scintigraphy and tests to exclude a plasma cell dyscrasia should be routine additional tests. In more difficult cases, laser-dissection with mass spectrometry and genetic testing provide further diagnostic accuracy. Most importantly, accurate diagnostic subtyping is the key goal as the treatment implications are highly significant, ranging from chemotherapy and stem cell transplantation for AL amyloidosis, to protein stabilisers, fibrillar disruptors and, most recently, novel antisense oligonucleotides for hereditary disease.[14–16]

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Blastic plasmacytoid dendritic cell neoplasm (BPDCN) in leukaemic phase without skin lesions: a diagnostic and management challenge

Sir,
We report a case of an 84-year-old female with blastic plasmacytoid dendritic cell neoplasm (BPDCN), having been diagnosed following an acute leukaemia-like presentation. There were no skin lesions. Full blood count was normal 7

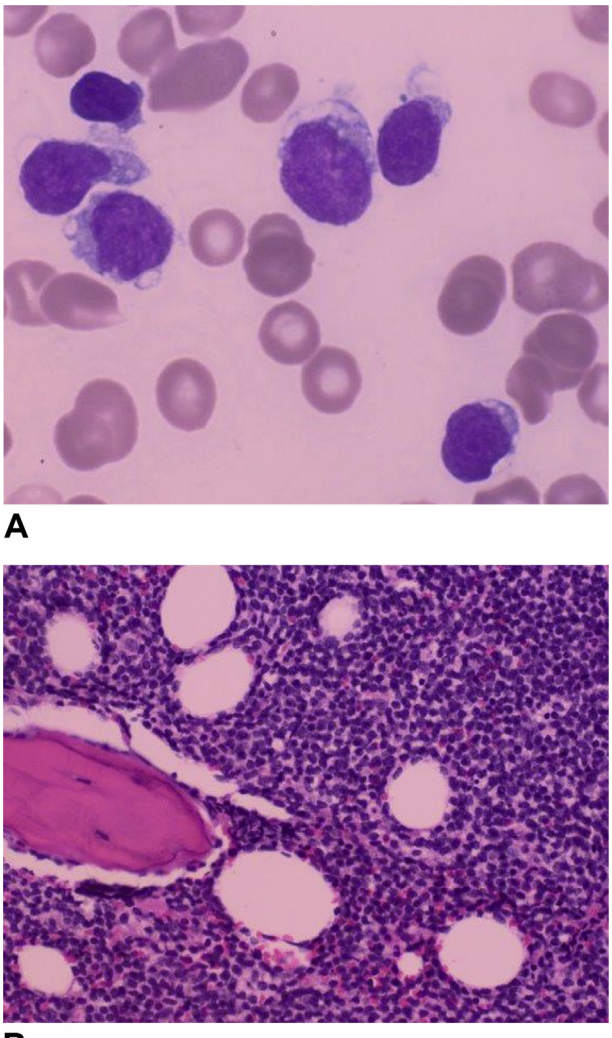

Fig. 1 (A) Bone marrow aspirate with peri-nuclear vacuolation – glycogen-containing microvacuoles in a pearl necklace pattern localised along the cell membrane. (B) Bone marrow trephine with heavy, diffuse infiltration of medium sized lymphoid cells.

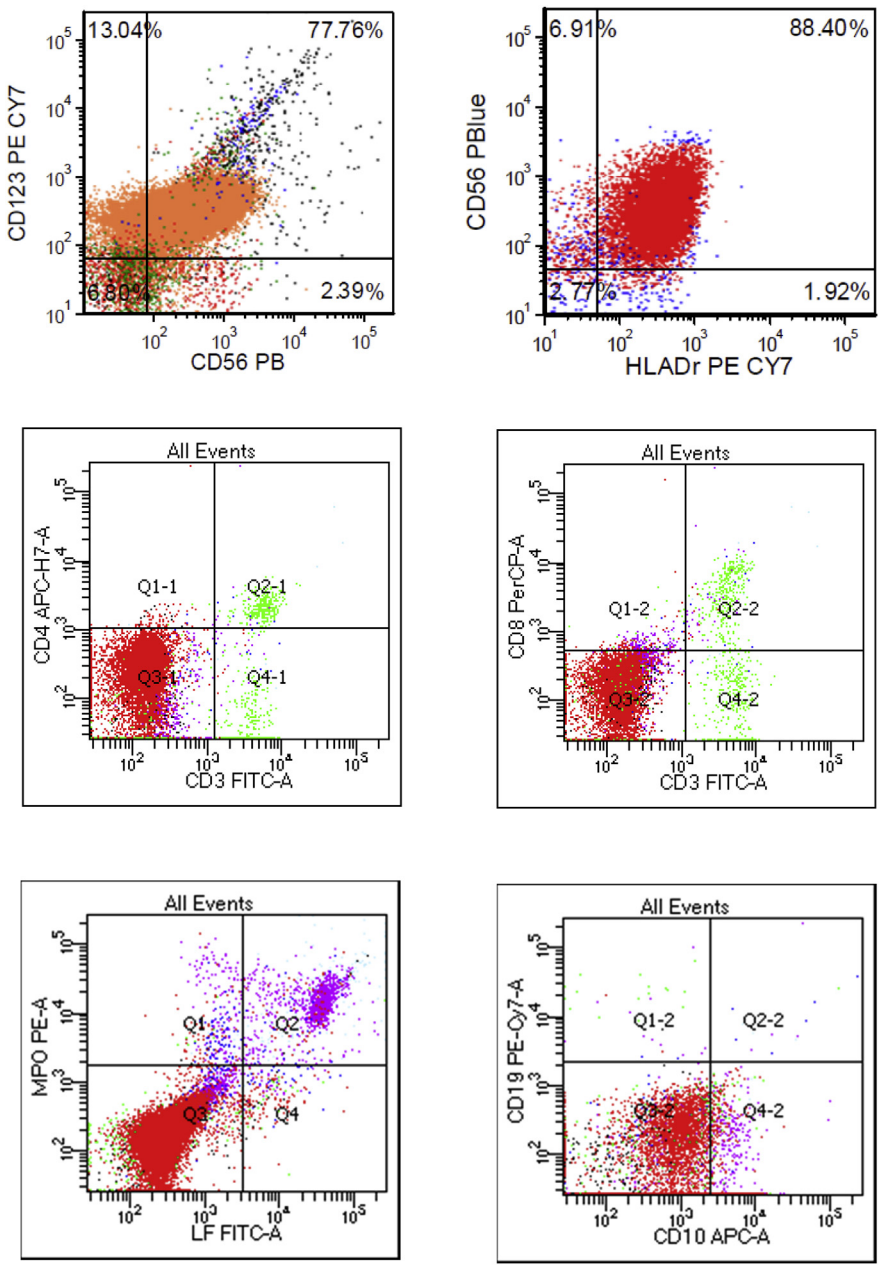

Fig. 2 Flow cytometry plots demonstrating key immunophenotyping findings. Lymphoid infiltrate is positive for CD2/7/56/123/HLA-DR and negative for CD3/4/5/16/34/79a/10/TdT/MPO.

weeks before the diagnosis, consistent with an aggressive clinical course. CD4 negativity is highly unusual in BPDCN, and a link to the leukaemic presentation is postulated by the author. Given the rarity of this entity, reporting of future cases is encouraged. In view of her age and frailty, the patient was not a candidate for intensive chemotherapy, and was commenced on cyclophosphamide/vincristine/prednisolone (CVP) therapy. She received a total of six cycles of treatment at 21 day intervals with normalisation of full blood count after two cycles, receiving minimal growth factor support. She had progressive disease with neurological decline (presumed CNS relapse) 7 months after commencing treatment and died.

BPDCN arises from the precursors of myeloid-derived type 2 dendritic cells.[1] Unlike type 1 dendritic cells, plasmacytoid dendritic cells are capable of producing copious amounts of interferons (IFN-α/β) in response to pathogenic stimuli.[2]

Tumour cells may show microvacuoles along the cell membrane (‘pearl necklace’ appearance) (Fig. 1A). Bone marrow involvement is present in over 80% of the patients with BPDCN (Fig. 1B). Skin involvement is present in almost 80−100% of cases.[3] BPDCN cells usually express CD4 and CD56. Variable terminal deoxynucleotidyl transferase (TdT) expression is observed in up to 40% of cases.[4] The expression of one or more of the following additional antigens should be demonstrated to establish a diagnosis of BPDCN: CD123, BDCA-2/CD303, TCL1, and SPIB.[5] Testing for CD303 and TCL1, both postulated to be highly specific for BPDCN, were not available. No Epstein−Barr virus (EBV) encoded RNA (EBER) is detected in BPDCN (Fig. 2).

Based on limited data and rarity of disease, preferred treatment strategies vary. Patients have generally been treated

with regimens used for acute myeloid leukaemia (AML), acute lymphocytic leukaemia (ALL), or aggressive non-Hodgkin lymphoma (NHL) with choice of therapy dictated by local experience. While the majority will achieve some form of response (complete or partial) to initial therapy, most adult patients will relapse.

Retrospective studies have suggested an advantage for ALL-like therapy. The largest study[6] was a retrospective analysis of 43 adults (median age 68 years) diagnosed with BPDCN across 28 Italian centres. Ten of 15 (67%) treated with an ALL- or NHL-like protocol achieved a partial response or better, while 11 of 26 (42%) treated with an AML-like induction regimen achieved partial response or better. The median overall survival was 8.7 months (range 0.2−33 months) with estimated survival rates of 28% and 7% at 12 and 24 months, respectively.

BPDCN is a rare disease treated heterogeneously depending on institutional preferences. Small series that have included patients with only cutaneous disease have reported somewhat better remission rates and a comparable advantage for ALL-like induction therapy. There may be correlation between the maturity of the tumour cells and response to therapy.[7]

Leukaemic manifestation without skin involvement should be distinguished from other leukaemias, the distinction relying heavily on flow cytometric findings. Of note, all of the antigens expressed in BPDCN, including CD4, CD56, and even CD123, can be expressed individually on myeloid or lymphoid leukaemias.

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Initial presentation of acute myeloid leukaemia as collision intradermal melanocytic naevus and myeloid leukaemia cutis mimicking naevoid melanoma

Sir,

We describe a case of a collision between an intradermal melanocytic naevus and myeloid leukaemia cutis (MLC) mimicking naevoid melanoma as the first presentation of acute myeloid leukaemia.

A 67-year-old male had an excisional biopsy of a clinically atypical naevus from the left chest. The lesion was a tan, well circumscribed macule, 7 × 6 mm macroscopically. Histological examination showed an asymmetrical intradermal melanocytic proliferation presenting in nests and sheets and exhibiting maturation with depth. It was composed of type A naevoid cells superficially possessing small nuclei, ample eosinophilic cytoplasm and focal cytoplasmic melanin pigment, and type B naevoid cells in the deeper part of the lesion with smaller nuclei and much less cytoplasm (Fig. 1). Intermingled with this population was a more cellular area composed of sheets of slightly larger cells showing high nuclear to cytoplasmic ratio, hyperchromatic nuclei, inconspicuous nucleoli and easily identifiable mitotic figures (Fig. 1). This second population also exhibited a linear arrangement and layering around dermal vessels and adnexal structures, in a pattern typically seen in congenital naevi. A junctional component was not identified and no epitheliotropism was seen. The primary differential diagnosis included naevoid melanoma. A panel of immunohistochemical stains was performed. S100, SOX10 and HMB45 were expressed in the bland naevoid cells only, with complete absence of staining in the closely associated mitotically active cell population. At this stage it became clear that there was a second non-melanocytic lesion present. Further immunohistochemical stains showed that the non-melanocytic cell population did not stain for cytokeratin AE1/3, CK20 or CK8/18, excluding Merkel cell carcinoma and metastatic carcinoma. The non-melanocytic cells stained weakly for CD45 and did not stain for CD20 or CD3. The Ki-67 index in the mitotically active population was up to 85%, and less than 1% in the melanocytic population. A third immunohistochemical panel showed the non-melanocytic population to stain for CD33, CD4, CD68 and lysozyme. These cells did not stain for myeloperoxidase, CD34, CD2, CD5, CD8, CD43, CD30, CD1a or CD117 (Fig. 1).

Based on the immunohistochemical findings, the lesion was diagnosed as collision intradermal melanocytic naevus and myeloid leukaemia cutis. The treating clinician reported that there were no other cutaneous lesions to biopsy and that a routine full blood examination seven months prior to the excisional biopsy was normal. Following diagnosis, repeat testing showed a mild macrocytic anaemia with anisocytosis (haemoglobin 127g/L, MCV 117 fL), mild thrombocytopaenia (139×10^9/L) and marked monocytosis with abnormal forms (2.2×10^9/L). Examination of a bone marrow aspirate and trephine confirmed the diagnosis of acute myeloid leukaemia (AML) with mutated NPM1 and 45% blasts in the peripheral blood (Fig. 1).