ECRONICON OPEN ACCESS

EC PAEDIATRICS
Case Report

A Rare Case of Pediatric Blastic Plasmacytoid Dendritic Cell Neoplasm: A Case Report

Mohamed Ahmed Maki Ebrahim[1]*, Mohamed Almuqamam[1], Alyosha Smolarski[2], Ying Xian Liu[2] and Aziza Sedrak[1]

[1]Department of Pediatrics, The Brooklyn Hospital Center, Brooklyn, NY, United states of America

[2]Department of Pathology, The Brooklyn Hospital Center, Brooklyn, NY, United states of America

***Corresponding Author:** Mohamed Ahmed Maki Ebrahim, Department of Pediatrics, The Brooklyn Hospital Center, Brooklyn, NY, United states of America.

Received: October 23, 2019; **Published:** December 06, 2019

Abstract

Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN) is usually diagnosed in men ages 65 - 67 years, presenting with cutaneous lesions. Our patient was a 9-year old male who presented with generalized joint pain and fatigue without evidence of skin involvement. Shortly after diagnosis by flow cytometry and bone marrow biopsy, this child completed 1800cGy cranial radiation therapy and currently undergoing chemotherapy with AALL1231 protocol and has shown complete response. This case is a reminder to clinicians to keep a high-index of suspicion of malignancy in children presenting with vague symptoms and adds to the limited number of BPDCN cases in children, thus acting as reference for physicians treating such patients.

Keywords: *Blastic Plasmacytoid Dendritic Cell Neoplasm; Leukemia; Acute Myeloid Leukemia; Pediatrics; Pediatric Oncology*

Abbreviation

BPDCN: Blastic Plasmacytoid Dendritic Cell Neoplasm; AML: Acute Myeloid Leukemia; WHO: World Health Organization; CD: Cluster of Differentiation; CT: Computed Tomography; MRD: Minimal Residual Disease; ALL: Acute Lymphoblastic Leukemia; SCT: Stem Cell Transplant

Introduction

Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN) is a rare and aggressive hematologic malignancy that is now categorized under Acute Myeloid Leukemia (AML) by the World Health Organisation (WHO) [1] and accounts for 0.44% of all hematological malignancies [2]. Accumulating phenotypic, functional, and genetic evidence including the finding of CD123 antigen expression, a key marker that was not routinely tested in the past, has pointed its derivation from myeloid precursors with commitment to the plasmacytoid dendritic cell lineage [3-9].

BPDCN presents as leukemia or evolves into acute leukemia and occurs more commonly in older men with very few pediatric cases reported [9]. Also, pediatric cases seem to suggest a more optimistic outcome than commonly seen in adults [10]. BPDCN has a heterogeneous presentation and although cutaneous lesions can often be seen, other organs such as the CNS can also be involved in addition to the peripheral blood, lymph nodes and bone marrow [2,4,9].

Case Details

We present a case here of a 9 year old male child with past medical history of sickle cell trait, complaining of generalized joint pain and fatigue without any evidence of skin involvement. Laboratory results revealed severe anemia, leukopenia and lymphocytosis. The patient was subsequently admitted for the management of severe anemia and was transfused with packed red blood cells. On physical examination patient was sick looking. There was conjunctival injection, rhinorrhea and tenderness to palpation over the bilateral hands, ankles, knees and lumbosacral spine. No lymphadenopathy or abdominal organomegaly was appreciated. The peripheral blood smear shows atypical lymphocyte blasts (about 40%) and blasts. Flow cytometry of peripheral blood was performed by Genpath showing 31.68% of CD123+ dendritic cells confirming the diagnosis of BPDCN (Figure 1).

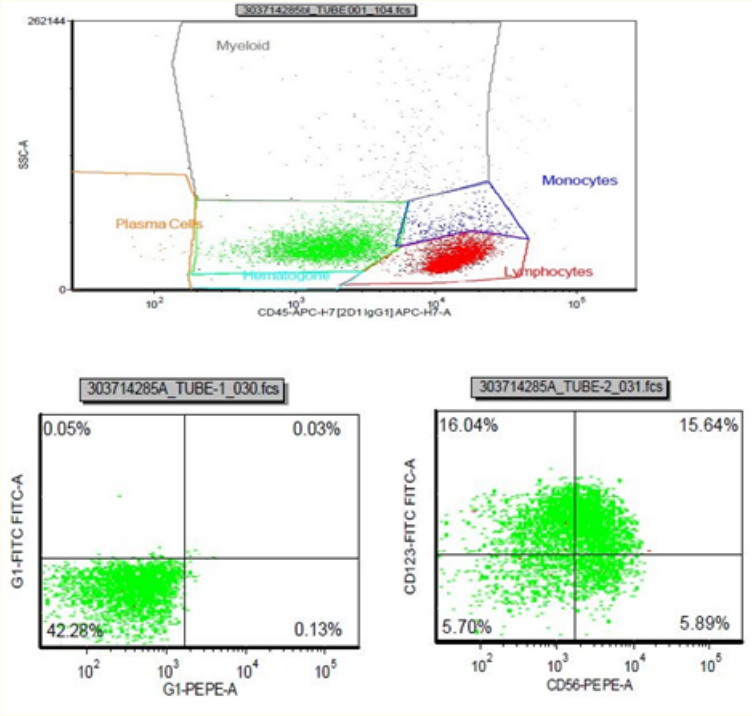

Figure 1: *Flow cytometry of peripheral blood by Genpath. The top graph shows the pattern of distribution of different types of white blood cells in the patient's blood according to the flow cytometry with the X-axis showing the Forward Scatter and the Y-axis showing the Side Scatter. The flow revealed numerous lymphocytes and blasts that are CD45 positive. The bottom 2 graphs show the pattern of immunoreactivity of these lymphocytes. The left graph clearly shows that the majority of the lymphocyte population are IgG1 negative but the right graph shows that at the same time at least 15.64% are positive for CD56 and CD123, 16.04% are only positive for CD123 and around 5.89% are CD56 positive only, while 5.70 are negative for both.*

The patient was then transferred to a tertiary center for further management. Computed tomography (CT) of the brain showed pansinusitis and bone marrow examination revealed infiltration by numerous neoplastic mononuclear cells that have fine nuclear chromatin, prominence of nucleoli and vacuolated cytoplasm and that tested positive for CD68 along with erythroid megakaryocytic hypoplasia. These cells accounted for 65% of the total cells. He was therefore started on AALL1231 trial protocol. AALL1231 is a phase III random-

ized trial investigating Bortezomib on a modified augmented Berlin-Frankfurt-Munster backbone chemotherapy protocol. The protocol contains the following medication Cyclophosphamide, Cytarabine, Daunorubicin Hydrochloride, Dexamethasone, Doxorubicin Hydrochloride, Etoposide, Hydrocortisone Sodium Succinate, Ifosfamide, Leucovorin Calcium, Mercaptopurine, Methotrexate, Pegaspargase, Thioguanine, Vincristine Sulfate and Radiation Therapy with Bortezomib. The patient has already completed the induction chemotherapy which he tolerated very well and has clinically showed complete response. During his first remission he showed signs of CNS involvement and thus was treated with cranial radiotherapy, which he completed successfully over a period of 11 days. Since then he has been in remission and continue to undergo the chemotherapy protocol. At the time of the submission of this article he continues to be on his 4th maintenance cycle of the AALL1231 protocol and tolerating the regimen.

Discussion

Cutaneous involvement is the main initial presentation in the majority of cases of BPDCN, but occasionally can present with leukemic symptoms alone [11]. Multiple organs such as the CNS, skeleton and GI tract are also often involved [11]. No standardized therapeutic approach has been established in BPDCN due to its rarity and recent recognition as a distinct clinicopathological entity [10]. Recent studies have reinforced the heterogeneous presentation of BPDCN and while some studies show longer mean survival of patients without cutaneous lesions, other studies seem to suggest that the increase in survival is due to the effect of acute lymphoblastic leukemia (ALL) chemotherapy which is generally not given in patients with cutaneous involvement. The consensus is that the disease progression in children is less clinically aggressive. While stem cell transplantation (SCT) has shown to be superior to ALL chemotherapy in reducing relapse and disease progression overall in adults, SCT has not be shown to have a superior impact in children. Recently, targeted IL3-receptor (CD123 is the alpha subunit) therapy by Diphtheria Toxin SL-401 has shown promising effects in patients in a small phase 1-2 study that have had high rates of complete remission [11-13].

This case report importance lies in showing a very atypical presentation of BPDCN in the pediatric population. Showing that children can be a potential victim of this disease, and that cutaneous manifestations are not necessary for its diagnosis. Hence this case serves as a reminder to pediatricians to keep a high index of suspicion of malignancy in children presenting with vague, chronic and nonspecific symptoms. It also adds to the limited number of observed BPDCN cases in children thus acting as a reference for physicians treating such patients.

Conclusion

BPDCN is diagnosed most commonly in older men and its presentation is varied, with cutaneous lesions being one the most common symptoms. This case demonstrates the possibility of children developing an atypical form of BPDCN, describes the diagnostic methods and successful treatment with AALL1231 protocol.

Statement of Ethics

The authors have no ethical conflicts to disclose. Informed Consent for participation was obtained.

Disclosure Statement

The authors have no conflicts of interest to declare.

Funding Sources

The authors have no financial support to disclose in the making of this article.

Authors' Contributions

Dr Ebrahim, Dr Almuqamam and Dr Alyosha Smolarski drafted the article, performed an in depth literature review and included critical revisions of pertinent academic and clinical content

Dr. Ebrahim, Dr Almuqamam and Dr Sedrak first diagnosed and treated the patient, provided clinical information and recommendations for the further clinical management of the patient, gave peer support and communication in the drafting of the report.

Dr Ying Xian Liu, Dr Smolarski, encountered the specimen taken from the patient, helped providing the pathological diagnosis in the interpretation of the peripheral blood smear. They also revised and gave final approval of the article.

Bibliography

1. Vardiman JW., *et al*. "The 2008 revision of the World Health Organization (WHO) classification of myeloid neoplasms and acute leukemia". *Blood* 114 (2009): 937-951.
2. Bueno C., *et al*. "Incidence and characteristics of CD4+/HLA DRhi dendritic cll malignancies". *Haematologica* 89 (2004): 58-69.
3. Lúcio P., *et al*. "CD123hi dendritic cell lymphoma: an unusual case of non-Hodgkin lymphoma". *Annals of Internal Medicine* 131.7 (1999): 549-550.
4. Chaperot L., *et al*. "Identification of a leukemic counterpart of the plasmacytoid dendritic cells". *Blood* 97.10 (2001): 3210-3217.
5. Petrella T., *et al*. "Agranular CD4+ CD56+ hematodermic neoplasm' (blastic NK-cell lymphoma) originates from a population of CD56+ precursor cells related to plasmacytoid monocytes". *The American Journal of Surgical Pathology* 26.7 (2002): 852-862.
6. Chaperot L., *et al*. "Leukemic plasmacytoid dendritic cells share phenotypic and functional features with their normal counterparts". *European Journal of Immunology* 34.2 (2004): 418-426.
7. Marafioti T., *et al*. "Novel markers of normal and neoplastic human plasmacytoid dendritic cells". *Blood* 2008 111(7): 3778-3792.
8. Dijkman R., *et al*. "Gene-expression profiling and array-based CGH classify CD4+CD56+ hematodermic neoplasm and cutaneous myelomonocytic leukemia as distinct disease entities". *Blood* 109.4 (2007): 1720-1727.
9. Pemmaraju N., *et al*. "Blastic plamacytoid dendritic cell neoplasm (BPDCN): a large single-center experience analysis of clinical and molecular characteristics and patient outcomes [ASH abstract 3746]". *Blood* 122.21 (2013).
10. Sakashita K., *et al*. "Usefulness of allogeneic hematopoietic stem cell transplantation in first complete remission for pediatric blastic plasmacytoid dendritic cell neoplasm with skin involvement: a case report and review of literature". *Journal of Pediatric Orthopaedics B* 60 (2013): E140-E142.
11. Rauh MJ., *et al*. "Blastic plasmacytoid dendritic cell neoplasm with leukemic presentation, lacking cutaneous involvement: Case series and literature review". *Leukemia Research* 36.1 (2012): 81-86.
12. Suzuki R., *et al*. "Blastic natural killer cell lymphoma/leukemia (CD56-positive blastic tumor): prognostication and categorization according to anatomic sites of involvement". *Cancer* 104.5 (2005): 1022-1031.
13. Kim MJ., *et al*. "Pediatric Blastic Plasmacytoid Dendritic Cell Neoplasm: A Systematic Literature Review". *Journal of Pediatric Hematology/Oncology* 39.7 (2017): 528.

Volume 9 Issue 1 January 2020