CASE REPORT

Blastic plasmacytoid dendritic cell neoplasm: a rare case of gingival lesion with leukaemic presentation

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SUMMARY

Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare haematological malignancy with an aggressive clinical course. It has been recognised as a distinct entity in the WHO 2008 classification of haematolymphoid neoplasm. This disease usually presents with cutaneous involvement as the first manifestation, with subsequent or simultaneous spread to bone marrow and peripheral blood with leukaemic dissemination. Gingival lesion as the first manifestation, in the absence of a cutaneous lesion, is an uncommon presentation of this rare disease. We report a case of an elderly woman, aged 84 years, who presented with a lump on the mandibular gingiva and ipsilateral otalgia without any cutaneous lesion and associated with an highly aggressive and rapid leukaemia. This case is an addition to the handful of those cases of BPDCN which presents without cutaneous involvement, but it is exceedingly rare for clinical features that make it a unique case in the literature.

BACKGROUND

Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare haematological malignancy with an aggressive clinical course. It manifests in two clinically and pathologically distinct variants. The first variant is represented by nodular aggregates of clonally expanded plasmacytoid dendritic cells found in lymph nodes, skin and bone marrow. This entity is rare and affects predominantly males. Almost invariably, it is associated with a myeloid neoplasm such as chronic myelomonocytic leukaemia or other myeloid proliferations with monocytic differentiation.

A second variant of plasmacytoid dendritic cell tumour has been recently reported and described as ‘blastic plasmacytoid dendritic cell neoplasm’. In this tumour, most patients have distinctive skin lesions and simultaneous involvement of bone marrow, and proliferating cells derive from plasmacytoid dendritic cells precursors.¹

The diagnosis of this form can be easily accomplished by immunohistochemistry, using a panel of plasmacytoid dendritic cell markers. The clinical course of BPDCN is characterised by a rapid progression to systemic disease via haematogenous dissemination. An oral manifestation as the first manifestation, in the absence of a skin lesion, is an uncommon presentation of this rare disease.

CASE PRESENTATION

An elderly woman, aged 84 years, was referred to the Emergency Department of Siena Hospital for pain on the right side of her face, lump on the right mandibular gingiva and ipsilateral otalgia. Her medical history indicated good health and absence of medications.

The first examination of oral cavity showed a hard, painful, reddish-pink, gingival swelling on the lower right mandibular gingiva which started about a week earlier after her dentist performed a second lower right premolar extraction (figure 1A).

Ear–nose–throat (ENT) examination was otherwise normal except for right laterocervical lymphadenopathy on palpation of the neck but on endoscopic evaluation, no irregularities or pathological processes in the nasal, pharyngeal and laryngeal regions were detected. Tonal audiometric examination showed a moderate, symmetrical and bilateral hearing loss typical for the elderly (presbycusis). The ENT specialist referred the patient for dental examination. Urgent orthopantomography showed dental avulsion of tooth 45 with radio-lucent area in the apex of the extracted element. The remaining mandibular bone appeared normal. The dentist decided to perform an incisional biopsy under local anaesthesia.

Ten days after the biopsy, the patient came back to the emergency department with intractable right mandibular pain, dysphagia and low-grade fever. Oral examination showed an important increase in the volume of the lesion, causing otalgia in the right ear and hypoesthesia of the ipsilateral lip and asymmetry of the face (figure 1B). Physical examination revealed pallor and dehydration. There was more palpable cervical lymphadenopathy, especially on the right side, in the absence of skin lesions.

Figure 1 Macroscopic features of the gingival swelling ostensibly mimicked common oral lesions. (A) Intraoral photographs of a painful, hard, reddish-pink, gingival swelling on the lower right mandibular gingiva before undergoing an excisional biopsy. (B) Ten days after biopsy, there was an important increase in the volume of the lesion, causing otalgia in the right ear and hypoesthesia of the ipsilateral lip.

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Figure 2 Histological and immunohistochemical features of gingival blastic plasmacytoid dendritic cell neoplasm. (A) H&E stain at x50 magnification showing a diffuse, monotonous neoplastic infiltrate. (B) H&E at x400 magnification showing small-to-medium size neoplastic cells exhibiting an irregular nuclear profile, one or more small nucleoli, mitoses (thick arrow) and apoptoses (thin arrow). (C–F) Immunohistochemistry chromogen diaminobenzidine stains at x400 magnification showing positive (brown) immunostaining of neoplastic cells for CD4 (C), CD68 (D), CD56 (E) and CD123 (F). (G) Immunohistochemistry chromogen diaminobenzidine stains at x100 magnification showing a high rate of tumour cell nuclei expressing the proliferative antigen Ki-67; the arrows indicate the normal proliferative compartment of the epithelial basal layer.

A complete blood count (CBC) showed white cell count of $11.4 \times 10^9/L$ (normal: $4\text{--}10 \times 10^9/L$); red cell count of $3.92 \times 10^{12}/L$ (normal: $4\text{--}5.5 \times 10^{12}/L$); haemoglobin 10.7 g/dL; platelets $74 \times 10^9/L$ (normal: $150\text{--}400 \times 10^9/L$). Examination of peripheral blood by flow cytometry revealed decreased platelets and a leucocytosis with 75% abnormal blasts stained positive for CD45, CD56, CD4, CD123 and CD43.

It was necessary to proceed with nasogastric tube placement to feed the patient.

At histology, the neoplasm was hypercellular and was constituted of a monomorphous, diffuse infiltrate of small-to-medium size cells, with a brisk mitotic rate and apoptosis. The neoplastic cells largely spared the epithelium, although in some areas epitheliotropism was noticed.

By immunohistochemistry, the neoplastic cells coexpressed CD4, CD45, CD68, CD56 and CD123 and were negative for CD15, CD2, CD3, CD8, CD34, CD117, TdT, myeloperoxidase and WT1. The proliferative index (Ki-67, clone 30–9, Ventana) was high, approximately 60%–70% (figure 2A–G).

An extensive infectious disease workup was repeated with several additional studies including cytomegalovirus, Epstein-Barr virus, HIV, Hepatitis B virus and Hepatitis C virus, all of which were negative. Bone marrow biopsy showed a hypercellular marrow, with CD4+, CD45+, CD56+, CD123+, Human Leukocyte Antigen-antigen D Related (HLA-DR)+ small blast cells accounting for 90% of cellularity. No other T and B cell lineage were observed. Based on clinical and laboratory findings, a final diagnosis of BPDCN was put forth. The most common presentation of BPDCN involves cutaneous manifestations, but in our patient, the physical examination performed at recovery by the dermatologist did not reveal plaques, nodules or other skin lesions.

CT scan of the head and neck revealed the presence of extensive neoplastic lesion of the horizontal hemimandible with deep bone erosion, pathological nodule at the base of the tongue and pathological lymph node in station 1b.

Thoracoabdominopelvic CT scan revealed mild splenomegaly, manifestations of peritoneal carcinomatosis in the left paracolic gutter and dimensional increase in bilateral inguinal lymph nodes (figure 3A–C).

During hospitalisation, the patient showed a rapid deterioration of her general condition: the CBC revealed worsening leucocytosis ($>70\,000/mm^3$), anaemia ($<3 \times 10^6/mm^3$), thrombocytopenia ($<30\,000/mm^3$). At the same time, the macular papular rash, the enlargement of the cervical mass and the deterioration of the mental state appeared.

The patient was initially managed with transfusional support, until a mutual decision was reached for transfer to palliative care.

OUTCOME AND FOLLOW-UP

Due to the impaired clinical conditions, only supportive care was provided. The patient succumbed to disease 7 days later from the diagnosis. Unfortunately, our patient died very early without giving us the opportunity to try a therapeutic approach.

DISCUSSION

BPDCN is a rare and aggressive haematodermic neoplasm derived from the precursor of plasmacytoid dendritic cells. It has been categorised into the group of myeloid malignancies in the 2008 WHO classification of tumours of haematopoietic and lymphoid tissues.

Its overall incidence is extremely low, accounting for 0.44% of all haematological malignancies and 0.7% of cutaneous

Figure 3 Radiological features (CT scan). (A) Extensive neoplastic lesion of the horizontal mandibula with deep bone erosion (thick arrow); pathological nodule at the base of the tongue (thin arrow). (B) Pathological lymph node of the neck in level 1b. (C) Manifestations of peritoneal carcinosis in the left paracolic gutter.

lymphomas.^{2,3} Median age at diagnosis is between 61 and 68 years, with males being affected three times more often than females. Adult cases are generally associated with an unfavourable prognosis.^{4,5}

BPDCN presents with cutaneous lesions as the first manifestation with subsequent or simultaneous spread to bone marrow and peripheral blood. Bone marrow involvement is also common which can lead to overt leukaemia. BPDCN has an aggressive clinical behaviour despite an initial apparent indolence. The median survival is approximately 12–14 months.⁶

It is rare to see BPDCN with a leukaemic presentation at the time of diagnosis, without a skin involvement, with only 30 cases reported in literature.^{3,7,8} Besides, considering the median age at diagnosis and the typical clinical presentation of BPDCN, our case is even rarer because the patient was an elderly woman, without skin involvement, but only with a gingival mass. In literature, there are no cases of BPDCN which debut with gingival lump, without skin lesion and leukaemic presentation.

With regard to the current patient, the macroscopic features of the gingiva ostensibly mimicked common oral lesions as epulis, haemangioma or squamous cell carcinoma. For this reason, the histopathological analysis has been critical to exclude other benign lesions such as fibromas, neurofibromas, schwannomas, peripheral giant cell granulomas or malignant lesions as, gingival leiomyosarcoma, myofibroblastic sarcomas, melanomas, rhabdomyosarcomas, lymphoma and spindle cell myoepithelial carcinomas.⁹

Historically, the tumour was variably thought to arise from either monocytes, T cells or NK cells giving rise to terms such as CD4+/CD56+ acute monoblastic leukaemia, primary cutaneous CD4+/CD56+ haematodermic tumour

and blastic NK cell lymphoma. In the literature, there are several cases of NK/T cell lymphoma which debut with destructive ulcer of the palate/uvulae.¹⁰ In this case, the differential diagnosis requires a characteristic immunophenotype with coexpression of CD4 and CD56, usually in combination with markers more restricted to plasmacytoid dendritic cells (such as CD123) and negativity for lymphoid, NK and myeloid lineage-associated antigens.⁶

Currently, there is no apparent consensus on the optimal treatment of BPDCN. Some cases have shown better response with acute lymphocytic leukaemia-like regimen. A diagnosis of oral BPDCN should be established histologically and supported by immunohistochemical analysis with specific markers. The triple-positive CD4+, CD56+, CD123+ phenotype combined with negativity for lineage-specific markers should represent a minimum requirement for BPDCN definition.

The present case is an addition to the handful of those cases of BPDCN which presents without cutaneous involvement and with leukaemia, but unlike other cases, it is exceedingly rare for both the age of the patient and because it began with an oral manifestation in the absence of a skin lesion.

Learning points

- ▶ Blastic plasmacytoid dendritic cell neoplasm (BPDCN) may begin with an oral manifestation associated with the leukaemia in the absence of a skin lesion.
- ▶ A diagnosis of oral BPDCN should be established histologically and supported by immunohistochemical analysis with specific markers.
- ▶ The macroscopic features of the gingiva ostensibly mimic other benign lesions such as epulis, haemangioma, fibromas, neurofibromas, schwannomas, peripheral giant cell granulomas or malignant lesions such as squamous cell carcinoma, gingival leiomyosarcoma, rhabdomyosarcomas and lymphoma.
- ▶ The diagnosis requires a characteristic immunophenotype with coexpression of CD4 and CD56, usually in combination with markers more restricted to plasmacytoid dendritic cells (such as CD123) and negativity for lymphoid, NK and myeloid lineage-associated antigens.

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