Blastic Plasmacytoid Dendritic Cell Neoplasm in a pediatric Peruvian patient

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Abstract

Blastic plasmacytoid dendritic cell neoplasm is an aggressive and rare hematologic malignancy, exceptionally presented in children. This case reports an 11-year-old Peruvian boy, with a 2-year history of a purple-violate tumor in a leg, lymph node involvement, and histopathological study with immunohistochemistry: CD4+, CD56+, Tdt+, CD45+, TCL1+. An institutional treatment protocol for high-risk ALL was given. There was a diagnosis delay in a pediatric patient with a rare but very visible neoplasm in a low-middle income country. Despite this, the clinical course was of an indolent evolution. The institutional protocol was efficient to achieve complete oncological disease response.

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Blastic plasmacytoid dendritic cell neoplasm is an aggressive and rare hematologic malignancy, exceptionally presented in children. This case reports an 11-year-old Peruvian boy, with a 2-year history of a purple-violate tumor in a leg, lymph node involvement, and histopathological study with immunohistochemistry: CD4+, CD56+, Tdt+, CD45+, TCL1+. An institutional treatment protocol for high-risk ALL was given. There was a diagnosis delay in a pediatric patient with a rare but very visible neoplasm in a low-middle income country. Despite this, the clinical course was of an indolent evolution. The institutional protocol was efficient to achieve complete oncological disease response.

Introduction

Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN) is a rare hematological neoplasm, which has its own category in the group of leukemias [1]. It usually presents in elderly people, and its clinical manifestations include nodular blue-violet skin lesions, bone marrow infiltration and, less frequently, extramedullary involvement [2]. These clinical characteristics do not differ significantly between age groups; however, better survival has been found in pediatric cases[2,3]. Despite some associations with other hematologic neoplasms, its etiology is still unknown [4]. Diagnosis is based on immunohistochemistry, it requires positive CD4 and CD56, and at least two positive dendritic cell markers[5].

Current literature, based on case reports, supports the use of acute lymphoblastic leukemia (ALL) treatment regimen as the most beneficial option [6]. While new therapies that target CD123 and SL-401 (tagraxofusp)[7] are currently being studied for a more specific treatment in adults, they still have to be tested in a pediatric population[8].

The objective of the present pediatric clinical case is to document both a diagnosis of this indolent and rare disease, whose natural history in Latin American patients is usually ignored in published reviews; and report complete remission after appliance of an institutional treatment regimen for high-risk acute lymphoblastic leukemia (HR-ALL).

Case report

The case of an 11-year-old boy, from Yungay (Ancash, Peru) is reported. He was referred from Ancash Hospital to the National Institute of Neoplastic Diseases (INEN) in Lima, with the diagnosis of 'Round Cell Neoplasia'.

This child presented with a 2-year clinical history, characterized by the presence of a growing tumour in the anterior inner middle third of the right leg, of approximately 5 centimeters by time of medical consultation, blue-violet colouring, increased consistency, poorly defined edges and little pain on palpation. No epidemiological, personal, family or medical history of importance was reported.

At physical exam he presented a 7 cm long surgical scar with ulcerated area and granulation tissue without signs of infection, presence of right inguinal adenopathies of 3x3 cm, mobile, painless, without phlogosis was found.

The child had a prior biopsy in Ancash, but it was insufficient tissue and INEN's oncopediatric team performed a new biopsy. Hematoxylin and eosin staining and immunohistochemical markers were studied. It showed CD4+ and CD56+; staining for more specific markers resulted in a local TdT+, CD45+, TCL1+ and CD34 -. In addition, a KI-67 score of 60%. (Fig. 1)

Significant lymphadenopathies in the right external iliac chain and right inguinal region were found through Multi-slice spiral computed tomography. Theses typical secondary lesions were considered as inguinal metastasis.

Laboratory values of hemoglobin, leukocytes, segmented, platelets, and erythrocyte sedimentation rate values were normal. Morphology, flow cytometry and bone marrow biopsy were negative to infiltration of neoplasm cells.

Final diagnosis was BPDCN. After the medical team discussion, an institutional HR-ALL treatment protocol, based on the pediatric one from the International BFM Study Group (BFM-95), was indicated (Table 1). The high-risk classification was mainly indicated because of the patient's age and the biological characteristics of this rare disease.

During treatment, two emergency admissions were required due to febrile neutropenia, both resolved without complications. By the date of submit of this report, the patient was in good general condition. He completed maintenance chemotherapy block in May 2020, and stays in controls without treatment related complications.

Discussion

By the year 2017, a review found only 74 pediatric cases of BPDCN worldwide [2]. However, it did not included data in Spanish or from Latin America, so these patients' clinical evolution has not been considered. Also, we reported a delay in diagnosis due to lack of resources at a hospital outside the country's capital (as seen in many low-middle income countries), and the indolent course of the neoplasm.

Various studies identify skin involvement as the initial manifestation (76% of adults and 79% of children) and also the most frequent[2]. These lesions are often asymptomatic and purplish or erythematous in appearance; however, they can also be pseudo-purple, plaque, nodular, equimotic, scaly or ulcerated [7]. The most compromised regions are usually the face, scapular region and to a lesser extent the trunk and extremities [3]. In this pediatric case of BPDCN, skin involvement was exclusively appendicular, it compromised soft tissue (solid tumor) and had a loco-regional presentation in the lower right limb (inner side of the right leg with a purplish tone).

Bone marrow compromise and leukemic expression can appear even without skin lesions in 60-90% of cases [2,3]. In this child, even after two years of evolution before the diagnosis, there was no bone marrow infiltration. Extramedullary manifestations can include involvement of the liver, lymph nodes (40%-50%), sinuses, orbits and central nervous system, rarely splenomegaly (20%) and fulminant leukemia (5-25%) [2,3], in this case only lymph node involvement was registered (right inguinal).

Diagnosis confirmation was made through immunohistochemistry and by excluding more frequent neoplasms. Thus, the positivity for CD4, but negativity of CD3, served to rule out a T cell neoplasm. In the same way, a positivity for CD56, but negativity for CD3, removed the possibility of T-NK lymphocyte involvement; and negativity for CD34 excluded the presence of myeloid cells [5]. Immunohistochemistry showed CD4+, CD56 +, in addition to 2 positive dendritic cell markers (CD123 and TCL1) which allowed confirmation of the diagnosis [9].Other dendritic cell markers not tested in this case are CD68, CD123 and BDCA-2/CD303[10].

It has also been documented that thrombocytopenia, anemia and, to a lesser extent, neutropenia can appear in these patients' blood counts[3]. On the contrary, this patients' initial values were within normal parameters.

Overall patient survival of 37 months was consistent with studies where the mean survival of patients under 40 years was 38 months[2]. And with other studies where the overall survival in children at 3 years was 57.4+/- 10.2 months [11].

Treatment of BPDCN in pediatric patients is still controversial. Even if some intents have been made to create a scheme of treatment[12], a gold standard is still far away. Most cases report good response with the same scheme used for ALL, recording remission rates of 93%, compared to 77% of the regimen for chronic myeloid leukemia and 80% of the scheme for lymphoma[2,5,12]. The most favorable results are usually seen in patients without skin involvement [3]. Protocol for ALL includes prophylaxis of the nervous system with intrathecal chemotherapy, since it is considered one of the main causes of morbidity and mortality in patients with this disease [7]. Bone marrow transplantation is usually reserved for cases with one or multiple relapses; in elderly patients is also used as a consolidation therapy after chemotherapy [8,11,13]. However, in pediatric patients it does not improve survival [2]. In this patient, institutional HR- ALL was given with good results, adding to the literature its efficacy in a different sociodemographic setting.[14]

BPDCN is a diagnostic and therapeutic challenge. Even with a very visible lesion, diagnostic delayed was presented in a peruvian setting. The decision of the oncopediatric team was based on literature and similar unpublished cases from the institution. Emphasis should be placed on timely diagnostic through the use of immunohistochemical markers. The treatment of BPDCN with an institutional high-risk ALL regimen has reached very good results in this pediatric case, achieving 37-month overall and progression-free survival.

Ethics Statement

Informed consent was signed by the patient's proxy.

Conflict of Interest Statement

The authors declare no conflict of interest.

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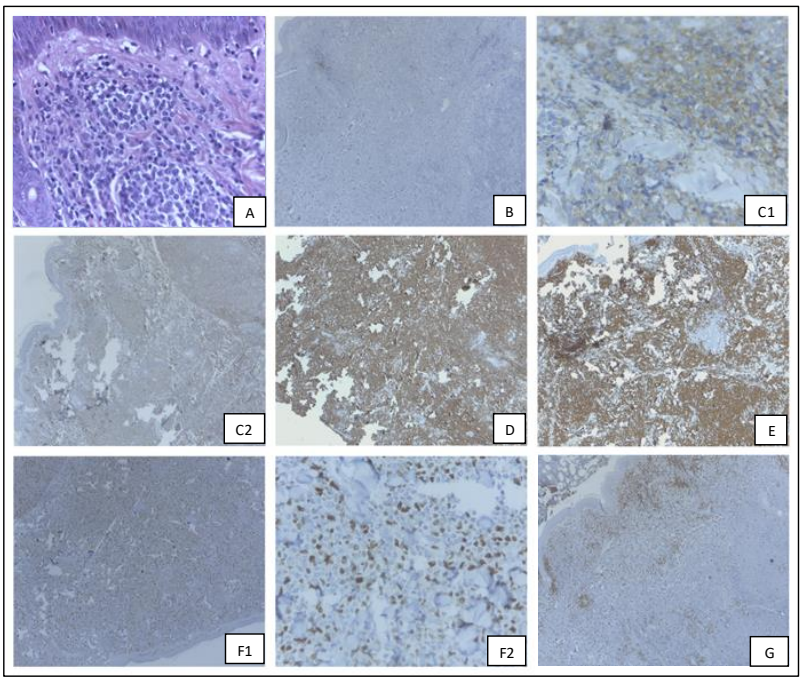
Legend list:

Figure 1. (A) Biopsy with Hematoxylin-Eosin 40x tumor tissue sample neoplastic proliferation in the dermis, without infiltration of adnexa. Immunohistochemistry showed results of tumor cell phenotype (B) CD20 negative, (C1 and C2) CD4 positive, (D) CD56 positive, (E) TCL1 positive, (F1 and F2) Ki-67 at 60 % and (G) CD 3 negative.



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