

incidence of gingival hyperplasia. These figures are assumed to be less in patients taking amlodipine (9). Literature about telangiectasia only consists of a few case reports.

For both symptoms it is likely that they are not always recognized as side-effects and are therefore under-reported. One can imagine that in the group of patients taking antihypertensive drugs, namely adults, telangiectasia is seen more often but not always related to medication and mistakenly diagnosed as a skin disease, such as rosacea. Hopefully, knowledge of the side-effects leads to faster recognition and better patient care.

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Skin Calcinosis Following Allogenic Bone Marrow Transplantation in an Acute Lymphoblastic Leukaemia Patient

Sir,

Skin calcinosis is a condition in which calcium salts are deposited in the skin. Such a deposition may be primary, without any known previous skin abnormality, or secondary to disturbances in calcium and phosphorus metabolism, which usually present with widespread metastatic calcification involving the blood vessels, kidneys, lungs and gastric mucosa.

The most common form of skin calcification is the dystrophic type, which occurs secondary to trauma or to pre-existing skin pathology. Iatrogenic calcification of the skin may also be seen following intravenous administration of calcium salts or after prolonged skin contact with saturated calcium chloride electrode paste (1). To date, bone marrow transplantation (BMT) has not been associated with skin calcinosis.

We report here a case of skin calcinosis following allogenic BMT.

CASE REPORT

A previously healthy 22-year-old Arab woman was treated for acute T-cell lymphoblastic leukemia.

She presented in June 1994 with weakness, arthralgia, weight loss, night sweats and fever. Physical examination and imaging at presentation revealed hepato-splenomegaly, para-aortic lymph nodes enlargement, large mediastinal mass and pleural and pericardial effusions.

Skin examination was normal. The peripheral white blood cell count was $90 \times 10^9/l$ with 58% lymphoblasts. Morphological, cytochemical

and flow cytometric analysis of bone marrow aspirate revealed acute lymphoblastic leukemia (L1). The serum lactic dehydrogenase level was 3136 U/ml.

Combination chemotherapy was instituted according to the Berlin protocol (2) and a complete remission was induced after 4 months. Complications of chemotherapy included severe sinusitis. One year later, a T-cell depleted (CAMPATH – 1G McAb) (3.9×10^8 nuclear cells/kg) allogenic BMT from the patient's fully-matched sister was performed after conditioning with total body irradiation (1200 cGy), cyclophosphamide (60 mg/kg), etoposide (1500/m²) melphalan (60 mg/kg) and total lymph node irradiation (720 cGy). Granulocyte col-



Fig. 1. Skin-coloured stone hard plaques on the patient's neck.

ony stimulating factor (5 µg/kg) was initiated on day +1 and was administered until WBC engraftment. Engraftment was rapid, WBC $>1 \times 10^9/l$ at day +12. The post transplant course was complicated by *E. coli* bacteraemia, which was treated with wide spectrum antibiotic therapy, including mezlocillin, cefazolin, gentamicin and later amphotericin, amikacin, ceftazidime and imipenem. Intravenous immunoglobulins were also administered. In addition, the patient developed transient disturbed liver function tests, with peak bilirubin levels of 125 µmol/l, and gamma-glutamyl trans peptidase levels of 474 U/ml, and acute colitis, which responded to steroids. Renal functions remained normal.

No cutaneous evidence of graft versus host disease was seen and bowel biopsy was non-specific. A month after BMT the patient gradually developed asymptomatic, skin-coloured, stone hard plaques on the neck and both axillae (Fig. 1). Chest radiograph revealed skin calcifications. Skin biopsy demonstrated normal epidermis, calcification of the upper dermis with no other abnormality. Therapy was not instituted, as the patient was asymptomatic.

The patient was discharged on prednisone therapy for colitis and on prophylactic valacyclovir and co-trimoxazole treatment. On follow-up, the skin calcinosis gradually resolved.

DISCUSSION

Several skin problems can be found in the early post-allogeneic BMT period. Among them, acute graft versus host disease is the most common, occurring in 50–80% of the patients (3). Other common skin problems are related to infectious complication of immunosuppression, such as molluscum contagiosum and verruca vulgaris, bacterial, fungal and protozoal infections (4).

Side-effects of multiple medication administration include bleeding, petechiae, ecchymoses, drug allergy, pigmentation and palmar erythema. An increased risk of skin malignancies is also a concern in immunosuppressed patients (4).

Reports of other dermatoses first developing in the early post BMT period include a case of generalized granuloma annulare (5). The present case of acquired skin calcinosis post-allogeneic BMT is, to our knowledge, the first to be reported. We have no doubt as to the timing of appearance of the skin calcinosis, numerous chest radiographs did not reveal calcinosis prior to BMT. We are also certain that the calcinosis was not a manifestation of graft versus host disease, since there was no clinical evidence of the disease, and histology showed the absence of an interface dermatitis. Metastatic calcification can also be excluded, as the patient's serum levels of calcium and phosphorus had been closely monitored (serum calcium was normal, albumin levels were 30–39 g/l, and phosphorus levels were, at times, mildly elevated at 1.5 mmol/l, with corresponding serum calcium of 2.43 mmol/l). Renal failure with secondary hyperparathyroidism was excluded by repeated blood creatinine monitoring. Post BMT reactivation of viruses can be a cause of dystrophic skin calcinosis. However, multiple

cultures and serological examinations for virus reactivation, including HTLV1 virus, were negative. Our pre-biopsy clinical diagnosis of pseudoxanthoma elasticum, a dystrophic type of skin calcinosis, was not confirmed histologically, nor were there any findings in her eye fundi or in family relatives.

This patient may represent a new type of iatrogenic calcification, secondary to BMT.

We do not know the mechanism of this complication. Possible contributing factors may include the chemoradiotherapy of the pre-transplant conditioning, although no radiodermatitis was seen histologically.

The many medications she received including chemotherapy, steroids, granulocyte colony stimulating factor and antibiotics, could have also been causative or contributory to the development of calcinosis. BMT itself may have been a factor. It seems unlikely that acute lymphoblastic leukemia was responsible for the calcification (6), as the patient was in complete remission from the disease during the period of BMT. However, it is possible that if the patient had subclinical cutaneous acute lymphoblastic leukaemia involvement which resulted in tumour cell necrosis with secondary calcifications.

Currently we cannot exclude the possibility of co-incidental development of primary skin calcinosis, unrelated to BMT.

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