

## **Blastic Plasmacytoid Dendritic cell neoplasm: Case report**

### **Neoplasia de células Dendríticas Plasmocitóides Blásticas: Relato de caso**

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#### **ABSTRACT**

Blastic plasmacytoid dendritic cell neoplasm is a rare neoplasm of hematopoietic origin with poor clinical evolution. Here we report a case of a patient who presented with blastic plasmacytoid dendritic cell neoplasm with cutaneous and nodal involvement. The patient was successfully treated with polychemotherapy followed by allogeneic bone marrow transplantation. The case described reaches, until the moment of this publication, disease-free survival of 32 months, superior to that described in the literature, which is from 12 to 18 months. We also did a brief review of the literature on this disease, including aspects relevant to diagnosis, treatment and prognosis.

**Keywords:** Blastic Plasmacytoid Dendritic Cell Neoplasm, Bone Marrow Cell Transplantation, Hematologic Malignancy.

#### **RESUMO**

A neoplasia de células dendríticas plasmocitóides blásticas é uma neoplasia de origem hematopoética rara e com evolução clínica ruim. Aqui relatamos um caso de paciente que

apresentou a neoplasia de células dendríticas plasmocitoides blásticas com acometimento cutâneo e nodal. O mesmo foi tratado com poliquimioterapia seguida de transplante alogênico de medula óssea com sucesso. O caso descrito alcança, até o momento desta publicação, sobrevida livre de doença de 32 meses, superior à descrita na literatura que é de 12 a 18 meses. Fazemos ainda uma breve revisão de literatura acerca desta doença incluindo aspectos relevantes para o diagnóstico, tratamento e prognóstico.

**Palavras-Chave:** Neoplasia de Células Dendríticas Plasmocitoides Blásticas, Transplante de Medula Óssea, Malignidade Hematológica.

## 1 INTRODUCTION

Blastic plasmacytoid dendritic cell neoplasm is a hematopoietic malignancy that was first described in 1994. In 2008, it was renamed in the 4<sup>th</sup> edition of the World Health Organization (WHO) classification of human tumors to more accurately reflect its cytological characteristics as a myeloid lineage neoplasm. In a dedicated chapter, the 2017 revised WHO classification asserted that this neoplasm has its origin in hematopoietic stem cells with the genetic signature being closer to the origin of myeloid precursors.<sup>3,5</sup> The association with myeloid disorders suggests a potential multilineage in some cases.<sup>5</sup>

Blastic plasmacytoid dendritic cell neoplasm is a rare disease that accounts for less than 1% of acute leukemias<sup>6</sup> and is more frequent in men than in women (3.3:1). It is particularly prevalent in the seventh and eighth decades of life, although it has been described in all age groups, including children. The neoplasm has no defined etiology, but it may be associated with myelodysplastic syndromes and myeloproliferative diseases, especially chronic myelomonocytic leukemia.<sup>3,4</sup>

The objective of the present report is to describe the case of one patient, of whom having presented blastic plasmacytoid dendritic cell neoplasm. We wish to show the clinical manifestations, immunophenotypic aspects for the diagnosis, the treatment administered and the response.

## 2 CASE REPORT

A 28-year-old man presented an initial itchy nodular lesion in his right calf. The lesion showed no purulent drainage, but it had undergone progressive growth for about 1 year before the patient sought care. The man was a rural worker who was obese, hypertensive, dyslipidemic, and also smoked. During the six months prior to the investigation, new diffuse nodular lesions with the same features had appeared in his

upper and lower limbs, trunk and cervical region, and he had lost nine kilos in one month and had shown sporadic episodes of fever.

Physical examination showed multiple hardened nodules of different sizes. The lesions were not painful to palpation, and they were located on the upper limbs, calves, thigh, chest, and back, as well as in the occipital, submental, and cervical regions. The calf lesions were ulcerated but showed no purulent secretion (Figure 1 - A).

Biopsy of these skin lesions showed dermal infiltration of immature malignant cells of intermediate size in a diffuse pattern and with nodular growth. The neoplastic cells had a scarce cytoplasm and irregular nuclei, with nucleoli occasionally evident. An immunohistochemical study revealed the expression of TCL1 and CD123, thus confirming the diagnosis of blastic plasmacytoid dendritic cell neoplasm. The expression of anti-apoptotic protein BCL-2 was also observed, and the cell proliferation antigen Ki-67 was expressed in 90% of the neoplastic cells.

Given this diagnosis, morphological examination and immunophenotyping were performed by flow cytometry analysis of bone marrow cells; the immunophenotyping showed only 0.4% of positive events for CD56, CD4, CD123, HLA-DR, and CD38, which correspond to plasmacytoid dendritic cells. Despite this finding, histological and immunohistochemical examination of bone marrow samples also gave negative results for neoplasia, therefore, we found this percentage not being sufficient to demonstrate the leukemic form of the disease.

Computed tomographic (CT) staging showed bilateral iliac and inguinal lymph node enlargement and an increased number of cervical lymph nodes, but with borderline dimensions. Sinus CT scan revealed possible infiltration in the paranasal sinuses and nasal fossae, as well as hypertrophy of the pharyngeal tonsils. There were signs of bronchiolitis in the chest, but no signs of neoplasia.

The HyperCVAD chemotherapy protocol was adopted, according to which hyperfractionated cyclophosphamide, vincristine, doxorubicin, and prednisone, high doses of methotrexate and cytarabine. Methotrexate, cytarabine plus dexamethasone were administered intrathecally for central nervous system prophylaxis. The lesions showed complete remission (Figure 1 - B) and the polychemotherapy was interrupted after seven cycles. Next, the patient was submitted to related-donor allogeneic hematopoietic stem cell transplant (HSCT) and, at the time of this publication, he has completed 32 months of remission after therapy with HyperCVAD followed by HSCT.

Figure 1: Skin lesions in the lower limb. A- Nodular and ulcerated lesions at the time of diagnosis. B- Scar appearance of skin lesions at the end of chemotherapy protocol.



### 3 DISCUSSION

Normal plasmacytoid dendritic cells were originally described by Lennert and Remmele in 1958,<sup>7</sup> and have had different names over time because their cellular origin is uncertain. The origin of blast plasmacytoid dendritic cell neoplasm also remained unclear for many years and only in 2008, the precursors of plasmacytoid dendritic cells were recognized as the normal counterpart of this neoplasm.<sup>3</sup>

The pathophysiology of blastic plasmacytoid dendritic cell neoplasm implies that it originates from clonal proliferation of plasmacytoid dendritic cell precursors. Morphologically, it is composed of monomorphic medium-size tumor blast cells with nuclei that have irregular contours, thin chromatin, and one or multiple eosinophilic nucleoli. The cytoplasm is scarce and azurophilic, but without Giemsa-positive granules, which is in accordance with our findings. Mitotic figures vary in number, without the occurrence of necrosis or angioinvasion.<sup>4,5</sup>

Immunophenotypically, the tumor expresses CD4, CD43, CD45RA, and CD56, as well as antigens associated with plasmacytoid dendritic cells, such as CD123, TCL1A,

CD303, and CD2AP. Neither CD4 nor CD56 are expressed in about 8% of cases. Some lymphoid or myeloid antigens, such as CD7 and CD33, are commonly expressed.<sup>5</sup> Some cases show expression of CD2, CD5, CD36, CD38, and CD79a, while CD3, CD13, CD16, CD19, CD20, LAT, lysozyme, and MPO are not expressed. Granzyme B can be detected by flow cytometry, but it is typically negative in immunohistochemical assays of tissue samples. Other cytotoxic molecules, such as Perforin and TTIA1, are not expressed.<sup>5</sup> The S100 protein is expressed in 25% to 30% of cases, especially in pediatric cases. TdT is expressed in about one third of cases, and CD117 is occasionally expressed. CD34 is not detected in immunohistochemical assays of tissue samples but it is detected by flow cytometry in 17% of cases.<sup>5</sup> The neoplasm can also express other antigens that are usually not expressed in normal plasmacytoid dendritic cells, such as BCL6, BCL2, and IRF4. In this case, BCL2 was positive.

The cutaneous tropism of blastic plasmacytoid dendritic cell neoplasm as observed in our patient, is attributed to its antigen expression, which includes CLA and CD56, and to the chemokine receptors expressed by the neoplastic cells, such as CXCR3, CXCR4, CCR6, and CCR7. Multiple skin lesions usually occur, which can affect any site and be present as nodules, plaques, or bruises of different sizes and colors.<sup>4</sup>

Epidemiological data show that in 90% of cases the patient presents skin nodules concomitant with the involvement of other sites, such as bone marrow, lymph nodes, spleen, or other organs before leukemic dissemination occurs, which would have a pattern similar to a myelomonocytic or monocytic leukemia. However, in approximately 10% of patients, acute leukemia is the first manifestation of the disease and the coexistence of myelodysplastic syndrome or the transformation into acute myeloid leukemia is observed in 15 to 20% of cases.<sup>1,2</sup> However, such manifestations were not observed in our patient.

The disease has an aggressive clinical progression, with an average survival span of 10 to 20 months. A total of 80% to 90% of cases show an initial response to polychemotherapy, but relapses with subsequent chemoresistance are often observed. Treatments based in acute lymphoid leukemia protocols are more effective than acute myeloid leukemia-based regimens.<sup>6</sup> Age has a prognostic impact, with the survival rates being higher in pediatric patients.<sup>5</sup> For patients in their first complete remission who are clinically fit, allogeneic hematopoietic stem cell transplantation is recommended as the first line of treatment to achieve long-term survival.

#### **4 CONCLUSION**

The present report describes a case of blastic plasmacytoid dendritic cell neoplasm presented as a lymphoma with extensive skin and lymph node involvement, but without bone marrow infiltration. This case showed a good clinical progression 32 months after diagnosis following administration of standard treatment according to literature (polychemotherapy according to acute lymphoblastic leukemia protocols, followed by HSCT). The patient in this case has already exceeded the overall survival estimate of 12 to 18 months described in literature.<sup>6</sup> It has not yet been possible to identify the specific immunophenotypic signature of the most severe cases of blastic plasmacytoid dendritic cell neoplasm. This would require larger studies, which are difficult to carry out as this is a rare neoplasm with a high mortality rate.

Although this neoplasm often has severe progression, with high relapse and chemoresistance rates, it can be treated, and the response is satisfactory in some cases, like this one reported.

#### **CONTRIBUTIONS**

Michel Hamui Sallum and Vanessa Afonso da Silva did the medical record review and literature review about the theme, as well as submission of the work to the ethics committee. Helio Moraes-Souza and Fernanda Bernadelli de Vito did the revision of the text including the translation into English.

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