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CORRESPONDENCE

Leukaemia cutis as the initial manifestation in a child with brachydactyly in chronic phase of chronic myeloid leukaemia

Sir,

Cutaneous infiltration by neoplastic leukocytes is defined as leukaemia cutis (LC) which results in clinically identifiable skin lesions.[1] It often occurs after the diagnosis of systemic leukaemia (55%), but concurrent (38%) or previous involvement (7%) can also be seen.[2] LC is a frequent manifestation in acute myeloid leukaemia (AML) and is usually the harbinger of a more aggressive phase in CML with poor treatment response and prognosis, but it rarely occurs in chronic phase.[1] LC has a wide range of clinical manifestations which makes it difficult to differentiate from other non-specific skin lesions, especially when occurring as the only symptom of systemic diseases.[1] Brachydactyly is either an isolated hand anomaly or part of a complex syndrome. Brachydactyly type B (BDB) as in our case, is characterised by hypoplasia of middle and distal phalanges and dysplasia of nails.[3] To our present knowledge, LC in chronic-phase CML in a child with brachydactyly is especially rare. The child showed good response and prognosis to the hydroxyurea therapy.

An 11-year-old boy accompanied by his parents visited the Dermatology Clinic of our hospital with erythematous macules and plaques over his trunk and four extremities for a month (Fig. 1A). The boy had no previous history of fever, allergy, abrasion or insect bite. He had taken no medication in the past the month. No obvious weight loss was noticed by his parents. The child also presented middle and distal phalange hypoplasia and nail dysplasia of the second to fourth fingers of the left hand, verified by X-ray diffraction (Fig. 1B). Splenomegaly was detected (10 cm below the costal arch reaching pelvic cavity by physical examination). Blood investigation showed a markedly raised level of white blood cell (WBC) count (443.8×10^9/L), slightly low haemoglobin (0.0106 g/dL) and normal platelet count (214×10^9/L). The boy was referred to the Department of Hematology in our hospital for further diagnosis.

On suspicion of haematological malignancy, we proceeded to bone marrow (BM) aspiration. The results revealed hyperplasia of myeloid series. Differential count showed myeloblast (2%), promyelocytes (2%), myelocytes (28%), metamyelocytes (14%), bands (25%), and segments (22%). Flow cytometry of the bone marrow sample showed myeloid-associated antigens (CD13+ and CD33+). Chest radiography was negative for lymphadenopathy. Ultrasonographic tomography showed splenomegaly (10 cm below the costal arch with no hepatomegaly) as examined physically.

Chromosomal analysis of the bone marrow specimen revealed a 46,XY chromosome with t(9;22), with a positive proportion of 34%, indicating the presence of Philadelphia (Ph1) chromosome positive cells. Polymerase chain reaction (PCR) was positive for BCR-ABL gene detection in the BM, as well as in the skin lesions. Because the patient and his parents refused to give permission for punch biopsy, we performed fine needle biopsy (FNA) of the skin lesions and smear of the sample revealed immature myeloid cells indicating leukaemic infiltration in the skin (Fig. 1C). Based on these findings, a diagnosis was set: LC in chronic-phase CML.

Considering the family's inability to afford imatinib therapy, we arranged chemotherapy of hydroxyurea. The patient responded well to hydroxyurea; at the same time, the erythematous macules and plaques began to regress and finally resolve to pigmentation within 2 weeks after treatment. Complete haematological response was achieved within 1 month and maintained in 1 year.

LC is a relatively rare condition coexistent with leukaemia. The manifestation of LC varies in cases clinically. Skin eruptions may manifest as papules, nodules, plaques, ulcers and ecchymosis.[4] The most frequent manifestation of LC is erythematous papules and nodules occurring in 75% of patients.[5] The frequency of LC differs widely in different types of leukaemia. The most common cause for LC is adult T-cell leukaemia/lymphoma (40–60%), followed by AML (13%).[6] LC is especially uncommon in CML (2–8%).[1] Mean age of the skin eruptions in CML was 60.6 years.[4] Previous cases concerning LC in CML mainly affected adults in an aggressive phase, with very little involvement in children.[4,5] Our case is a rare example of CML manifesting as LC in chronic phase in a child, which has not been reported before.

To make a diagnosis on LC is difficult and challenging. FNA is a less invasive and more convenient technique as a diagnostic tool and it allows better observation on cell morphology. In our

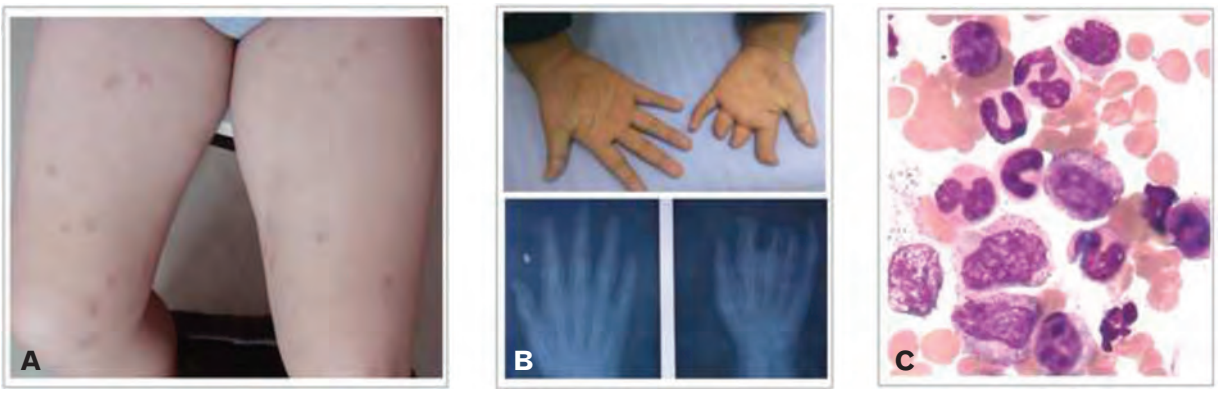

Fig. 1 (A) Erythematous macules and plaques on lower extremities. (B) BDB showing hypoplasia of fingers and nails on x-ray diffraction. (C) Spectrum of immature myeloid cells (FNA smear of skin lesions, ×1000).

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case, we clearly obverved cytoplasmic granules in myeloid cells which helped us to make the diagnosis. Genetic examination for certain abnormal chromosomes is also critical. Further more, patients with LC also have a high incidence of extramedullary involvement; therefore, it is important to reveal concomitant extracutaneous leukaemic infiltration like gums, pharynx and orbits when making the diagnosis.[4] Non-specific cutaneous lesions occur much more often. These lesions are mostly a manifestation of cytopenia, drug reaction and infection.[1,7] The patient in our case had no cytopenia, drug use history, or evidence of infection, and FNA showed immature myeloid cells which helped reach the correct diagnosis.

LC is reported to be refractory and responds poorly to chemotherapy.[5,8] The prognosis of LC is usually poor because the presence of LC indicates advanced disease and may be a marker of rapid progression. Studies showed that 88% of patients with leukaemia cutis died within 1 year of the diagnosis.[7] Some studies have suggested a subset of patients with AML-M4 shows a relatively poorer prognosis than other subtypes.[7,9] However, our patient responded well to the hydroxyurea chemotherapy. Skin lesions resolved within 2 weeks of therapy and complete haematological response was quickly achieved within 1 month and maintained in 1 year. This special case suggests that LC in chronic-phase CML in children has a better prognosis than LC in adult patients.

Brachydactyly represents the shortening of digits due to abnormal development during embryogenesis.[3] It occurs either as an isolated anomaly or part of a complex syndrome. BDB as presented in our case shows hypoplasia of the terminal part of the fingers with absence of nails.[3] Poland's syndrome, a rare congenital anomaly characterised by unilateral aplasia of the chest wall and ipsilateral hand anomalies, has been associated with leukaemia.[10] Brachydactyly coexisting with haematological malignancies, especially CML, has not been reported before. Furthermore, BDB gene mutation in affected pedigrees was shown in the receptor kinase-like orphan receptor 2 gene (ROR2) on chromosome 9q22. The parents and other family members are not affected, so further genetic studies are still needed to find whether there is a connection between the gene abnormality of BDB and CML.

Collectively, we report a rare case of LC in chronic-phase CML in a child with brachydactyly. The unusual presentation of CML alerts the clinicians that the skin eruption in children may be a sign of leukaemia. LC in children with chronic-phase CML may have a better prognosis than LC associated with other haematological malignancies.

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Beta thalassaemia intermedia due to silent alpha globin gene quadruplication in an infant

Sir,

We present the case of an 8-month-old girl born to a non-consanguineous Chinese couple in a dizygotic twin pregnancy. Her mother was found to be a β thalassaemia carrier during pre-pregnancy work-up, with mild hypochromic microcytic anaemia and a haemoglobin (Hb) of 9.8 g/dL (reference 11.5–14.8), mean corpuscular volume (MCV) 63.7 fL (reference 82–95.5), mean corpuscular haemoglobin (MCH) 19.7 pg (reference 27–32.4) and red cell distribution width (RDW) 15.3% (reference 11.8–14.6). As the father was haematologically normal with a Hb of 15.6 g/dL (reference 13.3–17.1), MCV 84.5 fL (reference 82–95.5) and MCH 28.4 pg (reference 27–32.4), further genetic testing for thalassaemia was not performed.

Elective lower segment Caesarean section was performed at 36+6 weeks because of gestational hypertension. Neonatal history was unremarkable. The patient was first found to be anaemic at 3 months of age. Physical examination at 8 months showed pallor and mild hepatosplenomegaly. A complete blood count revealed significant hypochromic microcytic anaemia with a Hb of 7.2 g/dL (reference 9.5–16.5), MCV 65.3 fL (reference 75.0–105.0), MCH 20.8 pg (reference 22.0–33.0) and RDW 22.6% (reference 11.5–14.5). Haemoglobin study