Spontaneous Regression of Cutaneous Blastic Plasmacytoid Dendritic Cell Neoplasm Followed by Acute Monocytic Leukemia Evolving from Myelodysplastic Syndrome

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Abstract

Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare and aggressive hematologic malignancy arising from plasmacytoid dendritic cell precursors. BPDCN typically manifests in the skin, but it can also evolve into a leukemic form or be complicated by acute myeloid leukemia, some cases with a preceding myelodysplastic syndrome (MDS). We herein report the first case of complete spontaneous regression of cutaneous BPDCN followed by acute monocytic leukemia evolving from MDS. This is also the first reported case of gastric BPDCN invasion.

Key words: blastic plasmacytoid dendritic cell neoplasm, CD4⁺/CD56⁺ hematodermic neoplasm, blastic NK cell lymphoma, spontaneous regression, gastric invasion


Introduction

Blastic plasmacytoid dendritic cell neoplasm (BPDCN), previously known as blastic natural killer (NK) cell lymphoma or CD4⁺/CD56⁺ hematodermic neoplasm, is a rare and highly aggressive hematologic malignancy (1). BPDCN typically manifests in the skin, but it can also evolve into a leukemic form or be complicated by myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML) (1-3). The treatment outcome is grim with a median survival of 12-14 months (1, 2). Spontaneous regressions have been reported in various hematological malignancies, but this is the first reported case concerning BPDCN. This is also the first report of BPDCN presenting with gastric invasion.

Case Report

In late December 2011, a 67-year-old man presented with multiple erythematous nodules on the trunk and limbs (Fig. 1A). A skin biopsy revealed medium-sized blastoid cells infiltrating the dermis and subcutis but sparing the epidermis (Fig. 2A, B). The immunohistochemistry findings showed tumor cells positive for CD4 (Fig. 2C), CD43, CD56 (Fig. 2D), CD123 (Fig. 2E), CD303 (Fig. 2F), and B-cell lymphoma 2 (Bcl-2) and negative for CD3, CD5, CD8, CD10, CD20, CD34, CD68, CD79a, CD117, Terminal deoxynucleotidyl transferase (TdT), T-cell leukemia 1 (TCL-1), Epstein-Barr virus-encoded RNA 1 (EBER1), and myeloperoxidase. The MIB-1 index was 80%. Based on these findings, a diagnosis of BPDCN was made. Upper gastrointestinal (GI) endoscopy revealed two polypoid lesions in the gastric corpus (Fig. 1B, C), and the biopsy again revealed medium-sized blastoid cells infiltrating the lamina propria which showed the same marker expression pattern as the cutaneous BPDCN cells, although CD5 and CD117 markers were not analyzed. Therefore, the gastric polypoid lesions were also pathologically determined to be BPDCN. Whole body CT scans did not detect any other sites of BPDCN involvement. Laboratory tests revealed a white blood cell (WBC) count of 6.0×10⁹/L with 4.0% bands, 57.0% neutrophils, 16.0% lymphocytes, 20.0%
monocytes, and 3.0% metamyelocytes. The patient’s hemoglobin level was 13.0 g/dL and his platelet count was 135×10^9/L. A bone marrow (BM) evaluation revealed a blast count of 13.2% along with dysplastic features, such as micromegakaryocytes and nuclear hypolobation of granulocytes, suggesting concomitant MDS. The BM blasts were morphologically atypical. We initially planned chemotherapy, however, the skin lesions spontaneously regressed and complete diminishment was seen by the end of February 2012. Careful outpatient observation was continued, but our patient was hospitalized in late March 2012 due to sudden hematemesis. Upper GI endoscopy showed multiple hemorrhagic ulcers in the gastric corpus, but a biopsy was not conducted due to the patient’s poor general condition. The patient’s WBC count was 44.4×10^9/L of which 67.0% consisted of monocytic cells. His hemoglobin, platelet count, LDH, and serum lysozyme levels were 8.8 g/dL, 59×10^9/L, 3,709 U/L, and 1,664 μg/mL, respectively. The BM was hypocellular, with monoblasts, promonocytes, and monocytes consisting over 80% of non-erythroid cells, which showed intense, non-specific esterase activity and negativity for myeloperoxidase. Monoblasts accounted for approximately 50% of the monocytic lineage cells in the BM (Fig. 2G). The patient’s leukemic cells were positive for CD11b, CD33, CD36, CD56, CD68, CD123 and Human Leukocyte Antigen DR (HLA-DR) and negative for CD3 (cytoplasmic), CD4, CD5, CD7, CD8, CD16, CD20, CD34, CD41, CD117, CD303, and TdT. A chromosome analysis revealed an abnormal karyotype of 47, XY, +8 [1] / 47, idem, i(8)(q10) [1] / 48, idem, +21 [1] / 49, XY, +20, +21, +21 [1] / 51, XY, +4, +7, +9, +10, +mar [1] / 46, XY [15]. Therefore, the evolution of MDS to acute monocytic leukemia with morphology resembling AML-M5b was confirmed. The patient achieved complete remission with one course of induction chemotherapy consisting of idarubicin hydrochloride (12 mg/m^2/day) on days 1-3 and cytarabine (100 mg/m^2/day) on days 1-7. Follow-up upper GI endoscopy on day 44 of chemotherapy revealed only mild gastritis, and the formerly found gastric ulcers had disappeared. Consolidation chemotherapy was suggested, but the patient opted for palliative care at another hospital, and he was discharged. The patient’s clinical course is shown in Fig. 3.

**Discussion**

BPDCN was previously thought to be of NK-cell lineage, but there is now general agreement that it is derived from plasmacytoid dendritic cell (pDC) precursors (1-3). BPDCN is typically positive for CD4, CD56, CD123, CD303, and TCL-1 and negative for all other lineage-specific markers. The neoplastic cells are also typically positive for CD43 and Bcl-2 (1, 3). TCL-1 negativity in neoplastic cells as seen in our case has been confirmed in about 10% of BPDCN cases, and this finding does not contradict the diagnosis (3). BPDCN itself often progresses to a leukemic phase, but about 10-20% of cases are known to be complicated by AML (1-3). Acute monocytic leukemia was distinguishable from a leukemic phase BPDCN in our case because BPDCN does not show non-specific esterase activity, and discrepancies in the surface antigen expression of CD4, CD68, and CD303 were found. Neoplastic cells positive for CD123 were found in both BPDCN and acute monocytic leukemia.
Figure 2. The patient’s skin biopsy. Hematoxylin and Eosin staining showed medium-sized blastoid cells with single to multiple nucleoli diffusely infiltrating the dermis and subcutis but sparing the epidermis (A, B). A distinct grenz zone can be seen (A). Tumor cells were positive for CD4 (C), CD56 (D), CD123 (E), and CD303 (F). The bone marrow squash preparation. May-Giemsa staining showed a mixture of monoblasts, promonocytes, and monocytes (G). Original magnifications were 200× (A-F) and 1,000× (G).

in our case, but CD123 is not a definitive marker because CD123 positive neoplastic cells can also be found in some cases of AML (4). The underlying mechanisms of AML complication in BPDCN have not yet been fully elucidated, but it has been speculated that the developmental plasticity of pDC precursors may potentiate the rise of both malignancies (2, 3). To investigate whether concomitant BPDCN and AML originate from the same clone, common genetic mutations should be investigated through methods such as a deep sequencing analysis in future cases.

Although a rare event, spontaneous regressions of hematological malignancies have been previously reported in acute myeloid and lymphoblastic leukemia, chronic myelogenous leukemia, chronic lymphocytic leukemia, Hodgkin and non-Hodgkin lymphoma, and plasma cell dyscrasias (5-10). Xie et al. recently reported BPDCN following spontaneous remission of AML-M5 (11), but this is the first case of spontaneous regression of BPDCN. The clinical
The patient’s clinical course.

The course of the current case does not represent typical BPDCN, and it cannot be denied that we are looking at a yet unknown entity or phenomenon. Further studies involving patients with a similar disease progression are necessary. In our patient, the gastric ulcers found on admission may have been side effects of loxoprofen sodium which was prescribed at the time, but other etiologic possibilities, such as BPDCN dissemination and invasion of acute monocytic leukemia, cannot be ruled out. Therefore, it remains unknown whether the gastric polypoid BPDCN lesions found at disease onset spontaneously regressed along with the cutaneous lesions or if they progressed to ulcerations and were ultimately eradicated with chemotherapy. In our patient, the gastric ulcers found on admission may have been side effects of loxoprofen sodium which was prescribed at the time, but other etiologic possibilities, such as BPDCN dissemination and invasion of acute monocytic leukemia, cannot be ruled out. Therefore, it remains unknown whether the gastric polypoid BPDCN lesions found at disease onset spontaneously regressed along with the cutaneous lesions or if they progressed to ulcerations and were ultimately eradicated with chemotherapy. BPDCN is known to involve the skin, lymph nodes, BM, peripheral blood, and less frequently the central nervous system and oral cavity, but this is the first report of BPDCN presenting with gastric lesions (1-4, 12).

In conclusion, we herein reported the first case of the complete spontaneous regression of cutaneous BPDCN followed by acute monocytic leukemia evolving from MDS. Furthermore, BPDCN may involve the GI tract more often than previously appreciated, and GI endoscopy should be considered as part of the routine examination in future cases.

The authors state that they have no Conflict of Interest (COI).

References