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Chemotherapy Induced Non-Hodgkin's Lymphoma in a Patient with Hodgkin's Disease - A Case Report

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Modern chemotherapy and radiation treatment of Hodgkin's disease has resulted in overall cure rates in excess of 60%[1]. However, the greatly improved survival rates have also led to increasing incidence of long-term side-effects of these treatment modalities[2]. The most serious consequence is the occurrence of second cancer[3]. We report a case of non-Hodgkin's lymphoma occurring in a patient who was previously treated for Hodgkin's disease.

Case Report

A 70 year old male presented with three months history of bilateral enlargement of cervical and supraclavicular lymph nodes. Excision biopsy of supraclavicular node revealed Hodgkin's disease, mixed cellularity type. Chest x-ray showed involvement of bronchopulmonary and perihilar nodes and CT scan of the abdomen revealed splenic enlargement and para-aortic lymphadenopathy. The patient was staged to have IIIA disease.He was started on the COPP/ABV hybrid regimen and received four cycles of chemotherapy. At the end of therapy, he was incomplete clinical and radiological remission except for the chest x-ray, which showed hazines of left hemithorax suggestive of diffuse pneumonic changes. Bronchoalveolar lavage revealed the presence of pseudomonas aeruginosa and acid fast bacilli. The patient was treated with appropriate antibiotics and was also started on anti-tuberculous therapy. He remained well in the following year, after which he was again found to have cervical lyniphadenopathy. A fine needle aspiration biopsy revealed features suggestive of non-Hodgkin's lymphoma. An excision biopsy confirmed the presence of mixed small and large diffuse non-Hodgkin's lymphoma (Intermediate grade according to the International Working Formulation). The patient was subsequently found to have stage IIA disease and was started on the CHOP regimen.

Discussion

Secondary cancers are important long term complications of the treatment of Hodgkin's disease[2,3]. Various types of secondaiy malignancies have been reported to occur. These include acute non-lymphocytic leukemia (ANLL), nonHodgkin's lymphoma (NHL) and solid tumours e.g., melanoma, breast, lung, thyroid and gastric cancer[4-6]. The overall risk continues to increase with the passage of time and is around 10% after 10 years of observation following the treatment of Hodgkin's disease. The risk is higher in ounger patients[6.7]. Secondary ANLL is widely thought to be due to the use of alkylating agents and procarbazine[8,9]. Secondary solid tumours are generally regarded to occur following radiotherapy[10,11]

The increased risk of developing NHL could be attributed to either chemo or radiotherapy oras a part of the natural history of Hodgkin's disease[4,5,6,11]. In one study, the actuarial risk of developing NHL was found to be 0.5% at 10 years and 1.6% 15 years after the successful treatment of Hodgkin's disease[5]. The risk was higher in patients who received a combination of chemo and radiotherapy as compared to those who were treated with either of the two The proposed mechanisms are either direct mutagenic effect of these two modalities orby activation of some latent oncogenic viruses. Alternatively, excessive

occurrence of NHL in such patients has been ascribed to the immunocompromised status of the host[4,6,13].

Our patient responded well to the initial chemotherapy and was clearly documented to be in complete clinical and radiological remission at the end of the fourth cycle. However, at the same time, he was found to have pulmonary tuberculosis and could not continue his chemotherapy to a total number of six cycles. During the full-length course of treatment fom tuberculosis, the patient remained in complete remission. The lymph nodes reappeared 15 months after the initial diagnosis of Hodgkin's disease, at which stage the diagnosis of NHL was made. To rule out the possibility of the disease being NHL all along, the histopathology slides were reviewed retsospectively by two pathologists. There was no suggestion of the existence of NHL in the specimen. Also, there was no evidence of Hodgkin's disease in the later specimen.

The question whether the drugs are implicated in the etiogenesis of NHL in this patient, or if it was the severely immunocompromised status of the host which led to the second cancer, cannot be answered. The patient received four cycles of cyclophosphamide. procarbazine and etoposide, all of whom have been known to be associated with the development of second cancers. On the other hand, the patient seemed to be immunocompromised, as suggested by the occurrence of various infections. immunosuppression is usually present at the time of the diagnosis of Hodgkin's disease and is known to persist long after the treatment is completed. Immunosuppression may lead to the clonal proliferation of B cells[14]. Although no uniform immunologic pattern of the secondary NHL has been documented in the literature, the muajority seem to be of B cell origin[12]. Our patient had diffuse mixed small and large type (intermediate graae) ot NHL which is usually of the B cell origin. Immunohistochemical studies were not done in this case. The relative risk of the occurrence of the second cancer decreases with the increasing age and was found to be 1.0% in patients older than 60 years of age.

The secondary NJHL is treated ill a similar wa as the de novo tumour. Response rates to the combination chemotherapy of more than 55% have been described in the literature[5].

This case signifies the importance of repeat biopsy in patients with apparent relapse of Hodgkin's disease, as the diagnosis of a second cancer has both therapeutic and prognostic implications.

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