Clinical Case Report

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Silent presentation of multiple metastasis Burkitt lymphoma in a child

A case report and review of the literature

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Abstract

Rationale: The Burkitt lymphoma (BL) is a very aggressive B-cell non-Hodgkin's lymphoma. It accounts for 34% of lymphoma cases in children.

Patient concerns: We present the case of a 6-year-old boy diagnosed with BL, who presented multiple contrasting elements of the disease: silent symptomatology, without involvement of the bone marrow at first, but with multiorgan infiltration and a fast evolution, despite starting the treatment shortly after the symptoms appeared.

Diagnoses: He was diagnosed with BL after immunophenotyping from the pleural fluid.

Interventions: After a week from admission, chemotherapy was initiated according to protocol NH-BFM therapeutic group III—cytoreductive phase in the acute care ward and subsequently the AA 24 treatment.

Outcomes: Following the treatment, the patient developed medullary aplasia and cutaneous toxicity. The patient's general state remained severe during the hospitalization.

Lessons: Even though the prognosis of BL has improved over time (up to 90% survival rate), in this case the evolution was unfavorable. In our patient, the symptoms appeared abruptly. They appeared late in the phase of multiple-organ dissemination, which generated the pessimistic prognosis.

Abbreviations: BL = Burkitt lymphoma, CT = computed tomography, IPPV = intermittent positive-pressure ventilation, LDH = lactate dehydrogenase.

Keywords: Burkitt lymphoma, child, multiple metastasis

1. Introduction

The Burkitt lymphoma (BL) is a very aggressive B-cell non-Hodgkin's lymphoma characterized by the deregulation and translocation of the C-MYC gene from chromosome 8.[1] BL is the most frequent non-Hodgkin lymphoma in children and adolescents, accounting for approximately 34% of the lymphoma cases in young age.[2] Three clinical BL subtypes are recognized: endemic, sporadic, and associated to immunodeficiency. The endemic form (the most frequent form) affects mainly the facial bones (typically the maxilla), the sporadic form affects mainly the terminal ileum, the cecum and the intra-abdominal lymph nodes, and the form associated to immunodeficiency appears in HIV-infected patients, patients with autoimmune `diseases or patients with primary immunodeficiency disorders.[3,4]

BL is common among the African children where the estimated incidence is 3 to 6 cases per 100,000 children/year.[5] The incidence is approximately 50-fold higher than that in the United States.[6] Sporadic form of BL is more common among Caucasians, than racial minorities and among boys than girls.[7] Age, performance status, LDH value, bone marrow, and central nervous system involvement are the most frequently used prognostic factors.[4]

The aim of this paper was to report a case of LB in a 6-year-old child, emphasizing the clinical features, radiographic findings, and the evolution of this lesion.

2. Case presentation

Male child aged 6, H = 110 cm, W = 33 kg, BMI = 27.27 with no significant personal pathological history, was admitted in the pediatric surgery ward for vomiting, mild temperature and abdominal pain, which started a week before admission. Because this symptomatology was persistent and the symptomatic treatment did not work, the child was referred to our hospital. Informed consent was obtained from the parents upon admission.

In the clinical examination upon admission, his general state was satisfying, he was afebrile and had normally colored teguments and mucous membranes. Auscultation of heart and lungs showed normal heart sounds, but no vesicular murmur in the right hemithorax, as well as the basal area of the left hemithorax. Examination of the abdomen presented a general enlargement (adipose tissue), tenderness in the right flank and right iliac fossa, where a solid, pseudo-tumoral mass was discovered (8 cm, tender, immobile). Bowel movements and

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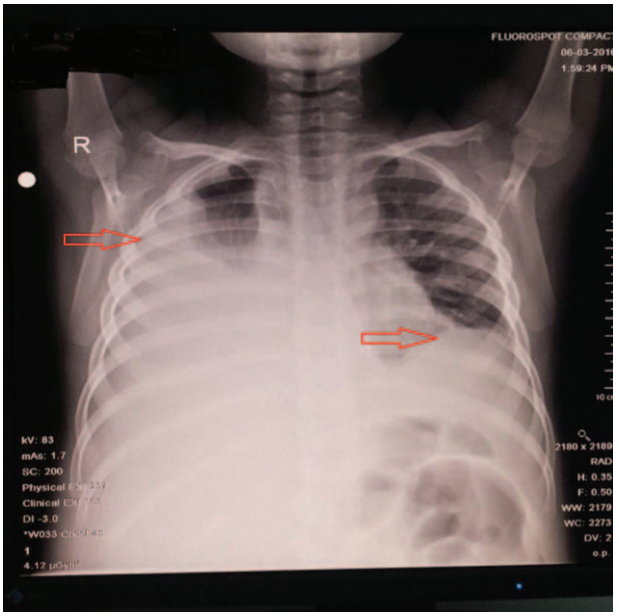

Figure 1. Chest x-ray—bilateral pleurisy.

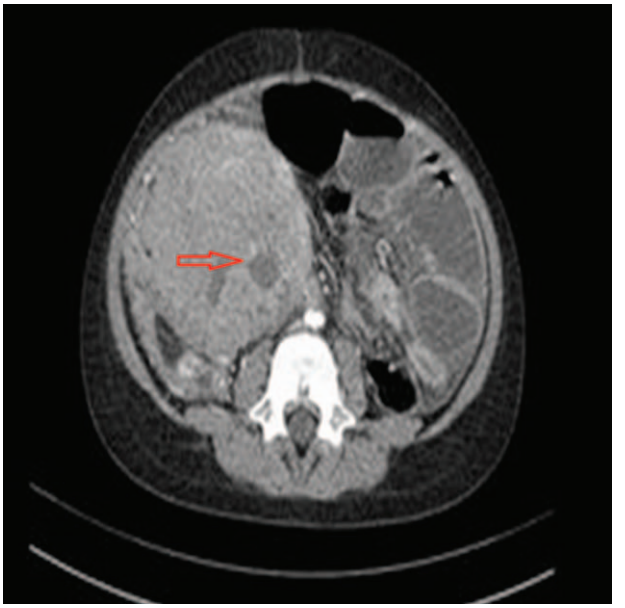

Figure 2. Abdominal CT—tumoral mass. CT = computed tomography.

micturition were physiological, without signs of meningeal irritation.

Biological tests revealed the presence of inflammatory syndrome and high LDH (2 × the normal value); anti-Epstein Barr virus IgM and Ig G antibodies—negative, anti-Cytomegalovirus IgM and IgG antibodies—negative, RPR Syphilis—negative, anti-HIV antibodies—negative, anti-HCV antibodies—negative, HBsAg—negative.

The chest x-ray revealed extensive pleurisy occupying more than 2/3 of the right hemithorax and medium pleurisy in the left hemithorax, widened mediastinum, bilateral interclavicular-hilar infiltrate (Fig. 1).

The computed tomography (CT) scan of the chest and abdomen, both native and with a contrast agent, described a solid tumoral mass sized 10.6/10.4/13.5 cm, located in the right flank and iliac fossa, with collateral tumor circulation, mediastinal adenopathies, bilateral pleurisy (more accentuated on the right side), pleural, pericardial, renal, muscle and peritoneal metastases, free fluid 4 cm thick in the peritoneal cavity, in the hypogastrium (Fig. 2).

Right thoracentesis was performed and 60 mL hematic fluid was extracted. The cytological examination revealed the presence of 66% blasts. Immunophenotyping from the pleural fluid was suggestive for the diagnosis of Burkitt lymphoma (CD19+, CD10+, CD20+, CD22+, CD79a+, CD45+, CD38+, CD33+, CD34+, CD15+, CD58+, CD9+, CD123+). The original cytological examination of bone marrow described efficient marrow on all series, noninfiltrated.

After a week from admission, chemotherapy was initiated according to protocol NH-BFM therapeutic group III—cytoreductive phase in the acute care ward and subsequently the AA 24 treatment in the pediatric oncology ward. Following the treatment, the patient developed medullary aplasia and cutaneous toxicity.

One month after beginning the treatment, the patient was transferred again to the intensive care unit because of sudden respiratory arrest and comatose state.

He was orotracheally intubated and mechanically ventilated in the IPPV mode. His state remained severe, he was afebrile, had facial contractures, anisocoria (following the neurological and neurosurgical examination, a cranial CT scan was recommended), oral bleeding, and epistaxis. Thrombocytopenia was treated with hemostatic agents, plasma, and platelet concentrate. The cranial CT examination showed the presence of subarachnoid hemorrhage in the left frontal lobe and a recent ischemic lesion in the area of the posterior cerebral artery.

During the entire period of hospitalization in the ICU, the patient's general state remained severe, 1st–2nd degree coma, with no communication or reaction to auditory stimuli. He presented cervical, axillar and inguinal eruptions covered by scabs, ecchymoses on the puncture spots, persistent respiratory symptoms, and persistent tumoral mass much smaller in size, though.

The patient was transferred to a palliative care center.

3. Discussions

In young age, BL can appear as an abdominal mass associated to symptoms such as: gastrointestinal hemorrhage, abdominal pain, nausea, and bowel obstruction caused by the direct compression or the involvement of the bowel lumen.[8] Intussusception upon presentation can be present in up to 18% of the patients with primary abdominal BL.[9] Although in our patient a solid pseudotumoral mass of approximately 8 cm could be felt in the right flank and the right iliac fossa, he had physiological bowel movements.

Sporadic BL appears mainly in children, mostly in boys. Like in our case, classical sporadic presentation is associated to an abdominal mass typically in the ileocecal region. Generally, the sporadic form is associated with involvement of the bone marrow and/or central nervous system.[10,11] In a study conducted both on adults and children with BL, bone marrow infiltration was reported in 67% of cases.[12] The original cytological examination of bone marrow described efficient marrow on all series, noninfiltrated.

The Epstein Barr virus plays an etiological role in different diseases, including infectious mononucleosis, nasopharyngeal

cancer, the Hodgkin disease and BL.[13,14] Approximately 30% of the sporadic BL cases suffer from an Epstein Barr infection.[10,11] In this case, anti-Epstein Barr virus IgM and Ig G antibodies were negative. We could not identify any trigger for the disease.

Currently, CT is widely used as an initial imaging method for BL patients. In our patient, the chest and abdominal CT both native and with contrast agent highlighted the existence of the abdominal tumor as well as mediastinal adenopathies, and pleural, pericardial, renal, muscle and peritoneal metastases. Upon admission, most children with BL come in an advanced stage of the disease and/or with metastases. The exact determination of the stage is essential for the appropriate treatment.[11]

Intra-aortic involvement is more frequent in Hodgkin's disease than in BL.[15] In the non-Hodgkin lymphoma, pulmonary involvement can be noticed when the diagnosis is set in less than 5% of the cases and can appear without concomitant mediastinal disease.[16] The most common mechanisms for the disease spreading at this level are hematogenic and lymphatic dissemination, direct invasion being less frequent.[17] Though our patient's parenchyma was not affected, we found pleural metastases and pleurisy. In BL, pleurisy can be noticed and sometimes it is extensive enough to generate mediastinal retraction and pulmonary atelectasis.[17]

Kidneys are affected in aggressive forms of non-Hodgkin lymphoma. Their infiltration is often present in terminal phases of non-Hodgkin lymphoma. In children, BL has the highest frequency of kidney infiltration. Hematogenic dissemination is the most common cause for renal lymphoma, though infiltration from adjacent ganglions can be present in 10% to 20% of the cases.[18]

The prognosis of children with non-Hodgkin lymphoma has improved in time. Studies conducted on children under 15 years showed that the survival rate at ages 5 and 10 increased from 76.6% and 73% between 1990 and 1994 to 87.7% and 86.9% between 2000 and 2004. The survival rate at the age of 10 for children diagnosed between 2005 and 2009 was reported as 90.6%.[19]

The authors of a study conducted during 26 years in Brazil on 45 children diagnosed with BL analyzed the potential factors for the negative prognosis of the disease (gender, age, stage, nutrition state, serum LDH, and kidney function). They noticed a significantly lower rate of revival in children and adolescents with uric acid $\geq$7 mg/dL, suggesting that a good marker for the tumor could be the metabolite concentration.[20] During the hospitalization period, our patient had uric acid values within normal limits or slightly increased, without exceeding 6.1 mg/dL. Other authors reported as a negative prognosis factor the increased value of serum LDH, which was confirmed by our patient, who had LDH values twice as high as the normal value.[21,22]

The particularity in our case was that the child had multiple contrasting elements of the disease: with apparently inoffensive symptoms, without initial involvement of the bone marrow, but with multiorgan infiltration and with a rapid evolution, despite the treatment initiated quickly from the occurrence of the symptoms.

4. Conclusion

In our patient, symptoms appeared abruptly. They appeared late in the phase of multiple-organ dissemination, which generated the pessimistic prognosis. We could not identify any negative prognosis factor associated to our case.

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