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Case Report

Richter's syndrome: a novel presentation

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Chronic lymphocytic leukaemia with transformation into a large cell lymphoma (Richter's syndrome) is usually associated with the rapid demise of these already immunocompromised patients. There have been no previously recorded cases involving the nose. We report such a case and describe a successful treatment approach combining monoclonal antibody therapy with a mini-allogeneic bone marrow transplant.

CASE REPORT A 54-year-old man presented to the otolaryngology department with a swelling on the dorsum of the nose, which had been rapidly enlarging for one month. Two years prior to this he was diagnosed with chronic lymphocytic leukaemia (CLL) and was stabilised initially with six courses of Chlorambucil. He relapsed one year later and bone marrow assessment following further treatment with six courses of Fludarabine showed only a partial response. One year further on he presented with the nose swelling. He had no symptoms suggestive of systemic involvement. On examination there was a 2 x 2.5cm soft mass on the dorsum of the nose continuous with a blue swelling obstructing the left nostril. The remainder of his physical examination was unremarkable. An axial CT scan (fig. 1) of his paranasal sinuses demonstrated a soft tissue mass, closely related to the left side of the anterior nasal septum, 2cm in diameter. Bowing of the nasal septum, as seen in the coronal reconstructions (fig 2) suggested the mass had been present for some time while the co-existing opacification of the left frontal air cell is a feature of sinus outflow obstruction.

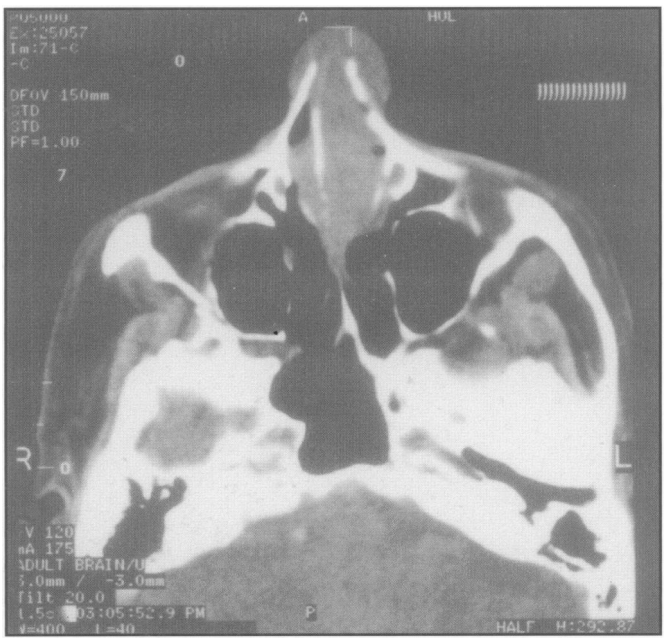

Fig. 1

An intranasal incisional biopsy confirmed a high-grade large cell transformation of the CLL - Richter's Syndrome.[1] He was treated with a six cycle chemotherapy regime of Cyclophosphamide, Hydroxorubicin, Vincristine and Prednisolone (CHOP) commencing two months after the swelling presented. It resolved and follow-up MRI scan at six months was normal.

The patient was subsequently treated with a further course of Fludarabine and the monoclonal antibody, CAMPATH-1H, before receiving a mini-allogeneic bone marrow transplant from his

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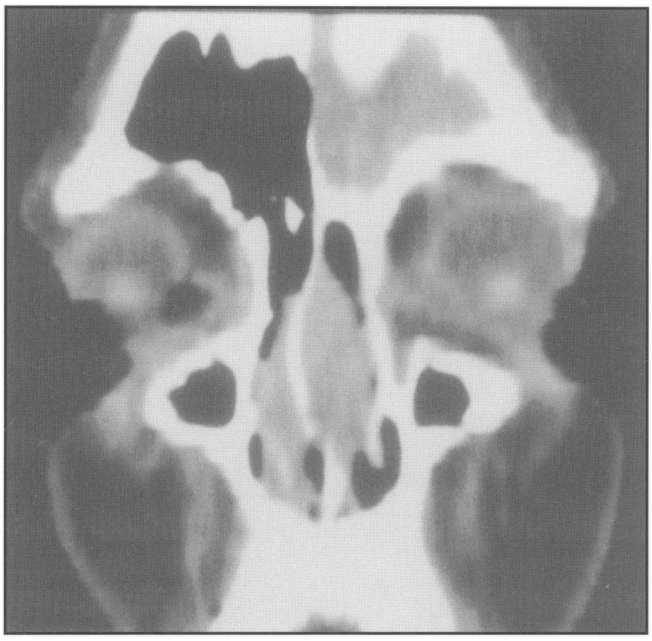

Fig. 2

brother one year from presentation. A PCR-based assay showed that complete haemotopoietic chimaerism was achieved after the transplant, however, he also had low-grade graft versus host disease.

Presently, three and half years from initial presentation, he has a normal quality of life in continuing complete remission from both the transformed disease and the CLL.

DISCUSSION

Richter's syndrome refers to the development of aggressive non-Hodgkins Lymphoma during the course of chronic lymphocytic leukaemia. Affecting 5% of these patients, it represents one of the possible anaplastic transformations of the leukaemia.[2] Disease onset is typically manifested by a sudden clinical deterioration of the patient and is characterised by rapid progression of lymphadenopathy, by extranodal disease and by constitutional symptoms. Histological examination is required to make the diagnosis of high-grade lymphoma. Immunophenotyping of the cells taken from the tissue biopsy and from a bone marrow aspirate expressed the same cell surface Kappa light chains suggesting clonal evolution rather than new disease.[3]

Robertson *et al* report a modest 5-month median survival despite multiagent therapy.[4] There is some evidence that patients may do quite well after high dose chemotherapy with stem cell support. Rodriguez *et al* have published data suggesting an improved prognosis in a series of patients receiving high dose chemotherapy followed by allogeneic bone marrow transplantation.[5]

Despite resolution of the nasal lesion following the CHOP regime the patient also underwent a bone marrow transplant and treatment with monoclonal antibody in order to provide him with the best chance of achieving complete remission. A high-dose conditioning regime is normally used prior to bone marrow transplantation. However, previous treatment with chemotherapy precluded mobilisation of autologous peripheral blood stem cells needed to compensate for the bone marrow suppression, which normally occurs following such a regime. He was therefore treated with a reduced dose of Fludarabine and CAMPATH-1H, a monoclonal antibody against CD52, an antigen expressed on greater than 95% of all normal human blood lymphocytes and most B and T cell lymphomas.[6;7] In the first report of the antibody, tumour regression was seen in two patients with advanced non-Hodgkin's lymphoma treated with CAMPATH-1H.[8] It is currently recommended for the treatment of patients with Fludarabine refractory CLL and preliminary data suggest it is effective as a first line agent in the treatment of B-cell CLL.[9;10] By activating various immune effector functions, including antibody-dependent cellular cytotoxicity, the antibody not only targets tumour cells, it temporarily destroys the recipient's T-cells. The resultant complete donor chimaerism may reduce the risk of transplant rejection and confer a survival advantage.[11] The "mini" from mini-allogeneic transplant refers to the reduced dose of chemotherapy used.

To the best of our knowledge there have been no previously reported cases affecting the nose to date. A handful of cases have been described with skin involvement, however, it is rarely limited to cutaneous locations.[12]

It is our aim to highlight not only this novel presentation but also the encouraging result obtained from new treatment techniques with monoclonal antibody and the reduced intensity conditioning chemotherapy regime.

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