RELAPSE OF HODGKIN'S DISEASE AFTER 10 YEARS OF COMPLETE REMISSION: CASE REPORT

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SUMMARY

A 17 year old male patient with nodular sclerosis Hodgkin’s disease had a relapse of lymphocyte depleted type ten years after entering complete remission with chemotherapy and radiotherapy. This is the first documented case in our experience of relapse after very long disease free interval. A review of the literature of late relapses in Hodgkin’s disease is also presented. Relapses have been recorded from three years to twenty years, although few very late forms are registered. Long term follow up will be necessary to document the role of the different therapeutic regimen.

INTRODUCTION

Hodgkin’s disease (HD) is ranking fourth overall among childhood malignancies seen at Kenyatta National Hospital, the referral, teaching and only major centre for management of patients with cancers in Kenya (Authors’ unpublished data). Since late 1970s Hodgkin’s lymphoma has been observed to be the childhood malignancy with the highest cure rates, even in emerging centres like ours in Kenya(1). Long term survival rates are greater than 90% and more than 80% of the patients survive in continuous complete remissions(1). With improved field radiotherapy and multi-agent combination chemotherapy, the five year survival rates in asymptomatic stage I and II HD is approximately 90% and upto 60% in stages III disease respectively(2-3).

Thus it seems inevitable that a substantial number of these would have late sequelae induced by treatment itself or live with the notion of potential relapse(4). The late effects of radiotherapy such as growth impairment, some endocrine organ dysfunction or the development of secondary solid tumours have been known(5,6). Complications include cardiac and pulmonary disease induced by radiation or chemotherapy(7). Vascular toxicity due to mainly several antineoplastic agents, thyroid, pituitary and gonadal failure have been seen in both males and females(8). Radiation has long term immunosuppressive effects with recognised changes in both humoral and cellular functions(9). Secondary acute non-lymphocytic leukaemia has been associated with node radiation and intensity of chemotherapy(10).

Late relapse those occurring more than three years after the initial complete remission have been described(11). Differences in the occurrence and histology of late relapses in the nodular versus the diffuse subtypes of lymphocyte predominant Hodgkin’s disease who was in complete remission for 10 years after he received chemotherapy and radiotherapy. His relapse which occurred in initially uninvolved site exhibited the histology of lymphocyte depleted Hodgkin’s lymphoma. A review of the literature of late relapsing Hodgkin’s disease is presented and the importance of studying these patients is discussed.

CASE REPORT

A 17 year old male presented in June 1987 with right cervical mass. The patient denied having weight loss, fever, night sweats or any other symptoms. His physical examination revealed several 4 x 6 cm right cervical nodes and a few 2 x 2 cm right root of neck nodes. His blood counts and serum chemistry were normal.

An excisional biopsy of a right cervical lymph node was performed and the pathological findings were consistent with Hodgkin’s Lymphoma of nodular sclerosis type. Chest X-ray was normal and abdominal ultrasound showed paraaortic lymphadenopathy. Bone marrow and trephine were negative. His final staging was III A.

He received chemotherapy consisting of cyclophosphamide, Vincristine, Prednisone, Procarbazine, Adriamycin (CHOP). He received also inverted Y (lower mantle) radiation, 1800 cgy over a period of four weeks. He was hospitalised twice over the next few months with infection complications, including an episode of pneumonia. He was regularly seen in the clinic for four years. He got lost to follow up for subsequent six years.

In August 1997, he was brought complaining of dyspnoea on effort, palpitations, abdominal distention, abdomen pains, weight loss, fever, night sweats and poor appetite, headaches and chest pains. A physical examination revealed generalised wasting, marked pallor of the mucous membrane, bilateral inguinal lymph node 2 x 4 cm. He was febrile, with a temperature of 39°C. He had hepatomegaly 4 cm below right lower coastal margin, and splenomegaly 12 cm below left coastal margin. His chest was normal.

Abdominal ultrasound showed massive splenomegaly and mild hepatomegaly. His blood counts showed severe anaemia, Hb 3.7 g/dl.

Serum chemistry results were as follows: uric acid 256 umol/l, albumin 29.6 g/dl, alanine aminotransferase (ALT) 60
DISCUSSION

This is a description of a patient who had Hodgkin’s disease stage III A in 1987 who relapsed in a clinically non-involved site 10 years after entering complete remission with chemotherapy and lower mantle (inverted Y) radiation. In 1987 the histologic type was nodular sclerosis and in 1997 he had lymphocyte depleted type.

The occurrence of late relapse in Hodgkin’s lymphoma is described in medical literature (13). Kanofsky et al (11) described late relapses in eight out of a cohort of 142 patients with pathologic stages IA through to IVB. The disease free interval ranged from 37 to 76 months.

Herman et al (13) followed 1460 patients with Hodgkin’s lymphoma and reported 52 late relapses. Duchesne et al (14) described different results in a cohort of 432 patients. They found an increased incidence of late relapse in patients with stages II disease and no association with the histologic sub-type. In their study the incidence of late relapse was higher in patients who received radiotherapy alone versus combined modality therapy. They reported that one of their radiotherapy treated patients had a documented relapse 20 years after diagnosis (14).

The occurrence of late relapses specifically in patients with lymphocyte predominant HD are of particular interest. Many studies demonstrating the existence of phenotypic differences in behaviour between nodular and diffuse variety of this sub-type (15) led Regula and co-workers to investigate any clinical differences between the two groups (12). The emerging report from this study and from other histologic studies is that nodular variant is a frequently relapsing but indolent disease which is distinct from the diffuse type and from all other types of Hodgkin’s disease as well (16).

Armata H. et al (17) reported on a boy treated at five years for Hodgkin’s disease IIA mixed cellularity type relapsing five years later. The boy had received MVPP, (Nitrogen mustard, Vinblastine, Procarbazine, Prednisone) five cycles combined with local irradiation 3900 Rads and complete remission was achieved. Relapsed HD was of lymphocyte depleted HD (17). In his series out of 10 children with relapses the histologic type changed only in one case. Our patient is one of the very few reported with relapse after a long disease free interval. He had a relatively advanced disease Stage III A at initial diagnosis.

Relapse in HD after 3.5 and 10 years are encountered respectively in 13 - 17% (16); 6-10% (18) and 0.6% (16) of patients. Very late relapses in HD (above 10 years) are rare but not exceptional (17). Green et al (18) made the observation that HD may occasionally develop twice in susceptible individuals and this is supported by the occurrence of a future malignancy in two patients (19). However, this is associated with early rather than late relapse following treatment. It is not clear if patients with late relapse have a different course from other patients with relapse following shorter disease free interval three to five years. As such, with significant advances in the treatment of Hodgkin’s disease and many getting remission, numbers of patients with very late relapse will rise.

Our patient demonstrates some features similar to the relapsed cases described by Green et al (18). It is important to continue to describe more of such cases along with the pertaining studies, so as to collect data in this subject that will tell the probable relapse or therapy related secondary disease. Several pathogenic mechanisms have been offered in an attempt to explain the occurrence of secondary malignancies and recurrence in these HD patients. Almost all cases have been linked to alterations in the immune system (20).

The behaviour of the relapsed tumour in our patient appeared more aggressive. This was at variance with the suspected indolent course predicted by the initial histology. It is therefore arguable whether histology alone could predict probability of relapse and clinical course, this should be a subject of further investigations. Efforts to reduce late sequelae will peg on the understanding of the clinical and biological HD tumour characteristics vis a vis the therapeutic modalities, specifically radiotherapy and chemotherapeutics possible roles in relapses and secondary malignancies. Overall objective will be to provide meaningful cure and high quality of life while predicting relapses and possibly secondary HD.

REFERENCES


