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Second malignancy following successful treatment for Hodgkin's disease: case report and literature review

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ABSTRACT

A 32-year-old male with a low grade non-Hodgkin's lymphoma (NHL) of the ascending colon presented 5 years after the successful treatment of Hodgkin's disease (HD). According to the literature, the occurrence of a second primary cancer is a great problem in the survivors of HD, which is the result of immunosuppression due to the disease itself or following chemotherapy and/or radiotherapy for it. Therefore, patients with HD must be followed-up regularly and for lifelong.

Keywords: Second cancer; Hodgkin's disease; Chemotherapy; Follow-up.

INTRODUCTION

In modern oncology, the combination of chemotherapy and radiotherapy either as a primary or as an adjuvant therapy has resulted in the long-term survival and cure of many patients. On the other hand, the long-term complications of cancer therapy has also increased.[1,2] The possible risk factors for developing a second primary tumour years later include the irreversible genetic damage by cancer therapy and congenital or acquired immunodeficiency of the patient. Moreover, patients with Hodgkin's disease (HD), testicular teratoma, ovarian carcinoma, breast cancer and paediatric cancers are at potential risk for developing a second primary tumour. HD has been treated with chemotherapy and/or radiotherapy. Therefore, the chance of developing a second malignancy in patients with HD is high and it warrants to develop the treatment strategies to minimize the long-term complications.[3] Herein we report a case of HD, who developed a second primary malignancy 5 years after the successful treatment.

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CASE REPORT

A 27-year-male patient from the Kathmandu Valley had presented to the Department of Surgery, Tribhuvan University Teaching Hospital, Kathmandu 5 years ago with chief complaints of weakness and multiple abdominal lumps of 2 months' duration. There was a history of empirical antitubercular treatment for 4-5 months elsewhere. Routine investigations were not conclusive except multiple intraabdominal lymphadenopathy. Subsequently, exploratory laparotomy revealed multiple mesenteric enlarged lymph nodes without caseation, and lymph node biopsy showed mixed cellular HD (Fig. 1). The patient received 6 cycles of chemotherapy with MOPP (mustine, oncovin, procarbazine and prednisone). The patient was doing well post chemotherapy and was in regular follow-up. After 5 years of treatment, he started having a slowly progressing lump in the right lower quardant of the abdomen. Investigations did not reveal disease recurrence. Then he presented with features of acute intestinal obstruction with a lump in the right iliac fossa. Emergency exploratory laparotomy revealed a huge mass of ileocecal junction including proximal half of the ascending colon. No lymphadenopathy was noted. Right hemicolectomy with complete tumour resection was done. Post operative period was uneventful.

Macroscopically, there was a huge growth of the ascending colon measuring 10X12 cm involving the iliocecal junction, which was firm and fragile. Histopathological examination showed a low grade NHL-lymphoplasmacytoid type (Fig. 2). The patient received 6 cycles of CHOP (cyclophosphamide, hydroxyrubicin, oncovin and prednisone) regimen of chemotherapy. After chemotherapy, the patient is doing well and he is on regular follow-up.

Fig. 1: The section from lymph nodes shows Hodgkin's disease of mixed cellularity. Arrow mark shows Reed-Sternberg cells. (H & E stain x 200).

Fig. 2a: The section from colon shows diffuse infiltration of atypical lymphocytes with plasmacytoid differentiation. (H & E stain x 100).

Fig. 2b: Magnified view of Fig. 2a showing small atypical lymphocytes with plasmacytoid differentiation. (x400).

DISCUSSION

HD is one of the curable malignancies; however, some patients may develop a second primary cancer many years after the successful treatment, especially children and adolescents.[4] These second malignancies have been linked to aggressive chemotherapy and radiation therapy.[2-9] Common second malignancies include leukemia, NHL, sarcoma, lung cancer and so on. However, the risk of gastrointestinal cancers following HD treatment is increased after combined modality therapy and treatment at a young age. As in our case, the excess risk of second gastrointestinal malignancy tends to be evident within 10 years after treatment.[10]

Although it is not possible to identify the exact cause for a second malignancy, several high risk conditions and drugs have been implicated (Table I and II). In malignant or non-malignant conditions causing chronic immunosuppression, it prevents the body's immune system from monitoring the production of abnormal cells during cell division. This leads to a failure to identify or attack the small cancers which may frequently develop in the normal person.

Table I: High Risk Factors for Second Malignancy

Malignant conditions:	Hodgkin's disease
	Ovarian carcinoma
	Testicular tumor
	Breast carcinoma
	Childhood cancers
Non-malignant conditions:	Prolonged immunosuppression
	Organ/tissue transplant
	Collagen diseases

Table II: Drugs Associated with Second Malignancy

Alkylating agents:	Chlorambucil
	Cyclophosphamide
	Melphalan
	Nitrosourea
	Thiotepa
Non-classical Alkylating agents:	Nitrogen mustard
	Procarbazine
Epidophyllotoxins:	Etoposide

The risk of patients' developing second primary malignancy after a long time-lapse is due to irreversible genetic damage caused by some chemotherapies. In general, drugs which interact with cellular DNA may not kill the cell but may induce sublethal changes which can be passed on to progeny and can be associated with later changes to the malignant phenotypes. Therefore, treatments with alkylating agents are associated with high risk of developing a second malignancy. Moreover, other features of treatment associated with high risk may include high doses, low doses chronically delivered, combination chemoradiotherapy and combination of high risk drugs.

The risk of second cancers after the treatment for HD is greatest for leukemia, NHL, soft tissue and bone cancers, lung cancer and some other solid tumours including stomach, colon, breast, thyroid, oral cavity and melanoma in decreasing frequency.[3,11] The high risk of NHL following the treatment for HD is controversial; however, several reports support the view that HD itself is immunosuppressive[3,11,12], also followed by its aggressive treatments.[2-9] Thus, both factors-immunosuppression as well as treatment maybe responsible for the development of NHL following HD. Most of these NHL are of intermediate or high-grade lymphomas, which is not consistent with our case and occur at extranodal site like in our case.[13,14]

Solid tumours are treated with drugs which best induce a remission, since the problem of cancer is paramount. High-risk agents, eg, alkylating agents, should be used with caution in the adjuvant setting or in neoadjuvant treatment of potentially curable tumours like HD. The risk of any new treatment need to be evaluated. In this regard, molecular techniques for genetic susceptibility or mechanisms of treatment - induced carcinogenesis should be studied in great detail. Moreover, patients with HD should be followed regularly and eventually lifelong.

CONCLUSION

Since the chance of developing a second primary cancer following HD treatment is high, lifelong follow-up should be a dictum. Frequent biopsies of suspected lesions may demonstrate NHL. Moreover, the treatment modality must be selected cautiously in order to reduce the late risks of second cancers.

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