bone marrow recovery could also exhibit unusual properties. These functional changes could lead to a release of cytokines and an upregulation of expression of some adhesion molecules such as α_4-integrin, all changes that might promote adhesion of neutrophils to vessel walls, damage to the endothelium, diapedesis and accumulation in some areas such as the dermis.[11,12] The earliest phase of this recovery is probably ongoing while the peripheral count still shows a sometimes deep granulocytopenia, the functional properties of these first neutrophils being more important than their absolute number. This theory could also possibly apply to usual cases of Sweet's syndrome, where a rapid increase in neutrophil count by bone marrow stimulation for various reasons could explain both the usual high neutrophil count and the unusual behaviour of these highly stimulated cells. A similar mechanism has been suggested by some authors to account for cases of Sweet's syndrome occurring during myelodysplastic syndromes.[13] Finally, a similar pathogenesis could also be hypothesized for ATRA-induced ND, as ATRA is a potent stimulator of some neutrophil functions.

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The importance of skin biopsy in the diverse clinical manifestations of cholesterol embolism

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SIR, Cholesterol embolism (CE) is a multisystemic disorder characterized by release of cholesterol crystal emboli from eroded atherosclerotic plaques of the aorta or large feeder arteries.[1–6] These lead to ischaemia and rarely cause infarction in tissue distal to the emboli. CE may occur spontaneously or after precipitating factors such as vascular surgery, angiographic procedures, or anticoagulant and thrombolytic therapies.[7] Although many organs may be targets of emboli, the most commonly involved organs are the skin and kidneys. We report a series of 52 patients where cutaneous lesions suggested a diagnosis of renal CE in 50 (96%) and skin biopsy provided the correct diagnosis in 27 patients (52%).

We surveyed 52 nephrology in patients consulting between 1989 and 1999 (44 men and eight women; mean age 68 years). The diagnosis of CE was made on clinical grounds alone in seven of 52 patients (13%). They presented a typical triad comprising a precipitating event, acute or subacute renal failure and ischaemic peripheral changes such as cutaneous lesions on the lower extremities, gastrointestinal bleeding or neurological involvement. The disease was spontaneous in 11 patients (21%); a triggering factor was identified in 41 patients (79%), such as angiography (50%), anticoagulant treatment (21%) and aneurysm resection (15%). Acute renal failure occurred in 18 patients (35%), subacute renal failure in 29 patients (56%) and chronic and stable renal failure in five patients (9%). Cutaneous lesions, which usually came before the onset of renal symptoms, occurred in 50 patients (96%). Patients had one or more characteristic skin lesions such as redness on the toes (79%) (Fig. 1a), livedo reticularis of the lower limb and abdomen (38%), or gangrene of the extremities (15%), leading to amputation of a portion of the lower extremity in three patients; two patients also showed ulceration of the scrotum and penis. The two patients without cutaneous lesions had a spontaneous form of renal cholesterol crystal embolization presenting as a chronic and stable renal impairment.

Skin biopsy provided the correct diagnosis in 27 patients (52%). The histological features of CE are highly characteristic, showing an occlusion of the lumen of small arteries and arterioles by atherosclerotic material. As the lipids are dissolved by the techniques used for preparation of the tissue for histological examination, the cholesterol crystals may be identified within lumina of small vessels by the presence of multiple, biconvex, needle-shaped clefts that remain after

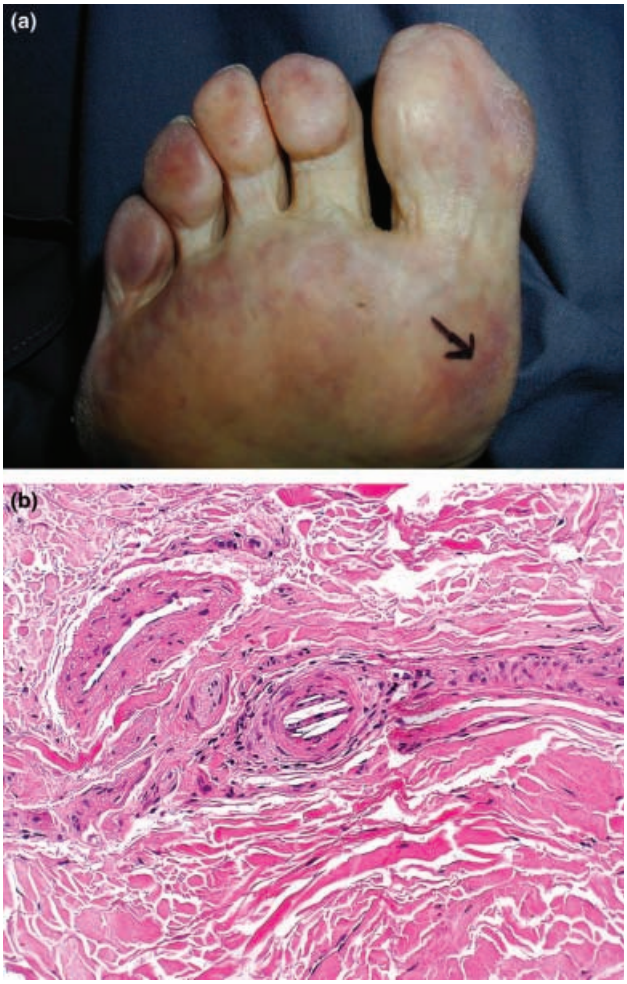

Figure 1. (a) Extent of redness on the toes. (b) Well-demarcated cholesterol crystals may be identified within the lumen of a small vessel.

cholesterol has dissolved during fixation (Fig. 1b). Percutaneous renal biopsy was performed in only four patients (8%). In two patients with a stable and chronic renal impairment, histological confirmation was obtained by nephrectomy specimens because of renal carcinoma in both cases. In four patients (8%), CE was confirmed histologically in the less likely target organs such as gastrointestinal tissue (stomach and colon) obtained on endoscopy. In one patient, who had an associated haematological disorder, the histological diagnosis was made when an iliac crest bone marrow biopsy showed cholesterol crystal emboli. Autopsy was the sole means of histological diagnosis in three patients. All patients had been followed for at least 2 years. The 1- and 2-year survival rate, estimated using Kaplan–Meyer actuarial curves, was 69% and 61%, respectively. Death was due to cardiac causes, gastrointestinal ischaemia and stroke.

Diagnosis of CE requires a high index of suspicion because the typical triad may be absent and clinical manifestations can be nonspecific. Renal biopsy should be considered the most definitive method of diagnosing renal cholesterol crystal embolization. However, during the acute phase of the disease many patients may be too ill to proceed with this invasive procedure. Moreover, as cholesterol crystal embolization is a patchy process, a focal lesion can elude histological examination.[8] Random muscle biopsy from the lower extremities may also have a high diagnostic yield, but the sensitivity of this procedure has never been evaluated. In contrast, biopsy of characteristic cutaneous lesions represents a more easily accessible site and may yield a positive diagnosis in many cases.[9] Cutaneous manifestations such as livedo reticularis, gangrene, cyanosis, ulceration, nodules and purpura are the most common signs of systemic cholesterol crystal embolization, and were found to occur in 35–90% of patients with CE in previous studies.[2,9,10] In our series typical skin lesions occurred in a greater number of patients (50 of 52 patients) than in previous studies because we looked for early cutaneous manifestations of CE and found 79% of our patients to have redness on the toes. Early recognition of CE skin lesions is not easy because lesions are often asymptomatic and weak, but looking for these is essential for early diagnosis of CE. Therefore, skin biopsy should be considered the best choice for histological diagnosis, because it is a simple and noninvasive procedure that avoids the increased morbidity of renal biopsy.

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Eccrine porocarcinoma and eccrine poroma arising in a scar

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Sir, Malignant tumours occurring at scar sites have long been reported in the literature. Most of them are squamous cell carcinomas and basal cell carcinomas. To our knowledge, eccrine porocarcinoma and eccrine poroma have not yet been described in association with scars. We report a case of eccrine porocarcinoma and eccrine poroma arising from a scar on the right foot.

A 74-year-old woman had had paralysis of the lower half of the body for more than 50 years from spinal injury due to tuberculosis. She had scars caused by skin infections due to osteomyelitis and recurrent decubitus on the lower legs and feet. She presented with a partly ulcerated, fresh, red nodule surrounded by a brownish macule, 5 cm in diameter, situated within a scar on the anterior surface of her right foot (Fig. 1a). In addition, there was a slightly elevated, reddish but partly white nodule surrounded by a brown macule, 4 cm in diameter, situated in a scar on the posterior surface of her right foot (Fig. 1b).

Histology of the nodule on the anterior surface of her right foot revealed a tumour composed of cords and broad columns of generally small basal-like cells extending into the dermis from the epidermis. The tumour cells were arranged irregularly and showed moderate atypia. The cells had large, hyperchromatic, irregularly shaped nuclei and some of them were multinucleated. Atypical mitotic figures were also seen. Ducts and small cysts were also seen within the tumour nests (Fig. 2a,b). The tumour cells stained positive with periodic acid–Schiff, alcian blue, epithelial membrane antigen, cytokeratin 7 (Fig. 2c) and carcinoembryonic antigen (Fig. 2d). However, diastase digestion, cytokeratin 20, S-100 protein and gross cystic disease fluid protein-15 were negative in the tumour cells. Based on these clinical and histopathological findings, the tumour on the anterior surface of the right foot was diagnosed as an eccrine porocarcinoma arising from a scar.

Histopathologically, the nodule on the posterior surface of the right foot showed nests and islands of uniformly small basaloid cells, which were sharply demarcated from the adjacent keratinocytes. Broad, anastomosing cords and solid columns and nests of large cells extended into the dermis to varying levels. Duct-like structures were also found. The tumour was diagnosed as an eccrine poroma that occurred in association with a scar.

Carcinomas are well known to arise frequently from a burn scar, and such carcinomas are termed Marjolin's ulcers. Skin malignancies are thought to occur in association not only with burn scars, but also with scars in chronically inflamed or traumatized skin. Among such malignant tumours, squamous cell carcinomas occur most frequently in association

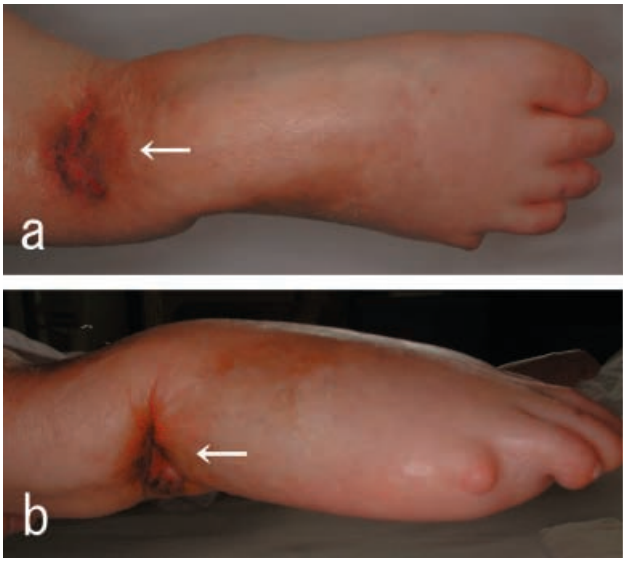

Figure 1. (a) Anterior view of the right leg upon initial examination. Note a partly ulcerated, fresh, red nodule surrounded by a brownish macule (arrow). (b) On the posterior surface of the right foot there was a slightly elevated, reddish nodule surrounded by a brownish macule (arrow).

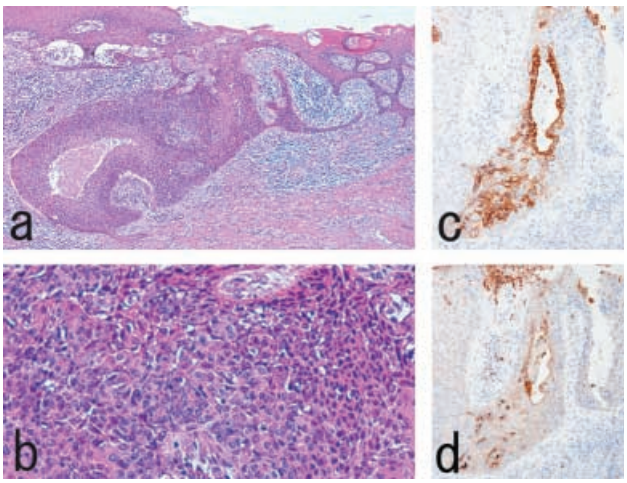

Figure 2. Histopathological features of the eccrine porocarcinoma on the anterior surface of the right foot. (a) The tumour was composed of cords and broad columns of basaloid cells extending into the dermis from the epidermis. Irregular-shaped ducts and small cysts were seen within the tumour columns (haematoxylin and eosin; original magnification ×40). (b) The cells had large, hyperchromatic, atypical nuclei (haematoxylin and eosin; original magnification ×200). (c) The tumour cells forming ductal structures were positive for cytokeratin 7 (original magnification ×120). (d) Carcinoembryonic antigen was also positive in the wall of irregular ducts (original magnification ×120).