UNIVERSITI TEKNOLOGI MARA

BLASTIC PLASMACYTOID DENDRITIC NEOPLASM

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MMed

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Introduction:

Blastic plasmacytoid dendritic neoplasm (BPCDN) is a rare entity and difficult to diagnose. It is highly aggressive with a poor diagnosis. Early diagnosis may help with treatment. Here, we report a rare case of co-existence of BPCDN with acute myeloid leukemia in bone marrow.

Case presentation:

Mr. R is a 42-year-old taxi driver, who presented to our hospital with three weeks history of lower back pain prior to admission. He denied history of trauma or fall. He had 1-2 episodes of diarrhea for two weeks. He also complained of lassitude and 7 kg weight loss. There were no fever, headache, vomiting, upper respiratory tract or urinary tract symptoms. He denies recent travels to other countries and No family history of malignancy. He is married for 2 years and has a son.

Physical examination was generally unremarkable. His vital signs were as follow, blood pressure 122/74 mmHg, pulse rate 120 beats per minute, temperature 38 degree Celsius and 98 percent oxygen on room air. No palpable lymph node at cervical, axillary and inguinal region. Cardiovascular and respiratory system examination were unremarkable. There was no hepato-splenomegaly on abdominal examination.

On presentation, his blood results were as follows; Full blood count revealed bicytopenia (Hemoglobin 105g/L, white blood cell 8.5 x 10^9/L, platelet 14 x 10^9/L). Renal profile showed acute kidney injury and hyponatremia (urea 7 umol/L, sodium 130 mmol/L, potassium 3.8 mmol/L, creatinine 120 umol/L)There was transaminitis and hypoalbuminemia (albumin 25 g/L, total bilirubin 29 umol/L, alkaline phosphatase 443 U/L, Alanine aminotransferase 138 U/L)upon performing the liver function test. We proceeded to performing a peripheral blood film which revealed a leucoerythroblastic picture with severe thrombocytopenia and suspicious mononuclear cell. The only abnormality seen on the whole body CT scan was the T9 compression fracture. An MRI of the cervicothoracic region showed T9 compression fracture with no evidence retropulsion or cord edema.

A bone marrow aspiration and trephine biopsy were done which showed extensive bone marrow fibrosis with limited viable marrow tissue consisting mainly histiocytes, plasma cells and lymphocytes suggestive of ongoing inflammatory process or infection. Bone marrow culture was positive for salmonella enteritis and he was continued on Ceftriaxone. He was febrile despite proper antibiotic coverage; antibiotic was further upgraded to Meropenem. On day 10 of admission, he developed papular rashes over his chest which rapidly spread to his limbs and face within a span of a few days (Figure 1, 2 and 3). Skin biopsy showed infiltrates of monomorphic neoplastic cells mainly around blood vessels and appendages involving the superficial dermis. These loosely cohesive neoplastic cells are vaguely plasmacytoid in appearance, exhibiting rounded to oval nuclei, fine chromatin, scanty eosinophilic cytoplasm and prominent nucleoli. Mitotic activity is also seen. The cells are diffusely positive for CD45, CD43, CD68 and CD4. Weak positivity for CD 56 noted. They are negative for MNF116, CD3, CD20, S-100, MPO, CD117, CD1a and Tdt. Ki67 is about 60 to 70 percent. Perivascular and peri- appendageal neoplastic infiltrate. The features favour blastic plasmacytoid dendritic cell neoplasm.

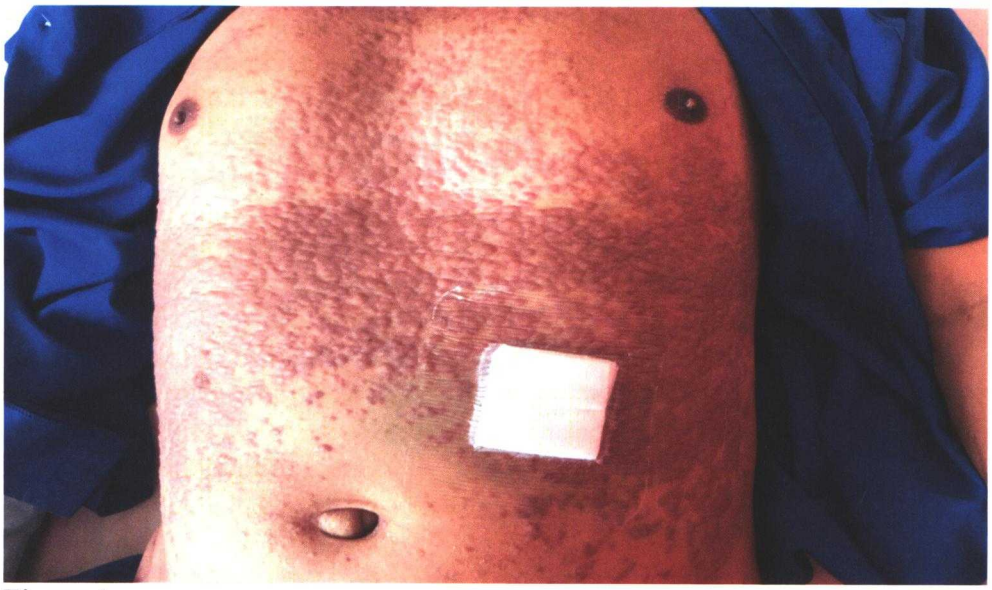

Figure 1

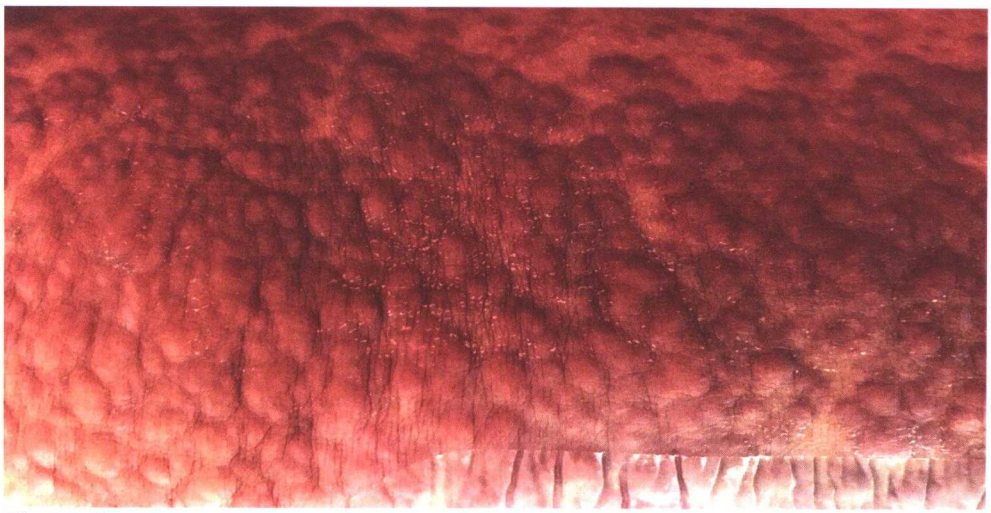

Figure 2

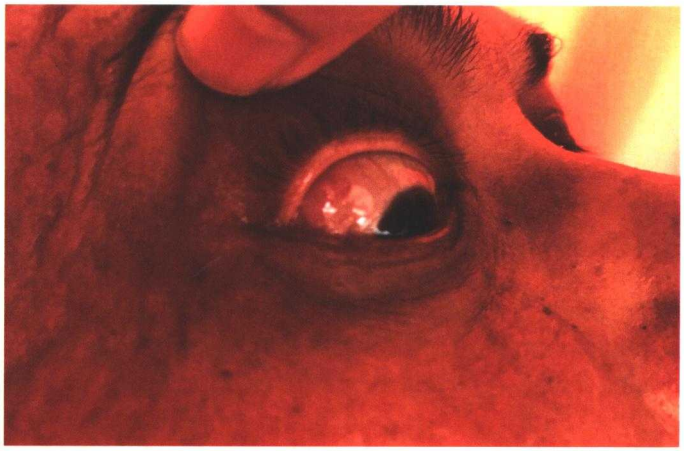

Figure 3

On day 22, he had left wrist drop with no other neurological deficit. A nerve conduction study showed sensory-motor neuropathy of which the cause was attributed to malignant infiltration of the radial nerve. During the admission there was rapid leukocytosis and presence of blast cells in the peripheral blood of 44%. A repeat bone marrow was done on day 30 of admission and showed monoblastic infiltration with positivity to CD33, CD13, CD64, CD14, CD4, CD15, CD11b, CD43, CD56 and HLA-DR (heterogenous). Nearly half (47%) of CD64+ cells show lack of CD14 expression and these cells are likely promonocytes. It is negative for CD117, CD34,cMPO, cTDT, cCD3, CD8, CD5, CD10, cCD79a and CD19 with negative to dim CD123 expression. Trephine biopsy showed marked hypercellular marrow tissue with diffuse infiltration of marrow spaces by sheets of medium to large sizes blast cells with round nuclei and prominent nucleoli. This is consistent with Acute Monocytic Leukemia (FAB-AML M5b). He was started on AML induction chemotherapy consisting of Daunorubicin and Cytarabine. Post chemotherapy his condition was complicated with prolonged febrile neutropenia however culture was negative. Counts subsequently improved and he was discharge with outpatient appointment.

Discussion:

Blastic plasmacytoid dendritic neoplasm (BPCDN) is a rare and highly aggressive malignancy derived from plasmacytoid dendritic cells (type 2 dendritic cell) (1). It is distinguished by its phenotypic expression of CD123 and CD56 (2). These cells are lineage negative and it may arise from either myeloid or lymphoid precursor (3). It generally occurs in elderly with the median age of 60 years old (4). Males are three times more susceptible compared to female. Plasmacytoid dendritic cells generally do not exist in skin but the disease typically presents as a cutaneous manifestation and subsequently or simultaneously spread to bone marrow and peripheral blood. Clinical presentation includes asymptomatic, solitary or multiple skin lesions such as nodules, plaques or bruise-like lesions that can range in size from a few millimeters to ten centimeters. It can be associated with erythema, hyperpigmentation, purpura, or ulceration. Purplish nodules are the most common lesions seen consisting about seventy three percent of patient (5). Interestingly, in our patient there is co-existence of BPCDN and acute monocytic myeloid leukemia (M5). According to literature 10-20% of BPDN will eventually transform to acute myeloid leukemia and it may occur in a patients with or without underlying myelodysplastic syndrome (6). However, this is associated with poor prognosis.

In the beginning, we suspected that the skin lesion was leukemia cutis as it is more common compared to BPCDN. Leukemia cutis is a nonspecific term used for cutaneous manifestation of any type of leukemia. It is difficult to differentiate between leukemia cutis and BPCDN. Both have similarities in clinical presentation and basic histopathology appearance. Histologically, both have been described in literature with pleomorphic cell and infiltrates prominent in the dermis, sparing epidermis, and occasionally extending to sub-cutis (2). Infiltration is describes as having perivascular or peri adnexal distribution. The chromatin is typically dispersed and nuclear membranes are irregular with prominent nucleoli and increased mitotic activity (7). Immunophenotype staining is very useful to established diagnosis and differentiates both lesions. Immunophenotypically, BPCDN express CD4 and CD56 in addition to at least one of the plasmacytoid associated antigens – CD123, TCL-1, CD2AP, or CD303/BDCA2, in the absence of lineage specific markers (7). MPO is negative in

BPCDN and variable in leukemia cutis. In our patient, the skin biopsy was positive for CD4 and CD56 and negative for MPO, which is consistent with BPCDN.

Other than skin manifestation, our patient also had neurological manifestation that is wrist drop but no other neurological symptoms. About ten percent of cases of central nervous system involvement at diagnosis has been previously reported mostly involving the brain and meninges (8). However, no case on peripheral nervous system was reported. We did not proceed with lumbar puncture for our patient. A study by Lourdes et al showed that among thirteen BPCDN patient evaluated, despite no neurological symptoms, all patients manifest with central nervous system at diagnosis or at relapse. It also suggested patients with occult CNS involvement might benefit from CNS-directed therapy e.g. intra-thecal prophylaxis (9). Eros et al, indicates that routine cerebrospinal fluid analysis and prophylactic intrathecal chemotherapy should be given in these patients. (10). The high incidence of CNS involvement suggests that CNS may be a persistent blast cell sanctuary in BPCDN patient with leukemic presentation, caused by limited ability of cytotoxic drug to cross blood brain barrier (9).

The prognosis of BPCDN is very poor. It is associated with short remission and survival (11). Currently, there are no established consensus guidelines or randomized controlled trial on the optimal therapeutic strategy of this disease. It is highly responsive to chemotherapy used for acute leukemia and aggressive lymphoma based protocol (12). Pagano et al shows that a higher percentage of patients achieved complete remission after acute lymphocytic leukemia or lymphoma regimen but relapse after treatment was higher compared to patient who treated with AML regimen (12). Thus, AML-like treatment regimens have are more commonly used to treat this disease (13). As our patient showed AML transformation, he was treated with AML chemotherapy regimen. High dose chemotherapy followed by allogenic hematopoietic stem cell transplant offers the possibility of long-term remission however outcome after complete remission is poor (14). Relapse occurs in majority of patient who treated with chemotherapy alone and about thirty percent relapse after stem cell transplant.

Conclusion:

In conclusion, BPCDN is a rare hematological malignancy and it poses a diagnostic challenge for the treating physician. There is limited literature on the disease so far. Our case taught a lesson that even though it is rare, it should be considered in differential diagnosis of skin lesions. Establishing a right diagnosis requires careful histological examination and appropriate immunohistochemical investigation and this will help in determining the proper treatment for the patient. Further studies and case accumulation should be done to help shed more light on this disease.