

Lymphoma in Two Siblings: A Plausible Case of Familial Lymphoma?

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Abstract

We report two cases of lymphoma manifesting in siblings, one is Hodgkin's lymphoma (HL) and the other is Non-Hodgkin's lymphoma (NHL) in a nuclear family. Each presented a year apart. The patients were well and alive as at the time of this report and did not show any signs of the disease. There was no history of tuberculosis (TB) or contact with any one with TB. Other common lymphadenopathy associated conditions were excluded and histology of excised lymph nodes was confirmatory of the lymphomas. We were constrained by facilities on the demonstration of Epstein Barr Viruses (EBV) or genetic associations. This is the first plausible case of reported familial lymphoma in Nigeria.

Keywords

Lymphoma, Hodgkin's Lymphoma, Non-Hodgkin's Lymphoma, Familial Lymphoma

1. Introduction

Malignant lymphomas are solid lymphoid tumors that occur in adults and in paediatric age groups. Previous studies [1]-[3] have indicated that lymphomas are the commonest type of malignancies in childhood in the tropics, and Burkett's lymphoma is by far the most common. The importance of malignancies as cause of death in children has been documented [3]. Lymphomas are categorized into two, Hodgkin disease (HD) and Non-Hodgkin Lymphoma (NHL) and have different clinical manifestations. Hodgkin disease constitutes about 13 - 43 percent of all cases of malignancies reported in the paediatric age group in Nigeria [4]. In Ibadan, it represents about 7% of all lymphomas [4], in Enugu it represents 5.4% in the age range 6-14 yrs, in Lagos it represents 5.1% [5] while in Uganda it represents 8.9% [6]. It is more commonly seen in adolescents, rare before the age of 10 years and often with a better prognosis than in adults. It is commoner in males than females. The etiology of Hodgkin disease (HD) is largely unknown and probably involves both environmental and genetic

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factors. The tumor appears to arise from the T-dependant areas of lymphoid tissue. There is considerable evidence supporting a chronic infectious process due to Epstein-Barr virus (EBV) infection [7]. Ferraris *et al.* [8] estimate that 4.5 percent of HD cases occur as familial cases. A link to HLA antigens HLA-B27, DR5, has been implicated in its aetiopathogenesis. EBV-encoded RNA has been detected in approximately 27 percent of tumors from familial HD cases [7] [8]. Non-Hodgkin lymphoma (NHL) results from malignant clonal proliferation of lymphocytes of T-, B-, or indeterminate cell origin [9]. Predisposing factors include EBV, which plays a major role, malaria, chromosomal anomalies and oncogens as well as congenital or acquired immunodeficiency states and exposure to toxic chemicals. Familial cases have been reported over the years [10] [11]-[20]. The present study is reported to show the probable occurrence of familial cases of lymphoma in the index family and in our environment. To the best of our knowledge, this is the first case of familial lymphoma reported from Nigeria. We are constrained by facilities to demonstrate EBV associations or do HLA studies.

2. Case Report A

P.I., 8 yrs male presented 8th June 2004 with swelling on the right jaw, multiple enlarged lymphadenopathies in the cervical, axillary and inguino-femoral regions; all were rubbery, mobile and non-tender. The right groin had a giant lymph node measuring about 8 cm × 8 cm, which was mobile, tender and attached to the skin and has been increasing in size slowly. There was associated weight loss but no fever, cough, vomiting, diarrhea or jaundice. Examination revealed a conscious and alert patient but wasted, weight 18 kg, height 116.5 cm and surface area 0.76 m². He was pale, afebrile, and anicteric; he had hepatomegaly of 6 cm and splenomegaly of 4 cm. The child was unimmunized. He had a hemoglobin of 8.7 g/dl, platelet count of 205 × 10⁹/L; Mantoux test induration measured 3.3 mm, HIV I & II antibody screening were negative, and ESR was >150 mm/hr. Chest x-ray revealed mediastinal lymph nodes.

Histology: The biopsy was a nodular lumpy irregular tissue measuring 2.5 × 2.5 × 1.5 cm, partially embedded in 2 blocks. Sections showed lymph node with effaced nodular architecture by extensive edema and necrosis. There were neoplastic cells with plasmacytoid features, having large oval-round nucleus that appeared vesicular. A few nucleoli are seen.

N. B. Several thinner sections also showed the real lesion. Diagnosis: NON-HODGKIN'S LYMPHOMA (large cell lymphoblastic).

3. Case Report B

P.C., male, 6yrs presented 18th August 2005 with enlarged lymph nodes in the cervical region. Multiple swellings were first noticed more than a year ago at the right side of the neck which progressively increased in size, with satellite swellings developing above primary swelling anteriorly and extending to the left. There was associated hepatosplenomegaly. Patient was fully immunized. He is the last of 5 children. Results obtained were as follows: PCV 0.44 (14 g/dl), WBC-7.8 × 10⁹/L, neutrophils 64%, eosinophils 6%, basophils 1%, lymphocytes 27%, monocytes 2%, ESR was 70 mm/hr Wintergreen, erythrocytes showed normocytic, normochromic cells. Leucocytes and thrombocytes appeared normal. Mantoux test induration measured 8 mm after 72 hrs. Total serum bilirubin was 3.8 mmol/L (3.4 - 17.1), conjugated bilirubin 0.5 mmol/L (<3.4), ALT 4.0 i.u/L (Up to 12 I.U/L), AST 14.0 i.u/L (Up to 12 I.U/L), ALP 37.9 i.u/L (25.0 - 92.0), Hb 8.0 g/dl, platelet count 110.0 × 10⁹/l. Lymph node (cervical) excision biopsy: Section showed lymph node with effaced nodular architecture by a tumor composed of proliferating lymphocytic cells on a background of inflammatory cell. Characteristically present was a tumor with giant cells, Reed-sternberg cells that are bilobed and binucleate. The nuclei were enclosed within abundant amorphilic cytoplasm. Prominent within the nuclei were large nucleoli surrounded by a halo. Necrosis and fibrosis were present. A diagnosis of Hodgkin's Lymphoma (mixed cellular-ity variant) was made.

Consent was obtained from the parents and the children regarding reporting/publishing and clinical photographs. They are members of Jehovah's Witness and have five children. Blood transfusion was refused; both patients are receiving erythropoietin for anaemia and combination chemotherapy for clinical stage IV NHL and HD respectively.

4. Discussion

This case is similar to the early descriptions of familial HD from the literature [11] [12]-[20] and thus represents

a case of familial lymphoma in Aba, Nigeria. In familial HD many factors may interplay. Many cases are of the nodular sclerosing Hodgkin's (NSHD) histology variety and even in this fewer than 27% have EBV encoded RNA in the tumours [7] [8]. Significant concordance of EBV status of tumors has not been found within families of familial HD cases. In contrast however, there is an increased risk of HD among monozygotic twins compared to dizygotic twins of HD cases as was found by Ferraris [8]. This suggests a probable role for shared genetic factors in familial HD. Recent studies have found histocompatibility antigen (HLA) class I region on chromosome 6 as the likely region where genetic and familial factors occur. Up to 60% - 70% of familial HD cases have been linked to this region where affected individuals may have significant HLA class I haplotype sharing. More recent evidence also suggest a role for several HLA class II antigen especially for nodular sclerosing NH and perhaps other yet to be identified loci [18]. Family and population studies [9] [10]-[18] have confirmed important familial components, which is stronger in families of affected individuals age <40 years, in males, and in siblings and is shared with some lymphoproliferative malignancies. Lynn *et al.* [11] estimated the absolute lifetime risk for a first degree relative of an NHL case to develop NHL is 3.6% compared with a population risk of 2.1%. Relatives of NHL cases were at significantly increased risk for NHL, HL and non-significantly for chronic lymphocytic leukemia. Findings with respect to siblings compared with parents and off springs or with respect to age at diagnosis of proband were inconsistent. In addition, relatives of cases with aggressive NHL were at substantially increased risk of NHL.

5. Conclusion

It is highly probable that these cases represent familial cases of lymphoma in the index family. Detailed genetic studies of these cases, siblings and close relatives will prove it.

6. Recommendation

- 1) Genetic studies of index families, high risk families and population samples of first degree relatives of index cases should be conducted.
- 2) There is need to use large databases for example of hospital records where available to conduct studies so as to overcome sample size limitations and recall bias.

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