

A new palliative treatment for blastic plasmacytoid dendritic cell neoplasm: a case report and review of the literature

Journal of International Medical Research

2019, Vol. 47(10) 5281–5288

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DOI: 10.1177/0300060519871860

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Abstract

Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare haematological malignancy that derives from plasmacytoid dendritic cells. The cancer is characterized by aggressive development and dismal prognosis, and due to limited prospective study, there is currently no established standard treatment. In this study, the case of a 77-year old female patient with BPDCN, who presented with a cutaneous lesion on the right of her face, is described. The lesion developed into a serious ulcer due to rapid disease progress, thus, a surgical excision was performed. As the patient refused to receive radiotherapy or haematopoietic stem cell transplantation following surgery, a new palliative combination chemotherapy was administered, comprising gemcitabine, nedaplatin and bleomycin. The therapy gave satisfactory results in terms of short-term treatment response and was well-tolerated. Published literature regarding BPDCN is also reviewed.

Keywords

Blastic plasmacytoid dendritic cell neoplasm, chemotherapy, CD4, CD56, CD123

Date received: 31 January 2019; accepted: 2 August 2019

Introduction

Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare and aggressive disease, accounting for approximately 0.27% of haematological malignancies.¹ As BPDCN is an extremely rare malignancy, a standard therapy regimen has not been

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established, and due to the aggressive progress and relatively short median survival from diagnosis in patients with BPDCN, optimal treatment has not yet been defined.² Herein, the case of an elderly female patient with BPDCN and a history of various diseases is described, in which the patient was treated with a new palliative chemotherapy regimen consisting of gemcitabine, nedaplatin and bleomycin. In addition, the published literature regarding BPDCN is reviewed.

Case report

A solitary soft tissue mass was reported to have appeared on the right side of the face of a 77-year-old female patient in October 2010. The mass was violet with a 3-cm diameter. As this lesion was painless, the patient did not go to hospital when she first noticed it.

In December 2012, the patient was referred to a local hospital in China, and a skin biopsy was performed in the outpatient clinic. The results revealed a diffuse infiltrate of medium-sized blast cells in the dermis, and the patient was diagnosed

with BPDCN. The patient also had a history of type 2 diabetes mellitus, stage 3 hypertension, hyperlipidaemia, coronary heart disease, cerebral infarction, glaucoma, lens extracapsular extraction and posterior chamber intraocular lens implantation, Sjogren's syndrome, rheumatoid arthritis, left axillary vein and brachial vein thrombosis, and she was receiving the following ongoing medications: heparin, felodipine, nateglinide and estazolam. Conventional Chinese medicine therapy for the BPDCN was then initiated, comprising the combined use of ginseng and Chinese Yew. The patient did not improve following treatment however, and the soft tissue mass grew progressively larger (Figure 1a).

In January 2013, the patient was admitted to the Department of Oncology, Fourth Medical Centre of PLA General Hospital, Beijing, China. Upon admission, a skin examination showed a skin nodule of 3 cm on the right of the face, with mild superficial ulceration. Laboratory blood results were unremarkable, (i.e., they were within normal ranges except for low lymphocyte [0.7%] and eosinophil [0%] counts).

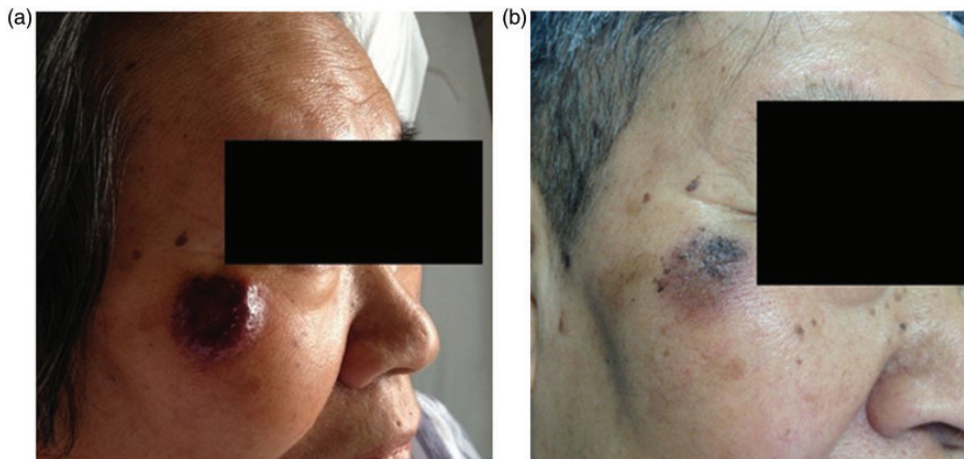


Figure 1. Images showing: (a) a soft tissue mass on the right side of the face in a patient diagnosed with blastic plasmacytoid dendritic cell neoplasm; and (b) the decreased lesion following combination chemotherapy using gemcitabine, nedaplatin and bleomycin treatment.

The patient then received a new palliative combination chemotherapy regimen, comprising 1.2 g gemcitabine (intravenous [i.v.]) on treatment day 1 and day 8; 70 mg nedaplatin (i.v.) on treatment day 1; and 15 mg bleomycin (i.v.) on treatment day 2. In February 2013, the patient received the second cycle of this chemotherapy regimen (delivered as before) and responded well in terms of an obvious decrease of the lesion on the right side of the face (Figure 1b).

One month later, however, the mass started to ulcerate. Because the ulceration was deemed incurable (due to lack of response to chemotherapy and the presence of type 2 diabetes), the mass was surgically removed (Figure 2a) and a biopsy was sent for histopathological assessment. Histopathology results confirmed that the dermis was infiltrated by blast cells with irregular nuclei and one to several small nucleoli, without epidermal involvement (Figure 3). Immunophenotyping revealed that the cells were positive for cluster of differentiation (CD)-4, CD56, CD123, and CD43, and the proportion of Ki-67 positive cells was 30–40% (Figure 4). Following

surgery, the patient and her family refused to allow her to receive radiotherapy, and the patient chose to continue with chemotherapy only.

The patient received a further two courses of chemotherapy in April and June 2013, with a good treatment response (the skin recovered well following surgery and laboratory blood results remained unremarkable) and the treatment was well-tolerated. The patient then refused to receive further treatment and self-discharged from hospital.

In December 2013, due to the appearance of a new tumour mass in the margin of the surgical area (Figure 2b), the patient agreed to continue chemotherapy, and received one cycle of the chemotherapy regimen described above. This was the last treatment this patient received. In April 2014, a soft violet tissue mass occurred in the patient's left upper arm, (Figure 5), but the patient refused any further treatment. There is no further available information regarding this patient.

The present study was approved by the Ethics Committee of the Fourth Medical

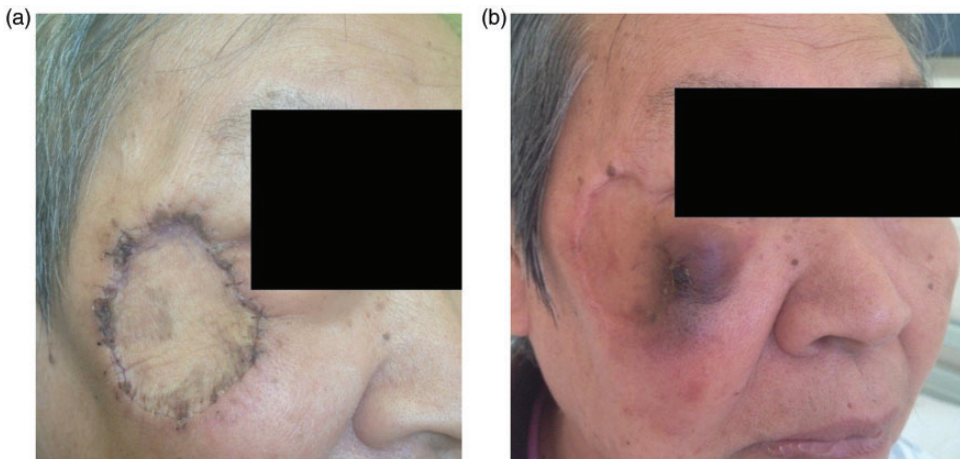


Figure 2. Images showing: (a) result of the surgical excision of an ulcerated soft tissue mass on the right side of the face in a patient diagnosed with blastic plasmacytoid dendritic cell neoplasm; and (b) the new tumour mass that appeared in the margin of the surgical area at 9 months following surgery.

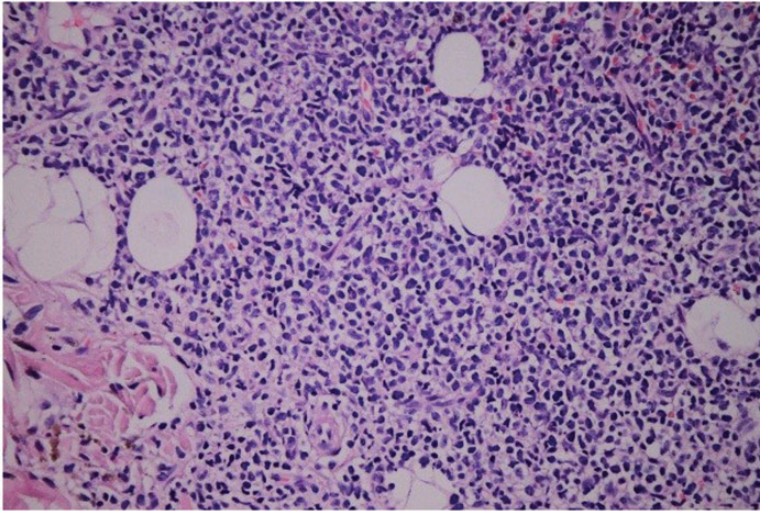


Figure 3. Photomicrograph from pathological examination of the soft tissue mass, showing haematoxylin and eosin-stained tissue section. The dermis was infiltrated by blast cells with irregular nuclei and one to several small nucleoli, without epidermal involvement (original magnification, $\times 200$).

Centre of PLA General Hospital and written informed consent to publish this case report was provided by the patient.

Discussion

The first case of BPDCN was initially reported by Adachi et al.³ in 1994, and was characterized by CD4 and CD56 positive cells found in skin lesions, with rapid involvement in the bone marrow and central nervous system. Identified as a malignancy arising from plasmacytoid dendritic cells,⁴ BPDCN was included in the same classification as haematological disease by the World Health Organization (WHO) in their 2008 publication.⁵ BPDCN was later classified as a distinct entity among myeloid neoplasms in the 2016 revision and 2017 WHO classification of lymphoid and haematopoietic tumours.^{6,7} BPDCN mainly occurs in elderly patients, with a male to female ratio of 3:1 and an overall survival time ranging between 9 and 13 months.^{2,4} In most patients, the primary manifestations of BPDCN are skin nodules, bruise-like infiltrates or plaques,

that rapidly develop to the involvement of bone marrow, peripheral blood, central nervous system and other systems. Approximately 23% of patients with BPDCN do not have symptoms involving the skin when diagnosed.⁸

Diagnosis of BPDCN is based on immunohistochemistry analysis and flow cytometry, as BPDCN cells can exhibit CD4, CD56 and other biomarkers that are specific for plasmacytoid dendritic cells, such as CD123, CD303 and T-cell lymphoma-1.⁹ Chromosomal losses and deletions in 5q, 12p13, 13q21, 6q23-ter, and 9 have also been observed in BPDCN cells.^{10,11} Inactivation of the tumour suppressors retinoblastoma-associated protein (RB1), tumour protein 53 (TP53) and cyclin-dependent kinase inhibitor 2A (CDKN2A), and activation of the oncogenes NRAS proto-oncogene, GTPase (NRAS), and KRAS proto-oncogene, GTPase (KRAS) has also been observed in many patients with BPDCN.¹²

The primary therapy that most patients with BPDCN receive is an acute

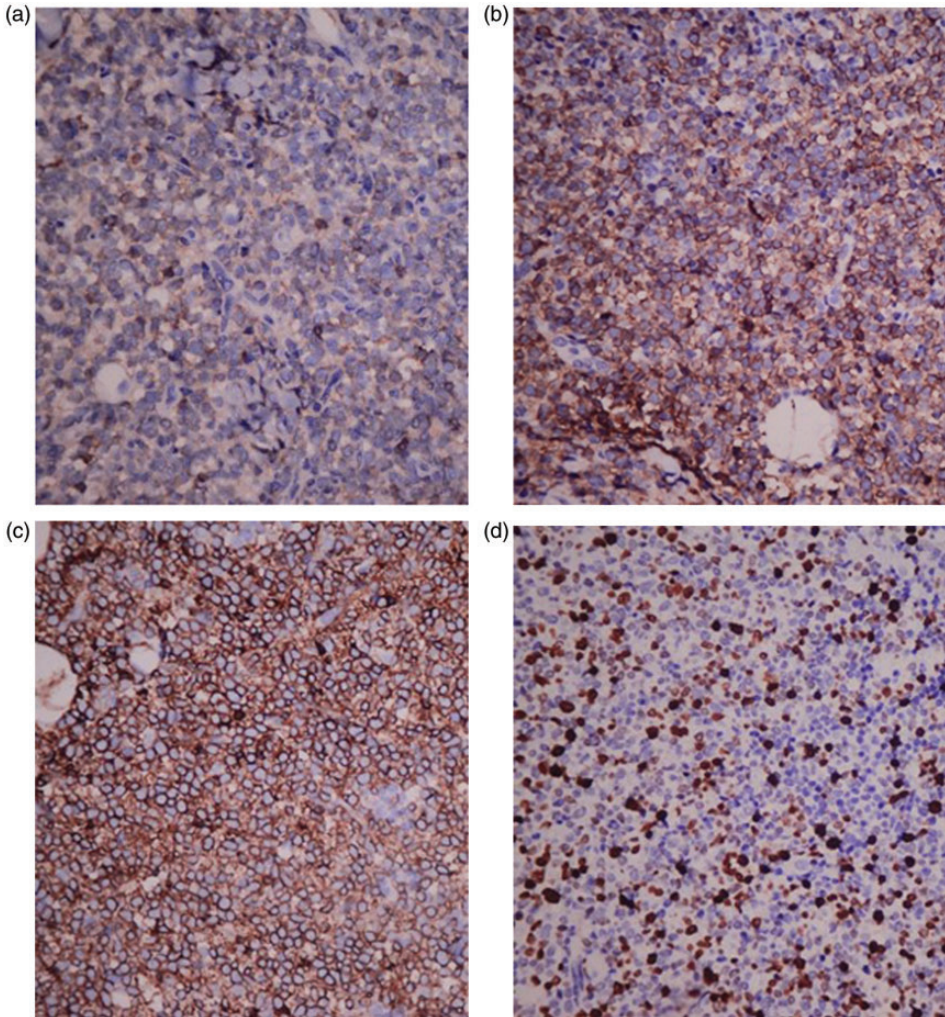


Figure 4. Photomicrographs showing immunophenotypic results revealing that the tumour cells were positive for (a) cluster of differentiation (CD)-4; (b) CD56; (c) CD123; and (d) Ki-67 (original magnification, $\times 200$).

lymphocytic leukaemia (ALL)-based or acute myeloid leukaemia (AML)-based chemotherapy regimen, after which, patients tend to rapidly achieve complete remission. Without any other subsequent therapies, however, most patients will relapse within one year with rapid disease progression.^{2,9} A previous study showed ALL-type therapy to possess a significant advantage in terms

of overall survival and complete remission, compared with AML-type therapy.⁸

Though radiotherapy alone is ineffective in treating patients with BPDCN,¹³ it can enhance the effects of chemotherapy, particularly in patients with skin located lesions.¹⁴ In a recent case report, two patients with skin located BPDCN who received combination treatment of an



Figure 5. Image showing a soft violet tissue mass that occurred in the left upper arm of the patient with blastic plasmacytoid dendritic cell neoplasm.

ALL-like (hyper-CVAD [cyclophosphamide, vincristine, doxorubicin, dexamethasone], A1B) chemotherapy protocol and consolidative localized radiotherapy without stem cell transplantation or other therapy, were reported to have achieved complete remission that was sustained for up to 9 years.¹⁵

To extend the overall survival of patients with BPDCN, many have been given hematopoietic stem cell transplantation after the first complete remission. In a retrospective study of patients with BPDCN, treatment with allo-haematopoietic cell transplantation or auto-haematopoietic cell transplantation during the first complete remission was shown to significantly prolong progress free survival and overall survival times.¹⁶

With the growing trend of targeted treatment, therapy targeting BPDCN has received much attention and is showing promising results. For example, a recombinant protein called SL-401, which links interleukin (IL)-3 to a truncated diphtheria toxin, resulting in diphtheria toxin that is targeted to CD123, has gained much interest as a targeted agent for treating

BPDCN.¹⁷ This targeted agent has been through phase I/II clinical trials and a phase II clinical trial in 45 patients with BPDCN is currently ongoing.^{18–20} According to a report of three cases, the effect of this treatment varies in different patients and some may exhibit serious adverse events.²¹

Many other new therapy modalities are also being investigated. For instance, stimulation of liver X receptors (LXRs) has been shown to reduce BPDCN spleen and bone marrow infiltrations;²² reduced intensity conditioning (RIC) regimens have been used to treat elderly and paediatric patients with BPDCN to decrease treatment-related toxicities;²³ early detection strategies may be applied in patients with a previous history of haematologic malignancy in order to provide early treatment before it transforms into BPDCN;²⁴ and venetoclax, an orally bioavailable inhibitor of BCL-2, has been used to treat patients with BPDCN.²⁵

In the present case, a new palliative treatment that comprised a combination of gemcitabine, nedaplatin and bleomycin was administered to an elderly patient with BPDCN who had a history of other diseases. The regimen was well-tolerated and a relatively long complete remission was achieved. Therefore, the present authors believe that this palliative chemotherapy regimen may be a treatment option for elderly patients in the same condition.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

Funding

This research was funded by the National Natural Science Foundation of China, Grant No: 81572953.

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