Calcinosis cutis: a rare complication of chronic myeloid leukemia

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Calcinosis cutis is a term for a group of disorders in which calcium deposits are formed in the skin. It is classified into 4 major types: dystrophic, metastatic, iatrogenic and idiopathic. In all cases insoluble compounds of calcium and/or phosphate are deposited within the skin due to local/systemic factors.

Case

A 65-year-old male patient was referred to our hospital with complaints of fever, weight loss and joint pains for the past 2½ years. He had also noticed extensive skin lesions over his knees, elbows and buttocks, which had developed during the last 4 months of his illness. Detailed examination and investigations found that he was suffering with chronic myeloid leukemia (CML). Physical examination revealed an enlarged spleen, which was palpable 18 centimeters below the costal margin. There was no lymphadenopathy. Skin examination showed well-demarcated and prominent shiny multiple firm whitish dermal nodules on the elbows, knees and larger lesions over the buttocks. The overlying skin, especially over the buttocks, was hard and tender, making it difficult for the patient to sit for a long stretch of time (Figures 1, 2). The lesions over the knees and elbows were also tender. Before reporting to us on two previous occasions large amounts of calcified material were surgically extruded from the lesions over the buttocks, which resulted in partial resolution and temporary relief. Laboratory tests on admission showed Hb 8.7g/dL (normal, 14-18g/dL), and WBC $48 \times 10^9/L$ (normal, $4.0-11.0 \times 10^9/L$). The differential count showed 50% segmented neutrophils, 3% band forms, 6% metamyelocytes, 12% myelocytes, 3% promyelocytes, and 3% nucleated RBCs. The number of eosinophils and basophils was also increased. The platelet count was $189 \times 10^9/L$ (normal, $150-350 \times 10^9/L$). Leukocyte alkaline phosphatase was 0, urea 6 mmol/L (normal, 3.6-7.1 mmol/L), and creatinine 100 $\mu\text{mol/L}$ (normal, $<133 \mu\text{mol/L}$). LDH was 800 IU/L (normal, $<480 \text{ IU/L}$) calcium was 3.7 $\mu\text{mol/L}$ (normal, 2.2-2.7 $\mu\text{mol/L}$), phosphorus 1.4 mmol/L (normal, 1.0-1.5 mmol/L). Parathyroid hormone level was 18 ng/L (normal, 10-55 ng/L). Bone marrow aspiration showed a hypercellular bone mar-

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Figure 1 (top): Multiple calcified nodules on the knees and elbows of the patient.

Figure 2 (right): Large calcified lesions on the buttocks.

row and there was hyperplasia of the myeloid series and megakaryocytes. Skin biopsy taken from one of the lesions from the right buttock revealed granules and deposition of calcium salts in the dermis (Figure 3). The clinical condition of the patient remained stable for a short while after which he went into an accelerated phase. The complete blood count showed a hemoglobin of 8.1 g/dL, WBC $278 \times 10^9/L$ with 8% myeloblasts. LDH was 1200 IU/L, blood urea was 28 mmol/L, serum creatinine 250 $\mu\text{mol/L}$, calcium 5.4 mmol/L, albumin was 38 g/L (normal, 36–47 g/L) and phosphorous 1.8 mmol/L. The patient was treated with hydroxyurea initially for a 4-month period and later diuretics and steroids were added but the response was minimal.

Discussion

Calcinosis cutis, initially described by Virchow in 1855, is characterized by the deposition of insoluble calcium salts in the skin and subcutaneous tissue. The pathogenesis of this condition is not understood completely and a variety of factors exist that allow different clinical scenarios to occur. Metabolic and physical factors also play a pivotal role in the development of most of the cases of calcinosis.

Metastatic calcification of the skin is defined as cutaneous calcification induced by disorders of calcium and/or phosphate metabolism. Causes of metastatic calcinosis include paraneoplastic hypercalcemia, malignancies, milk alkali syndrome, excessive vitamin D, and sarcoidosis and calciphylaxis, but the most common cause of metastatic calcification is still chronic renal failure. Paraneoplastic hypercalcemia usually occurs as a part of a malignancy syndrome due to bony metastases or the production of an abnormal hormone that directly affects calcium and bone metabolism.

Our patient presented with cutaneous calcinosis, which is a very rare complication of CML.¹ Hypercalcemia in an accelerated phase of chronic myeloid leukemia is thought to be caused by humoral factors mediated by parathyroid hormone-related protein (PTHrP).^{2,3} In severe cases calcifications can even occur in kidneys, blood vessels, heart, and stomach, and it usually predicts rapid deterioration and progression to blastic crises. Survival after diagnosis is usually extremely short despite intensive

treatment. However, hypercalcemia is a common metabolic complication of malignancies such as acute lymphoblastic leukemias, lymphomas and Paget's disease, which may induce enough bone destruction to cause hypercalcemia.^{4,5,6} The skin lesions in this case were characteristic, consisting of firm nodules around the joints such as knees, elbows and shoulders in a symmetrical distribution. At some sites the lesions were stuffed with a yellowish, white gritty substance, which was painful, hence limiting the mobility of the adjacent joints. The diagnosis of metastatic calcinosis accompanying hypercalcemia is usually missed as the lesions are too small to be diagnosed routinely. The condition of our patient remained stable for only a few weeks after being diagnosed as having CML and he later went into an accelerated phase of CML and ultimately died in hospital.

Calcinosis in itself is a benign process. However, morbidity is related to the size and location of the calcification. There is no specific treatment but when this condition is identified, the underlying problem should be corrected. Lesions which are large and tender require incision and drainage. In addition to painful lesions, conditions such as ulceration, functional impairment and recurrent infections are also indications for surgical management of the lesions. However, care has to be taken as the surgical trauma itself may stimulate calcification. It is thus advisable to treat a test site before managing a large lesion. In conclusion, this patient had an unusual presentation of two different complications of CML, hypercalcemia and cutaneous lesions.

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Figure 3: Photomicrograph showing calcified material in the upper dermis. (Haematoxylin & eosin x 25).

References

1. Miriam Q, Judith K, Janina S, et al. Accelerated phase of chronic Myeloid Leukemia presenting with Hypercalcemia and a mediastinal mass. *Acta Haematol* 1998;99: 231-233.
 2. Kwak HS, Sohn MH, Lim ST, et al. Technetium-99m MDP bone scintigraphic findings of hypercalcemia in accelerated phase of chronic myelogenous leukemia. *J Korean Med Sci* 2000; 15(15): 598-600.
 3. Oddel WD. Endocrine manifestations of tumours: Ectopic hormone production; in Wyn-gaarden JB, Smith LH. (eds): *Cecil Textbook of Medicine*. Philadelphia. Saunders. 1985. 1077-1080.
 4. Kornberg A, Amir G, Leizerowitz R, et al. Hypercalcemia complicating a megakaryoblastic crisis of chronic myelocytic leukemia. *Isr J Med Sci* 1988; 24:247-249.
 5. Ballard HS, Marcus AJ. Hypercalcemia in chronic myelogenous leukemia. *N Engl J Med* 1970; 282: 662-665.
 6. Joyner MV, Dujardin P, Cassout JP, et al. Hypercalcemia as complication of accelerated chronic granulocytic leukemia. *Br Med J* 1977; ii:1060.
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