BLASTIC PLASMACYTOID DENDRITIC CELL NEOPLASM
- A RAPIDLY EVOLVING ENTITY. CASE REPORT

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BLASTIC PLASMACYTOID DENDRITIC CELL NEOPLASM. - A RAPIDLY EVOLVING ENTITY. CASE REPORT (Abstract): blastic plasmacytoid dendritic cell neoplasm (BPDCN), CD4+/CD56+ hematodermic neoplasm was formally known as blastic NK-cell lymphoma. It is in fact a form of acute myeloid leukemia notable for highly aggressive behavior with cutaneous, lymph node and bone marrow involvement. This entity is derived from plasmocytoid dendritic cells and has a predilection for extranodal sites, especially the skin. Elderly male patients are the most affected and the prognostic is poor. The first case was reported in 1994 and since then, single cases and a few small series have been published. This article presents the case of a previously healthy 56-years-old man, who presented himself to a skin eruption consisting in multiple, large dermal ulcerated tumors, located on the trunk and scalp. The lesions were painless and grew in size rapidly. Physical examination was normal except for the skin lesions. Histological examination of a biopsy specimen and immunohistochemical studies (positive for next markers: CD4, CD 45, CD56, CD68, Ki 67) revealed the rare diagnostic - blastic plasmacytoid dendritic cell neoplasm. Keywords: BLASTIC PLASMACYTOID DENDRITIC CELL NEOPLASM, CD4+/CD56+ HEMATO-DERMIC NEOPLASM, IMMUNOHISTO-CHEMISTRY, SKIN CANCER.

Blastic plasmacytoid dendritic cell neoplasm (BPDCN) it is a rare disease, more prevalent in Asia and Latin America than in Europe, with predominance in males (1). Over the past decades, the understanding the biology of lymphoid cells has improved and so has the knowledge of primary cutaneous lymphomas. The current World Health Organization/ European Organization of Research and Treatment of Cancer (WHO/EORTC) classifications are based on clinical, pathological, immunopathological, molecular and cytogenetic findings. The hematodermic neoplasm is defined as a separate entity, CD4+/CD56+ hematodermic neoplasm (2). NK are a variety of cytolytic cells capable of killing a different target cells such as bacteria/viruses, infected cells or tumor cells (3). CD4+/CD56+ hematodermic neoplasm is an extremely rare, very aggressive form of acute myeloid leukaemia. Due to its rapid fatal course, no clinical trial has been conducted and the therapeutical options are
based on small retrospective cohorts of patients (4). Generally this type of lymphoma has a skin-tropism, with clinical presentation in the form of papules or nodules that vary in appearance and affects elderly adults, although BPDCN without cutaneous lesions has been described (5).

We report the case of a 56 years-old man, with CD4+/CD56+ hematodermic neoplasm, with rapid degradation of clinical status and severe reaction to the chemotherapy.

**CASE REPORT**

A 56-years-old man was admitted in the Dermatology Department of “St. Spiridon” Universitary Emergency Clinical Hospital, Iași with the suspicion of *Mycosis fungoides*. The clinical examination revealed many cutaneous painless tumors on the trunk and scalp, 5/10 cm in size, ulcerated, which appeared in the last 2 months and which rapidly, grew in size. Bilateral inguinal lymph node enlargement (less than one cm in diameter) was noted in physical examination. The patient was at first assessed in another hospital center, for red macules and joint pain, and was treated with corticosteroids. The lesions reappeared after he interrupted the treatment while the tumors progressed rapidly and became necrotic (fig. 1).

![Fig. 1. Clinical aspects of dermal necrotizing tumors, with rapid progression](image)

Laboratory data revealed: white blood cell count was 2.97 x 10⁹ cells (neutrophils 9.8%, lymphocytes 63.6%, monocytes 19.5%, basophiles 5.4%), hemoglobin level 12.1 g/dl, albumin level 51.2%, C-reactive protein (CRP) level was 1.52 mg/dl, and lactate dehydrogenase (LDH) level, 602 IU/l.

Computerized tomography showed:
- right parieto-occipital lesions involving the brain (fig. 2);
- dermal tumors on the anterior surface of the chest; note the presence of air bubbles within the tumor volume (fig. 3);
- systemic involvement of lymph nodes, especially in the armpit and inguinal areas;
- many cutaneous, expansive nodules, disseminated on the hole scanned area, but most consistent and larger in chest area;

- heterogeneous gas bubbles structure, calcification and contrast enhancement in the solid component of the tumor.

A skin biopsy was performed and pathologic exam established the final diagnosis. The immunohistochemical examinations showed diffuse dermal infiltration with neoplastic cells, showing blastoid morphology and positive reaction for: CD4, CD45, CD56, CD68, and Ki 67, whereas CD3, CD30, CD5, CD8 and CD15 were negative.

Figure 4 - tumor cells with intense CD4+ staining (ob.x 20), figure 5 - tumor cells with intense CD56+ staining (ob.x 40) and figure 6 with skin biopsy showing diffuse dermal infiltration with tumor cells.

Based on pathological findings, the final diagnosis was cutaneous CD4+/CD56+ hematodermic neoplasm, with systemic involvement. The patient began chemotherapy using a regimen combining vinblastine, lomustine and etoposide. After 14 days of chemotherapy, low neutrophil counts were detected, the chemotherapy was stopped and filgastrim treatment was initiated. The second day, the patient was found unconscious, with no reaction to verbal stimulus, and he was transferred to the Intensive care Unit. His recovered was slow after supportive treatment, correction of acid-base and hydro-electrolytic imbalance, mannitol, methotrexate, calcium folinate, phenobarbital and carbamazepine. Two weeks later his neurological status returned to normal, there were no neurological focal signs or evidence for brain bleeding. He was transferred back to Hematology Clinic and the therapeutic program was reconsidered with methotrexate. The oncology committee decided to start radiotherapy but during these sessions the patient became highly agitated, bewildered and aggressive and is treated with anti-edematous, phenobarbital, valium and haloperidol. The skin lesions were diminished rapidly and the patient was discharged.
DISCUSSION

BPDCN is characterized by positive results for CD4, CD43, CD56, CD68 and CD123 and negative results for conventional myeloid and lymphoid T and B-cell markers with involvement of the skin in the most cases. Recently, these immunophenotypical characteristics lead to the new terminology, BPDCN, instead of the blastic NK-cell lymphoma.

It has been thought that these cells arise from NK progenitor cell, but most recent studies suggested that the origin is a lymphoid related plasmocytoid dendritic cell. This idea is sustained by the expression of the blood dendritic cell antigen 2 (BDCA2) and interleukin-3 receptor alpha subunit (CD123) (6, 7).

As in others forms of leukemia, the atypical presentation is very common, the median survival rate is low, in this case about 12-14 months, so recognizing the clinical, pathological and immunohistochemical features are very important for finding a promising treatment (8, 9).

The differential diagnosis must include nasal type NK-cell lymphomas, cutaneous T-cell lymphomas and CD 56+ acute myeloid leukemia.

Mycosis fungoides, our first suspicion, is distinguished from BPDCN by the presence of epidermal involvement and CD3+, CD56− immunophenotype.

CONCLUSIONS

In our opinion, at this moment there is no consensus for the optimal treatment of BPDCN. Myeloablative treatment with allogenic bone marrow transplantation, within the first episode of remission has

After only one month, the patient’s state worsens and deceases with multiple organ and system failure.
resulted in a better survival (10). Other promising options are immuno-therapy with interleukin-3 or CD123 antibody. In conclusion, dermatologists must become aware of this rare form of leukemia and more informed about the use of CD cell markers in the field of cutaneous oncology.

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