

T-Cell Rich B-Cell Lymphoma– A diagnostic dilemma in paediatric oncology

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Abstract

T-cell rich B-cell lymphoma, most commonly seen in adults and rarely reported in children is a type of Diffuse Large B cell Lymphoma. (DLBCL). It has several clinical, histological and immunohistochemical similarities to commonly Nodular lymphocyte predominant Hodgkin's lymphoma. We report an 8 year-old boy who presented with a swelling over the right inguinal region for two months. FNAC of the swelling was inconclusive. MRI abdomen revealed multiple masses in right iliac fossa. Immunohistochemistry of the biopsy mass was consistent with T cell rich B cell lymphoma. T cell rich B cell lymphoma has a very low incidence in pediatric population and still remains unrecognized in most of the cases. When compared to adults, children have a better prognosis and hence stronger emphasis on immunohistochemistry is essential. Careful attention should be paid to differentiate the different neoplasms as each have a distinct course of clinical history and different therapies.

Keywords: T-cell rich B-cell lymphoma, Child, Hodgkin's lymphoma, Immunohistochemistry

Introduction

T-cell rich B-cell lymphoma (TRBCL) is considered a rare variant of aggressive B-cell lymphoma described by few neoplastic B-cells in a background of numerous benign T lymphocytes and histiocytes[1]. Not widely recognized in pediatric population, due to its extensive infiltrate of reactive T cells, causing diagnostic dilemmas, **only few cases are reported.** Often misdiagnosed as classical Hodgkin lymphoma or nodular lymphocyte predominant Hodgkin lymphoma or reactive lymphadenopathies, this entity should be

recognized in pediatric age group, as a less aggressive treatment results in relapses. When diagnosed accurately, children respond well to chemotherapy and exhibit good prognosis. We report a case of an 8 year old boy presenting with an inguinal swelling and abdominal mass which was initially thought to be Nodular lymphocyte predominant Hodgkins lymphoma and later confirmed by IHC as T cell rich B cell lymphoma, treated as per LMB 96 protocol and is in remission now for 4 years.

Case Report

An 8 year old boy presented with a swelling over the right inguinal region for a period of two months. The swelling was slowly progressive with an increase in the size of the lesion over last two weeks. There was no history of trauma, fever loss of appetite, weight loss, or night sweats. There was also no contact history of tuberculosis. On examination there was no generalized lymphadenopathy or hepatosplenomegaly. A 1 x 2 cms

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mass could be felt over the right inguinal region. It was non tender, not fixed to skin, and firm in consistency. Genital examination was normal. Baseline investigations including complete blood counts, renal and liver function tests, AFP levels, HCG levels and serum uric acid were normal. Serum LDH was elevated (980 units IU/L). Urine VMA was normal. FNAC of swelling was suggestive of reactive lymphocytosis. MRI abdomen showed extensive para-aortic, pre-caval, retro-caval and peri-pancreatic lymphadenopathy. Multiple soft tissue masses were seen in the right iliac fossa, also extending into the right side of the pelvis, engulfing the iliac vessels.

He underwent laparotomy and excision biopsy of the iliac mass, which was provisionally reported as Hodgkin's lymphoma-Nodular lymphocyte predominant type. By immunohistochemistry the atypical cells were immune positive for CD20 and PAX-5, negative for CD30, CD15, ALK-1 and LMP, while the background cells were positive for CD3 and CD68, making it most consistent with T cell rich B cell lymphoma. Bone marrow examination and CSF analysis was normal. The patient was started on chemotherapy as per LMB 96 (Group B) protocol and PET CT after 4 cycles of chemotherapy showed complete resolution. He completed 6 cycles and is disease free for 4 years.

Discussion

Originally, T-cell-rich B-cell lymphoma (TCRBCL) was introduced to describe several variants of B-cell lymphomas with a pronounced T-cell reaction mimicking T-cell lymphoma [2]. The presence of less than 10% (sometimes as low as 1%) of usually large, neoplastic B cells in a background of numerous T cells was the unifying feature of the diagnosis. It was originally described as T-cell-rich B-cell lymphoma in 1988 by Ramsay et al who reported five cases that had previously been misdiagnosed as peripheral T-cell lymphoma because of the presence of several T-cells surrounding a few large B cells [2].

Later in 1992 the definition was revised by Delabie et al who introduced the term histiocyte-rich B-cell lymphoma in characterizing six cases of large B-cell lymphoma identified by minimal neoplastic B cells amidst a large population of histiocytes and small lymphocytes [3]. In 2001, the World Health Organization formally defined TCRBCL as a morphologic variant of DLBCL characterized by fewer than 10% large neoplastic B cells amid a prominent inflammatory infiltrate, the majority of which are small polyclonal T cells, with or without the presence of histiocytes [4]. In 2000, a Children's Cancer Group study reported that out of a total of 86 studied cases, 30% were diagnosed to have DLBCL. Furthermore, only 6 cases out of these were found to have TCRBCL.

The common age group affected was between the ages of 12-16 [5]. TCRBCL can be similar to other peripheral B cell lymphoid neoplasms, most commonly nodular lymphocyte predominant

Hodgkin's lymphoma (NLPHL) making its diagnosis pathologically more challenging and thus may attribute to the low yield in the above mentioned study. The main histopathological differential diagnoses for TCRBCL are Lymphocyte rich classical HL (cHL) and Nodular lymphocyte predominant Hodgkin's lymphoma (NLPHL).

Classical Hodgkin's Lymphoma (cHL) can be mistaken for TCRBCL due to similar features of scanty neoplastic cells and abundant host inflammatory response that is further complicated by the occasional presence of HRS (Hodgkin & Reed-Sternberg) - like neoplastic cells [6]. The majority of HRS cells are negative for CD45, CD20, and CD79a and positive for CD15 and CD30 [7].

The reactive cells in cHL include a high number of small B cells along with other inflammatory cells, including eosinophils, neutrophils, and plasma cells. The absence of this inflammatory milieu differentiates TCRBCL from classical Hodgkin's Lymphoma [8].

NLPHL and TCRBCL can be immunophenotypically similar with tumour cells that are positive for CD20 and CD79a in both. It is the presence of reactive CD3+ T cells in the background that differentiates both entities. In addition, the background in NLPHL has CD57+ rosettes and CD21+ follicular dendritic cells, while TCRBCL shows CD68+ macrophages [9]. In our case, the HPE reports showed atypical reactive

lymphoid cells that stained positive for CD20, CD79 and CD68 making this a diagnosis that leaned more towards TCRBCL.

B symptoms, extra nodal involvement and advanced stage disease are commonly seen in TLCBCL, unlike in other types of DLBCL.

NLPHL usually present with isolated cervical or inguinal lymphadenopathy and are at lower stage at the time of diagnosis [10]. The child in our case presented with a inguinal lymphadenopathy but constitutional and B symptoms were absent.

TCRBCL is treated like DLBCL through R-CHOP chemotherapy and children had better prognosis when compared to adults. Tiemann et al has reported an event free survival of 86% and overall survival of 94 % at a median follow up of 23 months [11]. Those who were misdiagnosed and treated less aggressively had poor prognosis as they relapsed and had poor response to salvage therapies thereby highlighting the importance of accurate diagnosis at presentation [12].

Conclusion

Careful immunohistochemical analysis of both tumour cells and inflammatory micro environment is essential for accurate diagnosis of T cell rich B cell Lymphoma in children and adolescents as Hodgkin lymphoma is also of higher incidence among these age groups and the histological similarities of these two entities adds to the diagnostic dilemma. This case study highlights the difficulties in defining the specific subtypes of DLBCL and the importance of immunophenotyping in accurate diagnosis of such cases.

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Case Report

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