CASE REPORT

BURKITT-LIKE LYMPHOMA IN AN INFANT: A CASE REPORT

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Childhood non-Hodgkin's lymphomas, including Burkitt and Burkitt-like, are rarely diagnosed in infants. A case of B-cell lymphoma in a 13-month-old girl with extensive abdominal disease, ascites, pleural effusion, and tumor lysis syndrome is reported. Phenotypic analysis showed a germinal center B-cell phenotype, and a B-cell clonality was confirmed by polymerase chain reaction. There was no evidence of Epstein-Barr and HIV infection. The case herein reported emphasizes the need for considering the diagnosis of lymphoma even in very young children.

DESCRIPTORS: Non-Hodgkin lymphoma. Burkitt lymphoma. Burkitt-like lymphoma. Infant. Childhood cancer.

INTRODUCTION

Non-Hodgkin's lymphoma (NHL) is a rare disease in the very young children[1,2]. Small noncleaved cell lymphoma (SNCCL) and Burkitt's and Burkitt-like lymphomas comprise 40% - 50% of childhood lymphomas[3]. The incidence of SNCCL is age-dependent, being much higher in the first 2 decades of life; SNCCL has not been reported in children under 2 years of age. These lymphomas are B cell in origin and have the immunophenotypic characteristics of a subset of germinal center cells. Rare cases of Burkitt and Burkitt-like lymphoma have been reported in infants[2,3]. We herein describe a case of a Burkitt-like SNCCL in a very young child.

CASE REPORT

A 13-month-old female infant developed diarrhea and failure to thrive. Physical examination revealed a mass in lower abdominal quadrant and ascites. Computed tomography showed extensive intra-abdominal disease and right pleural effusion. Laboratory findings showed: red blood count, 3.67 x 10^{12}/L; hemoglobin concentration, 9.5g/dL; haematocrit, 29%; platelet count, 514 x 10^{6}/L; white blood cell count, 10.9 x 10^{6}/L with 31% lymphocytes and 76% neutrophils. High blood levels of lactic dehydrogenase (LDH), 2171 IU, and uric acid (9.2 mg/dL) were consistent with mild tumor lysis syndrome. An exploratory laparatomy was performed and revealed diffuse abdominal involvement including omentum and ovaries, which were biopsied. The histopathological analysis showed neoplastic cells similar in appearance to those of Burkitt's lymphoma, but there was increased pleomorphism over that accepted for Burkitt's lymphoma (greater variation in cell size and shape). The cells tended to have a more finely dispersed chromatin pattern and sometimes had a single prominent eosinophilic nucleolus. Burkitt-like SNCCL was diagnosed. Cytogenetic analysis was not performed in this case.

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Immunohistochemistry showed strong positivity for CD20 (L26 DAKO). Pleural effusion phenotypic analysis by flow cytometry was positive for HLA Dr, CD19, CD20, IgM, and CD45 and negative for CD34, CD3, CD4, and CD8. The cerebrospinal fluid and bone marrow were negative for the disease. The St. Jude staging system was applied, and the patient was classified as having stage III disease.

B-cell clonality was detected by PCR using oligonucleotide primers to amplify rearranged CDRII and CDRIII regions (semi-nested FR2-JH and FR3-JH PCRs) of immunoglobulin heavy chain (IgH) as described elsewhere[4,5] (Fig. 1). The HIV test was negative in the child and her parents. In situ hybridization for Epstein-Barr encoded RNAs was negative. No evidence of immunodeficiency was found in this child. The patient was treated with a BFM (Berlin-Frankfurt-Münsten)-based protocol[6] and developed markedly elevated serum uric acid levels, severe electrolyte imbalance, and renal failure, but recovered with appropriate treatment. She remains alive, in complete remission for 30 months.

DISCUSSION

Burkitt's lymphoma (BL) is a B-cell neoplasm classified in the National Cancer Institute Working Formulation as small, noncleaved cell lymphoma[7]. In Equatorial Africa, BL is the most common childhood malignancy, accounting for approximately 80% of childhood cancers and is called "endemic" (eBL). In contrast, outside Equatorial Africa, BL occurs in a sporadic form (sBL). Epstein-Barr (EBV) viral DNA is found in virtually all cases of eBL, but in only 15% - 30% of sBL from the United States [8]. In South America, high association of EBV with BL was reported in the Northeast area of Brazil and these EBV associated BL were observed in young children[9]. Both eBL and sBL are characterized by specific chromosomal translocations that juxtapose areas within or near the c-myc proto-oncogene locus on chromosome 8 to an Ig gene locus on chromosome 2, 14, or 22. The resulting deregulation of the c-myc gene has been implicated in the pathogenesis of the disease[10]. Previous studies have shown that the cases classified as Burkitt-like lacked c-myc rearrangement and had different molecular pathogenesis than BL[11,12]. Unfortunately, in this case, the molecular distinction between the two categories was not performed, and the diagnosis was made according to the morphologic criteria defined by the REAL classification [13].

This patient presented a B-cell lymphoma at an unusually young age at diagnosis. The histological examination revealed a Burkitt-like SNCCL. Non-Hodgkin's lymphoma (NHL) including Burkitt and Burkitt-like, are rarely described in infants. In 338 consecutive newly diagnosed children with NHL, Murphy et al., found that 4.8% of them were younger than 3 years of age[1]. Evans et al., reported 6 children who developed NHL before the age of 3 years associated with mother-to-child HIV transmission[14]. In another report of NHL in children with vertical HIV infection, 21.7% were under 2 years old[15]. We have identified 1 infant patient with a Burkitt-like SNCCL whose HIV test was negative in the child and her mother, and the EBV genome was not detected by *in situ* hybridization, despite the previously described relationship between young age and HIV infection and these lymphomas[10,11].

Prior to the last two decades, childhood Burkitt's NHL was a fatal disease in most of the cases. In 1976, Wollner et al. reported the excellent results on the treatment of childhood NHL using a novel multiagent chemotherapeutic regimen, LSA_2L_2[16]. Several reports in the past 10 years have shown that event-free survival has significantly improved[6,17-19]. Patients with limited disease currently have an excellent prognosis (90% - 100%)[6,17]. The probability of cure is obviously influenced by many factors, among which the most important are the total body burden of tumor and intensity of chemotherapy[6]. The former is reflected

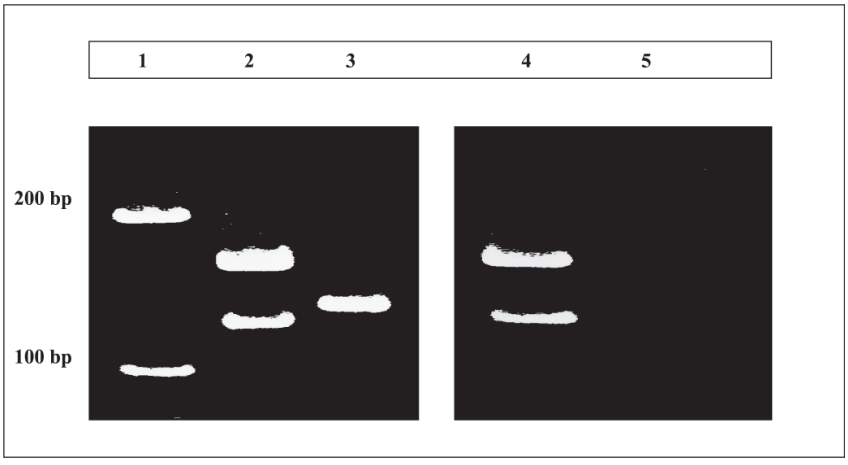

Figure 1 - Clonal IgH (CDRIII) gene rearrangement detected by FR3-JH polymerase chain reaction (PCR). Lane 1: 100 bp ladder (GIBCO-BRL) size marker; lane 2: biallelic rearrangement in pleural liquid, lane 3: positive control (Cemo-1 cell line); lane 4: rearrangement in abdominal tumor, identical pattern as pleural liquid; lane 5: PCR amplification without DNA template. Negative image of an 8% polyacrylamide gel with silver staining.

mainly by the stage of disease and LDH serum level at diagnosis[20]. In the past, the prognosis for patients with high tumor burdens or with central nervous system involvement was very poor[21]. This situation has changed markedly in recent years, and patients with stage III Burkitt and Burkitt-like SNCCL including those with extensive intra-abdominal disease, have a 60% - 80% long-term survival rate[6,18]. Tumor lysis syndrome is often present at diagnosis or after initiation of treatment. This emergent clinical situation should be anticipated prior to starting treatment. Despite the high tumor burden found, our patient achieved long-term complete remission, probably related to the intensive therapy.

The current report illustrates the importance of considering NHL in the differential diagnosis of neoplasia in very young children, even when HIV is not present.

RESUMO

KLUMB CE e col. - Linfoma burkitt-*like* em um lactente: relato de caso. **Rev. Hosp. Clín. Fac. Med. S. Paulo 58**(1):33-36, 2003.

Os linfomas não Hodgkin da infância, incluindo os linfomas de Burkitt e Burkitt-*like* são raros em lactentes. Um caso de linfoma não Hodgkin B em uma lactente de 13 meses de idade é descrito. Ao diagnóstico a paciente apresentava extenso comprometimento abdominal associado à ascite, derrame pleural e síndrome de lise tumoral. A análise imunofenotípica mostrou um fenótipo compatível com células linfóides oriundas do centro germinativo e a origem clonal dessas células foi demonstrada por reação em cadeia da polimerase. Não foi demonstrada associação do linfoma com infecção pelo vírus Epstein-Barr e/ou virus da imunodeficiência adquirida. O caso apresentado enfatiza a necessidade de considerar o diagnóstico de linfoma mesmo em lactentes.

DESCRITORES: **Linfoma não-Hodgkin. Linfoma de Burkitt. Linfoma Burkitt-*like*. Lactente. Neoplasias na infância.**

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