with erythroderma, diffuse cutaneous induration, excoriations, crusting, subtotal alopecia, lymphadenopathy and hepatosplenomegaly (Fig. 1a). She was admitted for investigation with the following abnormal laboratory findings: haemoglobin 10.3 g/dl, platelet count  $441 \times 10^9/l$ , white cell count  $444 \times 10^9/l$ ; bone marrow aspirate contained abundant small cells with convoluted nuclei. Serum gamma glutamyl transferase 68 IU/l, alkaline phos-

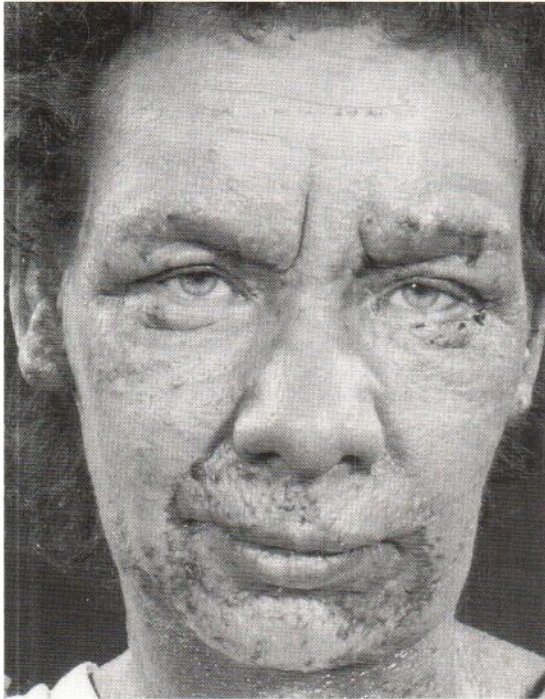


Fig. 1a. Appearances at presentation.

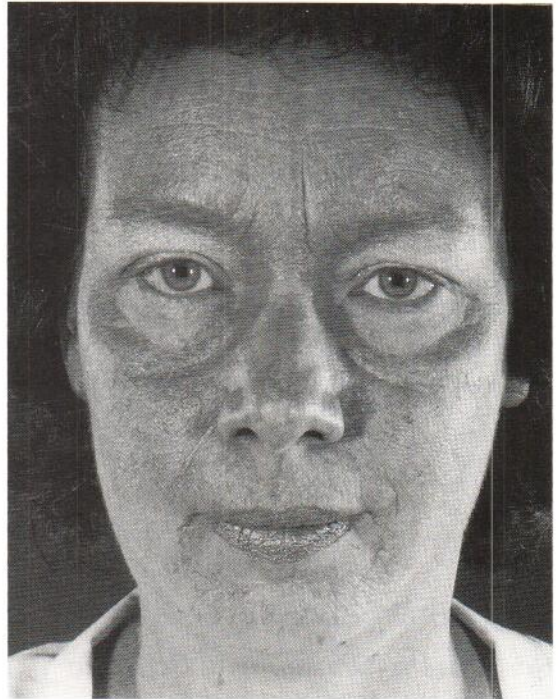


Fig. 1b. Marked improvement after 4 weeks of treatment.

phatase 641 IU/l, bilirubin 33 IU/l. Chest X-ray and CT scan revealed mediastinal, para-aortic and pelvic node involvement and enlargement of liver and spleen.

Prior to chemotherapy, histology of skin showed a dense, band-like upper dermal and perifollicular cellular infiltrate. The cell population was mixed, consisting of lymphoid cells, occasional plasma cells and eosinophils. Atypical lymphoid cells with convoluted nuclei were the predominant cell type, and formed Pautrier microabscesses in the adnexal epithelium and epidermis (Fig. 2). The lymph node architecture was replaced by polymorphous lymphoid infiltrate containing atypical cerebriform cells. A panel of monoclonal antibodies was used to stain frozen sections of skin and lymph node. The predominant cell type in both sites was of peripheral T-cell (CD2, CD3 positive) and expressed the helper-inducer marker CD4.

Small T-cell Sézary syndrome with frank leukaemia was diagnosed. Chlorambucil (0.1 mg/kg/day), prednisolone (60 mg/day) and topical clobetasol propionate (*Dermovate*<sup>®</sup>) resulted in marked clinical improvement (Fig. 1b). Persistent pruritus and patchy erythematous induration were controlled by PUVA. The patient's overall well-being was greatly improved; 6 weeks later she was discharged from hospital. Out-patient treatment consisted of prednisolone (20 mg/day), topical betamethasone valerate (*Benivate*<sup>®</sup>), weekly PUVA, and intermittent pulse therapy of chlorambucil (0.2 mg/kg/day). CT scan examination 3 months after diagnosis indicated reduction in lymphadenopathy, normal size liver and spleen; repeat skin histology

confirmed partial remission. The white cell count remained constant at  $30 \times 10^9/l$ , but Sézary-type cells persisted.

Seven months after diagnosis she developed a spiking fever, oro-perineal candidiasis, staphylococcal skin infection, lymphadenopathy and hepatosplenomegaly. The fever persisted despite repeatedly sterile blood cultures and courses of ketoconazole and parenteral broad spectrum antibiotics. Following MCOP (mitozantrone, cyclophosphamide, vincristine and prednisolone) the fever settled, but she subsequently developed neutropaenia and septicaemia and died 8 months after diagnosis. Post-mortem examination showed widespread leukaemic infiltration of lymphoreticular system, kidneys, lungs and brain.

## DISCUSSION

Sézary syndrome was diagnosed in view of a preceding history of cutaneous involvement, Pautrier abscesses in the epidermis, and the presence of peripheral, cutaneous and nodal atypical helper-inducer T-cells. According to the clinical type and extent of skin involvement (T4), lymph node grading (L4) and combination staging procedure which accounts for visceral involvement, blood smear positivity and lymph node effacement (IVB), this case had the most advanced form of cutaneous T-cell lymphoma (4, 5). Bone marrow involvement corroborated the



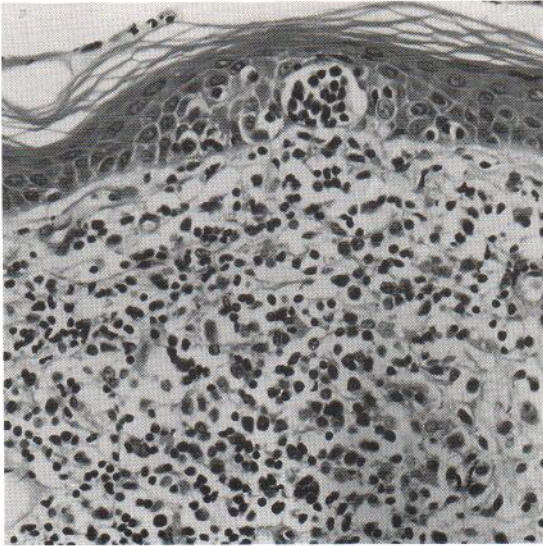


Fig. 2. Photomicrograph showing dermal infiltrate which consists mainly of atypical lymphocytes. A Pautrier microabscess is seen in the epidermis (right of centre). ( $\times 230$ )

diagnosis of T-cell leukaemia. The prognostic indicators included in the staging and grading methods would indicate that this patient had less than 50% chance of surviving 12 months after diagnosis despite treatment (6), although small circulating malignant T-cells are associated with better survival. In Schechter's series disruption of lymph node architecture with small cells occurred in 2 of 17 patients (12%) at initial diagnosis and visceral involvement was present in 4 of 17 cases (23%). Our patient had small T-cell morphology, diffuse visceral and lymph node involvement with disruption of nodal architecture with an associated adverse prognosis. This case, therefore, represents an unusually malignant variant of leukaemic small cell Sézary syndrome.

Poor risk patients with advanced CTCL may not be suitable for extensive electron-beam radiation with chemotherapy; preliminary analysis suggests a trend toward impaired survival of those treated aggressively (2). The Winkelmann regimen of chlorambucil and systemic corticosteroid is an established therapy in the control of advanced Sézary syndrome when the peripheral white cell count is elevated (3). A useful partial remission was achieved with this relatively non-toxic therapy and PUVA also confer-

red further palliation by controlling intractable pruritis and persistent skin lesions. To date, there are promising reports of other treatment modalities, such as interferon, retinoids and cyclosporin, but studies are small and fail to make comparisons with other established treatments (7-8). However, adverse side effects and complications of treatment should be seriously considered, particularly those of cyclosporin (9). Other systemic treatments with tolerable side effects should be evaluated in order to improve palliation of advanced Sézary syndrome, and CTCL in general.

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