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A child with Non-Hodgkin Lymphoma presenting with haemorrhagic pleural effusion

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Abstract

Lymphoma is the third common malignancy of childhood, presenting with rapidly or slowly growing mass, systemic B symptoms (fever, night sweats and weight loss), hepatomegaly and splenomegaly. Here, we report an eight year old male child who presented with fever, dyspnoea and weight loss of three kilograms over the last month; had right pleural effusion and was investigated for both infectious and non-infectious causes and later was diagnosed as Non-Hodgkin lymphoma. It emphasizes the importance of high suspicion, especially in the presence of haemorrhagic pleural fluid, to differentiate it from other common causes of pleural effusion in childhood.

Key words: Non-hodgkin lymphoma, Pleural effusion

INTRODUCTION

Lymphoma, being the third most common malignancy is still rare with incidence of 11% of childhood cancer, and is twice common in boys than girls[1]. There are two main types of lymphoma: Hodgkin lymphoma and non-Hodgkin lymphoma (NHL). NHL accounts for more than half (53%) of all lymphomas in children[1]. The incidence of NHL in Nepal is not known as there is no national population based cancer registry, but NHL stands as the fourth common malignancy and comprises almost eight percent of childhood cancer in Kanti Children Hospital[2]. It presents either as a rapidly growing mass or systemic B symptoms (fever, night sweats and weight loss) or slowly growing lymphadenopathy, hepatomegaly or splenomegaly. Other presentations include skin rash, pruritus, pyrexia of unknown origin, ascites and pleural effusion. Here we are discussing a child with haemorrhagic pleural effusion who was later diagnosed as NHL.

CASE REPORT

An eight year old male from Dang presented to the outpatient department of Kathmandu Medical College Teaching Hospital with fever since five days and acute onset of MRC grade III dyspnea (The Modified Borg scale)[3] for three days. He also had history of weight loss of three kg over last one month. His development was appropriate for age and he had no significant illness in past. He was born out of non-consanguineous marriage with uneventful birth history and a negative family history of malignancy. On detailed examination, the child was malnourished (Protein energy malnutrition Grade II as per Indian Academy of Paediatrics Classification based on weight for age) with Tanner stage I. The child was tachypnoeic and with oxygen saturation of 94% in room air. He had palpable lymph nodes in central axilla and right inguinal region with a size of 0.5 cm × 0.5 cm, which was single, firm, non-tender and fixed. On respiratory examination, there was decreased chest movement on right side, along with marked dullness on percussion, decreased vocal resonance and breath sound over the right chest. Other systemic examination revealed no abnormality.

On investigations, Chest-X-ray showed right sided pleural effusion. Erythrocyte sedimentation rate (33 mm/1st hour) and lactate dehydrogenase (LDH: 1332 U/L) was high while haemoglobin, complete blood count, renal and liver function tests, and peripheral blood smear were normal. Pleural fluid analysis revealed haemorrhagic fluid with low sugar (4 mg/dl), high protein (5.5 g/dl), high total count (32,200/mm^3) with predominant lymphocytes (85%), serum: pleural fluid

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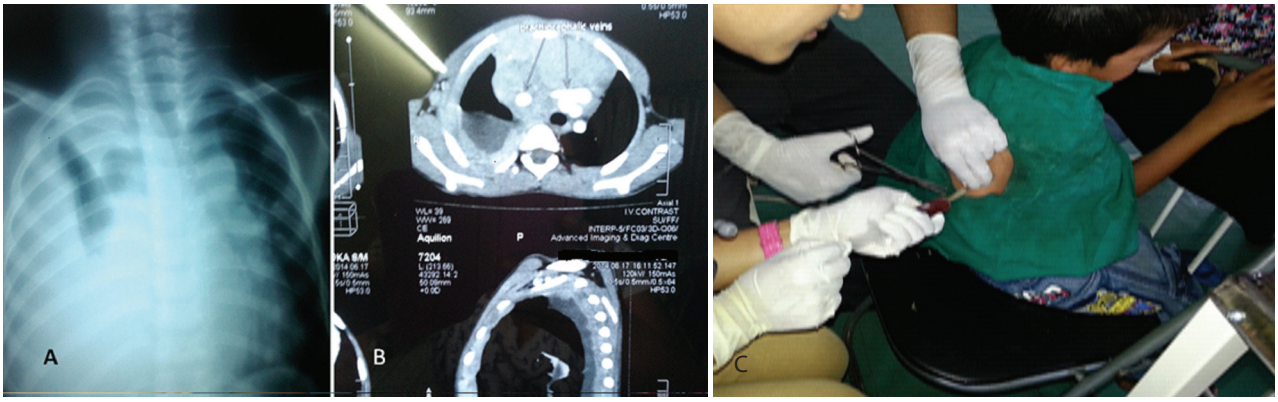

Figure 1: (A) Chest X-ray showing right pleural effusion. (B) Contrast CT scan showing mediastinal tumour in the anterior mediastinal space. (C) Haemorrhagic pleural tap.

LDH ratio was 0.46, serum: pleural fluid protein ratio was 0.6, high adenosine deaminase (404 U/L) but negative for acid fast bacilli and malignant cells. During the hospital stay, therapeutic pleural tapping was done which provided symptomatic relief to the child. The child was further investigated with contrast enhanced computed tomography scan of chest which revealed large heterogeneously enhancing soft tissue mass (65 mm × 95 mm) predominantly in the anterior mediastinum with infiltration of mediastinal great vessels and diffuse pleural thickening in right thoracic cavity. Ultrasound guided fine needle aspiration cytology (FNAC) was done which confirmed Lymphoblastic NHL. The metastatic spread of tumour to bone marrow and central nervous system was absent. The child was referred to Bhaktapur Cancer Hospital for chemotherapy and is being treated with maintenance treatment of high dose Methotrexate which will be continued for two and half years.

DISCUSSION

NHL consists of a diverse group of malignant neoplasms of the lymphoid tissues variously derived from B cell progenitors, T cell progenitors, mature B cells, or mature T cells[4]. NHL in most children develops without no obvious genetic or environmental aetiology but a small number of patients have secondary aetiologies like inherited or acquired immune deficiencies (Severe combined immunodeficiency syndrome, Wiskott-Aldrich syndrome), viruses (Human Immunodeficiency Virus, Epstein Barr Virus, Human herpes virus 8), chemical exposure (chlorophenol, benzene, or immunosuppressive drugs) or as a part of genetic syndromes like ataxia-telangiectasia or Bloom syndrome[5,6,7]. Childhood non-Hodgkin lymphomas can be classified as one of the following types[7]:

a. Lymphoblastic lymphomas
b. Burkitt lymphomas
c. Diffuse Large B cell lymphomas (DLBCL)
d. Anaplastic Large cell lymphoma

The incidence of Burkitt lymphoma is higher (38%) in children between 0-14 years of age whereas diffuse large B cell lymphoma (DLBCL) is higher (39%) in children between 15-19 years of age[8].

The clinical manifestations of NHL in childhood and adolescent depend on site of involvement (primary or secondary) or on pathological subtype. Most of the patients with NHL are diagnosed late with advanced disease at stage III or IV, including extra-nodal disease with gastrointestinal, bone marrow and CNS involvement. Our patient was diagnosed as a lymphoblastic lymphoma (stage III as per St. Jude staging system[7] for childhood Non-Hodgkin Lymphoma) with high Lactate dehydrogenase (1332 IU/l) without any involvement of CNS and bone marrow. There is unfavourable prognosis if age at diagnosis is late (i.e. the older paediatric patient: adolescent or young adult have poorer prognosis), involvement of CNS and bone marrow, and the serum level of lactate dehydrogenase is more than 1000 IU/L[9,10].

Lymphoblastic lymphoma comprises approximately 20% of childhood NHL, and often presents with intrathoracic or mediastinal involvement as an anterior mediastinal mass (75%)[11]. It may manifest as dyspnoea, wheezing, stridor, dysphagia, or swelling of the head and neck. The frequency of pleural effusions is 20% in NHL which has unclear prognostic implication[12]. The primary pathogenesis of pleural effusion is due to the direct pleural infiltration in NHL. Lymphoblastic lymphoma may also involve bone, skin, bone marrow, central nervous system, abdominal organs (but rarely bowel), and occasionally other sites such as lymphoid tissue of Waldeyer ring and testes. As soon as the

diagnosis of NHL is suspected, immediate assessment and stabilization of the patient's metabolic status is necessary with rehydration of child with 3000 ml/m2/day with 5% dextrose in 0.25% isotonic saline intravenously without supplementary potassium to prevent tumour lysis syndrome which results in hyperkalaemia, hyperuricaemia, and hyperphosphataemia[10]. This is followed by addition of sodium bicarbonate to maintain alkaline urine (pH 7-7.4) for 24-48 hours and [Xanthine oxidase inhibitors: Allopurinol (10 mg/kg/day, divided into two to three doses)[10]. But the primary modality of treatment for childhood and adolescent NHL is multi-agent systemic chemotherapy with intrathecal chemotherapy[7]. Surgery is used mainly for diagnosis and staging. Systemic chemotherapy includes acute lymphoblastic leukaemia regimens like eight drug induction (Corticosteroid, vincristin, daunorubicin, asparaginase, cyclophosphamide, cytarabine, 6-mercaptopurine and intrathecal methotrexate) therapy and a consolidation (6-mercaptopurine, high-dose methotrexate, intrathecal methotrexate) and re-intensification (dexamethasone, vincristin, doxorubicin, asparaginase, cyclophosphamide, cytarabine, thioguanine and intrathecal methotrexate) therapy, which is followed by maintenance therapy (6-mercaptopurine and oral methotrexate) for a total therapy duration of 24 months.

CONCLUSION

The burden of acute infectious disease in the developing countries is still heavy, but this does not exclude the need to identify rare malignancies. A high degree of suspicion, especially in the presence of haemorrhagic pleural fluid, is required to differentiate it from other common causes of pleural effusion in childhood. Its early diagnosis and management are important to prevent further complications of the disease.

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