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HODGKIN'S DISEASE AFTER TREATMENT FOR BURKITT'S LYMPHOMA: CASE REPORT

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SUMMARY

Hodgkin's disease and non-Hodgkin's lymphomas are interrelated disorders which have been reported to occur either simultaneously or sequentially in the same patient. We report here the development of nodular sclerosing type Hodgkin's disease in a patient two decades after successful treatment for Burkitt's lymphoma with cyclophosphamide and abdominal resection (AR). While the onset of symptoms after treatment for Burkitt's lymphoma was seven years definitive diagnosis of Hodgkin's disease was only made 22 years after the initial diagnosis of Burkitt's lymphoma. The recurrent and solitary nature of the lymphadenopathy and the fact that it was initially reported as reactive hyperplasia is typical of nodular lymphocyte predominant Hodgkin's disease. We believe that there was a transitory period of the malignancy as nodular lymphocyte predominant Hodgkin's disease.

INTRODUCTION

A most serious consequence of curative therapy for malignancies is the development of a secondary malignancy(1). The occurrence of Hodgkin's disease (HD) and non-Hodgkin's lymphoma (NHL) in the same anatomical site (composite lymphoma) or in separate sites (synchronous or metachronous) have suggested a closer association between these two disease entities(2).

Burkitt's lymphoma (BL) is a malignant lymphoma of B-lymphocyte origin(3). It is endemic in tropical Africa. It is of interest because of its dramatic response to chemotherapeutic agents, which initially was to cyclophosphamide as a singular agent(4) but lately combination chemotherapy which included cyclophosphamide has not shown such a dramatic response with some requiring bone marrow transplantation. BL has been reported to have occurred following treatment for HD(5,6). A review of such cases showed a male/female ratio of 3.75, with 78% occurring after treatment with a combination of chemotherapy and radiotherapy(6). The median interval between HD and the diagnosis of BL was eight years. There is, however, no report in the literature of the development of HD following treatment for BL. We report the development of HD in a patient who had shown a good response to the treatment of BL using cyclophosphamide and abdominal resection (AR).

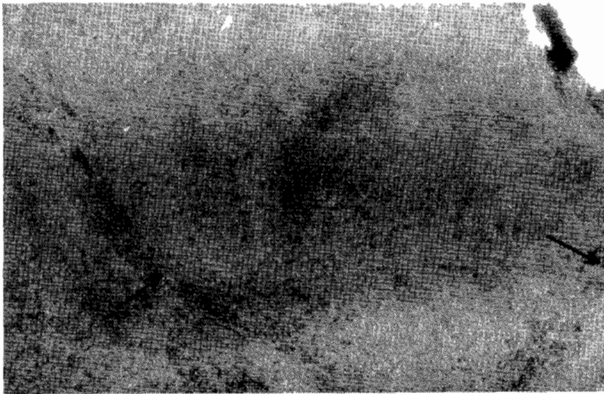
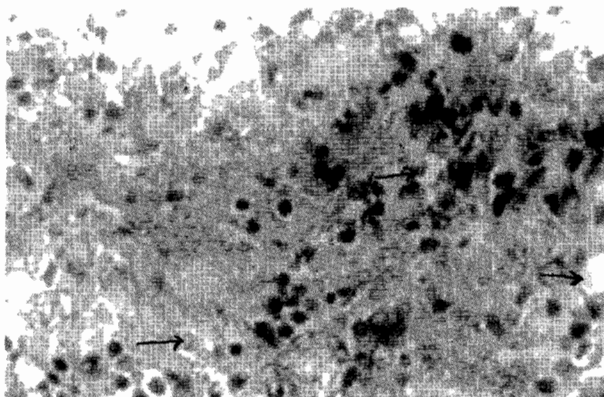
This case is being reported because of the rarity of the

development of a second malignancy following the treatment for BL despite the fact that it is a malignancy that occurs early in life and responds well to therapy. More often treatment for HD is followed by a secondary malignancy, either as acute myeloid leukaemia or BL(5-7). This case will draw further the attention of physicians to the possibility of secondary lymphoma following treatment for BL.

CASE REPORT

A 38-year old female nursing staff was referred because of a solitary left neck swelling of 15 years duration. A diagnosis of chronic tonsillitis had earlier been made following a lymph node biopsy done which was reported as reactive hyperplasia. The swelling responded to antibiotic therapy but recurred. She had a repeat biopsy done at a later date. This was reported as Hodgkin's disease but could not be sub-classified. Hence the need for referral. The patient presented with a left sided neck swelling and recurrent fever but no history of weight loss or night sweats. Twenty two years prior to presentation she had presented at a teaching hospital with an enlarged thyroid gland, nodular masses in the left breast and lower abdomen. At laparotomy, she had bilateral oophorectomy and a histological diagnosis of Burkitt's lymphoma was made. She was treated with a single intravenous infusion of cyclophosphamide to which she showed good response with the disappearance of the masses.

On examination she looked well nourished. There was a firm non-tender mass measuring 4cm by 2cm in the left supraclavicular fossa. There was no other organ enlargement.

Figure 1*Low power magnification showing fibrosis***Figure 2***High power magnification showing Reed Sternberg cell (left hand corner) and lacuna cells*

Staging done did not reveal the involvement of any other organ. A working impression of lymphoma stage 1B was made. A biopsy of the supraclavicular node confirmed nodular sclerosing Hodgkin's disease (Figures 1 and 2). She was sent back to the referring hospital due to an industrial dispute in the health sector and was lost to follow up.

DISCUSSION

The development of a secondary leukaemia is a known complication following treatment of Hodgkin's disease, especially with the use of both chemotherapy and radiotherapy(7). The risk of developing secondary malignancy depends on age, the particular drug or

combination of drugs used, the dose and duration of chemotherapy and most importantly, whether or not chemotherapy is combined with radiotherapy.

Alkylating agents are associated with leukaemogenesis, but the nitrosoureas are probably worse. Patients above the age of 40 years and those who have undergone splenectomy may also be at a higher risk. The median interval from stopping treatment to the development of leukaemia has been calculated at three years(8). Hodgkin's disease has also been described in patients previously treated for non-Hodgkin's lymphoma but the median interval from the diagnosis of NHL to the diagnosis of HD was five years (range 2 - 12 years)(9). In the case reported here, HD was diagnosed 22 years after treatment for Burkitt's Lymphoma, even though the onset of symptoms was seven years after the treatment for Burkitt's. Lymphadenopathy was recurrent and was reported as reactive hyperplasia before the final diagnosis of Hodgkin's disease.

The patient's presentation is unusual not only in the long interval between the two malignancies but occurred after treatment with a single dose of cyclophosphamide which was the initial mode of treatment for BL(4,10). The recurrent and solitary nature of the lymphadenopathy is typical of nodular lymphocyte-predominant HD, which belong to the indolent group of small lymphocyte lymphoma(11). The initial histological classification of the disorder as reactive hyperplasia is also not unusual with nodular lymphocyte predominant HD(12). In 10% of patients with nodular lymphocyte-predominant HD, the disease may evolve into a B-cell malignant lymphoma of large cell type after an interval of up to 16 years(13). It could be inferred that there was a transitory period of the malignancy as nodular lymphocyte predominant HD before its evolution into nodular sclerosis HD. The histological sub-classification of nodular sclerosis in this patient is however not unexpected since nodular sclerosis or mixed cellularity HD are mostly found in association with NHL(8,9).

Reports of patients with a low grade B cell lymphoma or leukaemia who have developed HD has given rise to speculations that the neoplastic cells from the two conditions are related. This has also led to the hypothesis that HD is probably a B cell process (11,14). Burkitt's Lymphoma is a B cell neoplasm, which has been associated with infection with Epstein Barr Virus (EBV). The identification of EBV in NHL of composite NHL and HD, suggest a common origin from an EBV infected progenitor cell (15). There is also recent evidence that the EBV is associated with a significant proportion of cases of Hodgkin's disease, with the detection of EBV genomes in affected tissues and that EBV gene products confer a growth advantage on Reed- Sternberg cells (15). The development of Hodgkin's disease after Burkitt's lymphoma further strengthens the suggestion that HD may be clonally related to an underlying B-cell malignancy and that the Reed-Sternberg cell may be an altered B lymphocyte.

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