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*Case Report*

# Lymph blastic plasmacytoid dendritic cell neoplasm: a case report and review of literature

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**Abstract:** Objective: To investigate the feature, pathological diagnosis and differential diagnosis of blastic plasmacytoid dendritic cell neoplasm in the lymph node. Methods: The clinical and histological findings, immunophenotype, treatment and prognosis of one patient with blastic plasmacytoid dendritic cell neoplasm in the lymph node were evaluated with review of the relevant literature. Results: The male patient with age of 72 years presented as cutaneous lesions. Pathological examination detected that blastic plasmacytoid dendritic cell neoplasm affected the skin and bone marrow. Under microscopical observaion, the tumor consisted of diffuse blasts with small to medium size, scant cytoplasm, highly irregular nuclear contours, dispersed nuclear chromatin and faint indistinct nucleolus. Immunohistochemical characteristics of the tumors were positive for CD43, CD56 and CD123, and negative for ALK, CD30, CD117, MPO and CD4. Conclusion: Blastic plasmacytoid dendritic cell neoplasm is a rare and highly aggressive hematopoietic neoplasm. Besides the skin, lymph node can also be involved. The differential diagnosis is necessary from other hematopoietic and lymphoid tumors.

**Keywords:** Blastic plasmacytoid dendritic cell neoplasm, differential diagnosis, lymph node, treatment

## Case report

The male patient, aged 72 years, was admitted to our hospital due to thirst and frequent urination symptoms for over 10 years, which were significantly aggravated in the recent 3 months. He reported that these signs and symptoms were present without known causes, accompanied by excessive intake of diet and drinking. He did not receive any intervention or treatment since no other symptoms were noted. Approximately 3 months ago, the patient notified that the symptoms of thirst and frequent urination were aggravated and he was subsequently admitted to our medical institution. Blood glucose detection test revealed that the fasting blood glucose level was 9.9 mmol/L and the 2-h postprandial blood glucose level was detected up to 23 mmol/L. The status of blood glucose control was not explicit. His body weight was decreased by approximately 10 kg in the recent 6 months. He had a medical history of herpes zoster. Previously, he was physically healthy and had no medical history of allergy. Physical examination demonstrated no signs of yellow skin or sclera, no edema or rash was seen. Superficial lymph node enlargement was palpable. In addition, no nasal secretion, throat hyperaemia or tonsil enlargement was observed. Heart and lung function tests yielded normal results. Neither liver nor spleen enlargement was detected. No percussion pain was detected in the kidney. Lumbar puncture was performed for subsequent laboratory examination. Routine blood examination revealed that the quantity of white blood cells was decreased, lymphocytes accounted for the dominant proportion, the percentage of cells with abnormal morphology was approximately 3% and the percentage of mononuclear cells was significantly elevated with evident vacuolization in the cytoplasm. The mature red blood cells were observed in varying size. Red blood cells with nucleus were counted among 100 white blood cells. The quantity of cell platelet was relatively large. Peripheral immunotyping of these cells were carried out and demonstrated that CD56 and CD123 were abnormally expressed and

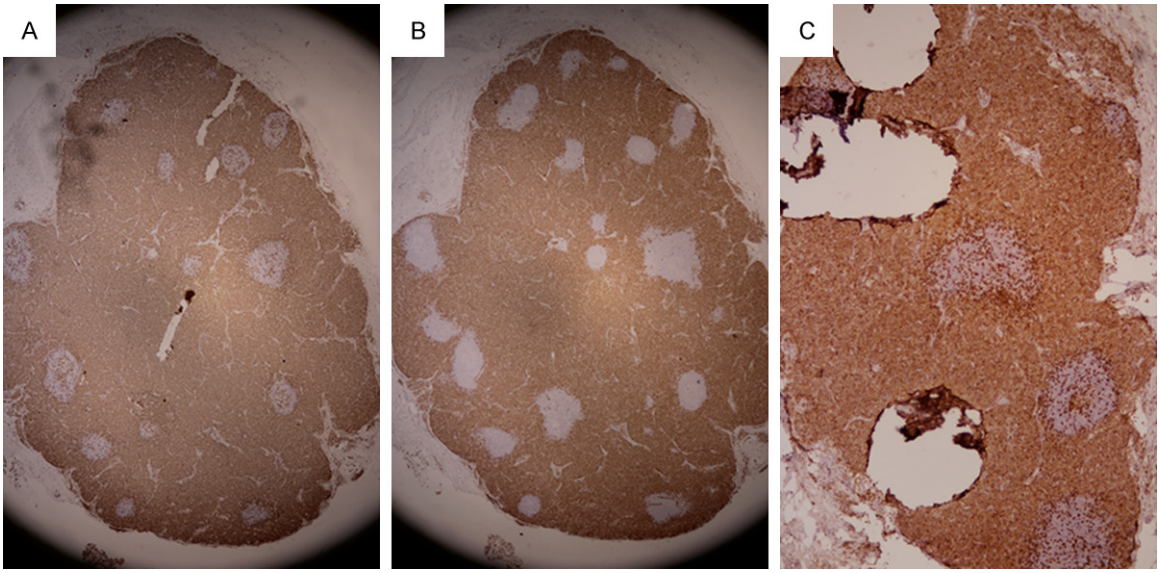


**Figure 1.** Immunohistochemical staining of CD34, CD123 and CD4.

cTDT was partially expressed. Based upon these findings, he was primarily diagnosed with blastic plasmacytoid dendritic cell neoplasm. Chest CT scan revealed that multiple lymph node calcification was detected in the bilateral lung and pulmonary mediastina.

Pathological examination demonstrated that the quantity of lymph node was subject to gross examination. Under microscopic observation, the lymph node structures were partially destroyed. The quantity of lymph follicle was declined and the intracellular space was enlarged. Even lymphocyte infiltration was equally observed. The cells were seen in moderate size, round, oval or irregular cellular nucleus. Staining examination detected the signs of cellular nucleus and slight nucleus division in partial cells. Immunohistochemical staining test was performed by the Department of Pathology, the Affiliated Hospital of Jining Medical Hospital. The cells were detected positive for CD43, CD56 and CD123, negative for ALK, CD30, CD117, MPO and CD4, as illustrated in **Figure 1**. KI-67 was highly expressed in a slight quantity of secondary lymph follicles. The proportion of positive cells within the lymph follicle region was approximately 20%. The lymph follicles were positive for CD20 and negative for CD3. However, the CD3 was positive surrounding the lymph follicles. Regular FDC network was noted in the CD21. The staining examination performed by Department of Pathology, Beijing Friendship Hospital, Capital Medical University revealed that CD4 and CD99 were positive within the lymph follicle region. In addition, CD43, CD123 and TDT were positive, whereas CD117, MPO, CD8 and CD10 were negative within the lymph follicles, as illustrated in **Figure 2**. KI-67 was highly expressed in few secondary lymph follicles. The proportion of positive cells within the lymph follicle region was approximately 20%. CD20 and PAX-5 were not expressed in the lymph follicles. CD3 and CD7 were equally negative in the lymph follicles but positive adjacent to the lymph follicles. The diagnosis of lymph node blastic plasmacytoid dendritic cell neoplasm was confirmed by subsequent bone marrow pathological examination. Written informed consent was obtained from the patient. The study procedures were approved by the ethics committee of Affiliated Hospital of Jining Medical College.

## Discussion

Blastic plasmacytoid dendritic cell neoplasm, first described in 1994, is a rare, aggressive, haematologic malignancy, which is originally derived from precursor of plasmacytoid dendritic cells [1]. Blastic plasmacytoid dendritic cell neoplasm probably presents with cutaneous lesions or as acute leukemia with systemic involvement since the beginning. In both cases, the course of blastic plasmacytoid dendritic cell neoplasm is aggressive and the median

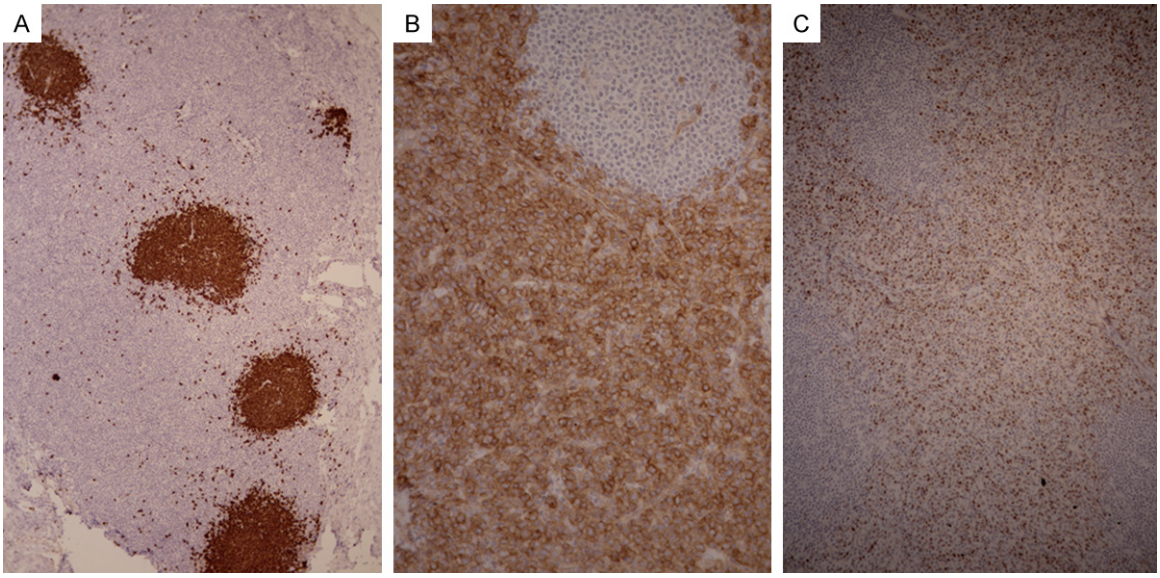


**Figure 2.** Immunohistochemical staining of CD20, CD43 and TDT.

survival of these patients is approximately 12 to 14 months.

In 2001 [2], blastic plasmacytoid dendritic cell neoplasm is classified into malignant tumors without definite origin or differentiation stages due to rapid progression and poor prognosis, which is defined as NK cell lymph tumor. Nevertheless, blastic plasmacytoid dendritic cell neoplasm is grouped with the acute myeloid leukemia-related precursor neoplasms in the 2008 World Health Organization classification [3]. It was previously postulated to originate from natural killer cells, T cells, or monocytes but is now proven to arise from the plasmacytoid dendritic cells.

The pathogenesis of blastic plasmacytoid dendritic cell neoplasm remains largely unknown, although it has frequent deletion of multiple tumor-suppressor genes including RB1, TP53, CDKN1B and CDKN2A. Blastic plasmacytoid dendritic cell neoplasm presents with phenotype characteristics of CD4 and CD56 positive lymphocytes with over 90% of cases expressing CD123, a marker for plasmacytoid dendritic cells. Blastic plasmacytoid dendritic cell neoplasm frequently occurs in the elderly patients with a median age of 61-67 years. It equally affects pediatric patients, a 15-year-old patient as previously reported [4]. A literature review of approximately 200 reports of blastic plasmacytoid dendritic cell neoplasm has found involvement limited to the skin in 50% of cases. Cutaneous involvement may present as solitary or multifocal nodules, patch-plaques, or ecchymoses. Blastic plasmacytoid dendritic cell neoplasm can be limited to the skin or the bone marrow, but several reports have shown that tumor infiltration can involve the lymph node. Previous study [5] reported one 21-year-old male patient suffered from lymphadenopathy in the right inguinal site as the initial symptoms for 4 months. Subsequently, lymph node biopsy was performed. Morphological observation and immunohistochemical staining were also conducted to make a diagnosis of blastic plasmacytoid dendritic cell neoplasm. The patient recurred 10 months after corresponding interventions, which were mainly involved with the skin and bone marrow. Blastic plasmacytoid dendritic cell neoplasm can be manifested with multiple initial symptoms, such as fatigue, asthenia, fever and weight loss, *etc*. Once recurs, it dominantly affects the skin. Previous studies [6, 7] have demonstrated that patients diagnosed with blastic plasmacytoid dendritic cell neoplasm limited to the skin have a higher survival rate compared with their counterparts without cutaneous involvement. In terms of the morphological features [8-10], blastic plasmacytoid dendritic cell neoplasm is manifested as diffusive parent cell infiltration with moderate size, round or oval cells, irregular cancer cell nucleus ranging from 1 to 3 nucleoli. Previous research [11] has reported an atypical case of

blastic plasmacytoid dendritic cell neoplasm, who was manifested as evident large nucleoli. The possibility of blastic plasmacytoid dendritic cell neoplasm cannot be excluded if the immunohistochemical results are qualified. Giemsa staining revealed that the cell cytoplasm was slight in blue color without granules. The sign of nuclear division is extremely rare even if blastic plasmacytoid dendritic cell neoplasm is highly malignant.

Blastic plasmacytoid dendritic cell neoplasm is manifested as malignant cutaneous tumors and masses. Under microscopic observation, it primarily invades into the corium layer rather than the cuticular layer. The pathological lesions can spread to the subcutaneous adipose layer. The pathological changes of lymph node are mainly manifested as diffuse infiltration within the lymph follicles in the pattern of leukemia infiltration. Bone marrow biopsy demonstrated a majority of patients presented with mild interstitial infiltration, and extensive interstitial infiltration was noted in few cases. Immunophenotype analysis should be performed for partial cases. The residual hematopoiefic tissues were manifested as abnormal development, especially the megakaryocytic cells.

The tumor cells primarily expressed CD4, CD43, CD123, CD56, CD45RO and TCL1 rather than B cells, T cells or myeloid cells. Previous studies [12] have demonstrated that the tumor cells express myeloid cell antigen CD13. Hence, the sign of positive CD13 cannot be utilized to exclude the diagnosis of blastic plasmacytoid dendritic cell neoplasm. The possibility of blastic plasmacytoid dendritic cell neoplasm cannot be fully excluded if the patient is negative for CD56 but positive for CD4, CD123 and TCL1. Recently, SPIB [13] has been proven to be a transcription factor of mature B cells, T cells and plasmacytoid dendritic cells. SPIB is over-expressed in patients diagnosed with blastic plasmacytoid dendritic cell neoplasm and those are lack of CD4, CD56, TCL1 and CD123. Consequently, SPIB can be utilized as a biomarker for the incidence of blastic plasmacytoid dendritic cell neoplasm. Certain blastic plasmacytoid dendritic cell neoplasm patients are negative for CD2, CD36, CD38, CD3, CD5, CD13, CD16, CD19, CD20, CD79a, LAT, MPO, CD34 and CD117 expression. Especially, negative MPO can be used to exclude the diagnosis of blastic plasmacytoid dendritic cell neoplasm. Granzyme B, TIA1 and perforin are detected negative in a majority of cases. Approximately one-third of blastic plasmacytoid dendritic cell neoplasm cases express TDT. The proportion of positive cells does not exceed 80%. The EBER is detected negative.

The challenge in this case is that the patient did not present with cutaneous symptom, whereas he mainly suffered from lymphadenopathy. Under microscopic observation, the degree of lymph node injury was not evident. Immunohistochemical staining examination detected the signs of follicular dendritic cells, primarily manifested as tumor cell infiltration in the follicular region, which was likely to miss the diagnosis. The following aspects should be emphasized to make a differential diagnosis of blastic plasmacytoid dendritic cell neoplasm. First, the lymph node structure was destroyed, a slight quantity of lymph follicles was observed, the lymph sinus was evident with disperse activated immune parent cells.

Immunohistochemical staining examination demonstrated a slight quantity of CD20-positive cells in the follicular region, whereas the amount of CD3-positive cells was large. The large cells positive for CD30 were noted within the follicular region with different positive intensity. The quantity of CD5/CD2/CD7-positive cells was equivalent to that of CD3. No loss of T-cell antigen was noted. Positive EBER was also detected. Moreover, blastic plasmacytoid dendritic cell neoplasm should be differentially diagnosed from invasive NK cell leukemia. The signs of necrosis and blood vessel infiltration can be observed. Immunohistochemical staining reveals positive CD2, CD56, cytoplasm CD3, granzyme B and EBER.

To conclude, blastic plasmacytoid dendritic cell neoplasm is an extremely rare and highly-aggressive hematopoietic neoplasm. In addition to the skin involvement, lymph node can also be invaded. It is of great significance to implement differential diagnosis from blastic plasmacytoid dendritic cell neoplasm to alternative types hematopoietic and lymphoid tumors.

**Disclosure of conflict of interest**

None.

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