Reactive Angioendotheliomatosis Associated with Myelodysplastic Syndrome

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Sir,

Although Gottron & Nikolowsky (1) probably reported the first case of angioendotheliomatosis in 1958, this term was proposed in 1963 by Tappeiner & Pfleger (2), who described a proliferation of endothelial cells within the lumen of dermal vessels with secondary necrosis and infarction of the skin. To our knowledge, only 39 cases of reactive angioendotheliomatosis have been reported in the literature, usually as isolated cases, except the series of 15 cases published by McMenamin & Flether (3). The association of reactive angioendotheliomatosis with systemic diseases is common, but some exceptional cases have been described without any association (4). Several factors may play an important role in this process, including angiogenic circulant factors (5) such as VEGF, procoagulant factors and localized hypoxia that produces oxidative stress with release of free radicals. We report here a case of reactive angioendotheliomatosis with crusted-necrotic ear lesions after cold exposure. The patient also had a myelodysplastic syndrome.

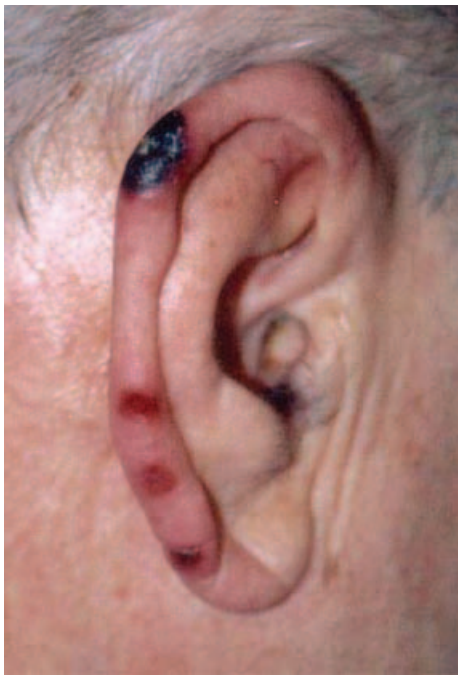

Fig. 1. Necrotic, purpuric, crusted lesions on the ear.

CASE REPORT

A 75-year-old man presented in December 2002 with necrotic, purpuric, crusted lesions on his ears with 6 weeks of evolution (Fig. 1). No other localizations were seen. Histopathological examination of a cutaneous biopsy revealed a benign angiomatous dermal proliferation with fibrin thrombi in some vessels. A CD31 stain confirmed the endothelial origin of this proliferation, which was diagnosed as reactive angioendotheliomatosis.

Laboratory analyses revealed thrombocytopenia (platelet count 58×10^9/l), slight anaemia (haemoglobin 11.5 g/dl), megathrombocytes in the peripheral blood extension, and mildly elevated erythrocyte sedimentation rate (27 mm in the first hour, normal <20), mildly elevated alkaline phosphatase (286 UI/l, <250 UI/l), lactate dehydrogenase (526 IU/l, <190 IU/l) and creatinine (200 μmol/l, <101 μmol/l) levels.

Basic coagulation investigation, including activated partial thromboplastin time and fibrinogen, was normal. Calcium, phosphorus, complement values, serum protein electrophoresis, rheumatoid factor and antinuclear antibodies were normal or negative. Serology for hepatitis B virus, hepatitis C virus, HIV and *Treponema pallidum* was negative. Epstein-Barr virus and cytomegalovirus serology showed residual values. Thyrotropin-stimulating hormone and T4 were normal. Direct Coombs test was negative. No cryoglobulins or cold agglutinins were seen. Anti-platelet antibodies, platelet adhesion and aggregation studies were normal.

The patient was evaluated in the Haematology Department, where a histopathological study of the bone marrow revealed a myelodysplastic syndrome. Cutaneous lesions were resolved within 1 month after cold protection and a topical antibiotic (mupirocin).

In November 2003 the patient presented similar lesions accompanied by slight general involvement. A new analytical study and bone marrow biopsy revealed similar results to those obtained before. A complete hypercoagulability study revealed negative antiphospholipid antibodies but elevated levels of D-dimer. Periodic follow-up showed no significant changes.

DISCUSSION

Sustained and intense cold exposure may induce vessel spasm, causing hypoxia and local ischaemia and resulting in endothelial damage. The reperfusion after the heating of damaged endothelial cells induces platelet aggregation and thrombus formation. This increases tissue ischaemia, with possible development

of necrosis and additional liberation of local proangiogenic factors, such as VEGF.

It is known that myelodysplastic syndrome may promote a procoagulative status and the release of circulant angiogenic factors like those seen in acute leukaemia (6). We have not found any previous references to angioendotheliomatosis associated with myelodysplastic syndrome.

Our patient had increased levels of D-dimer, which is a usual event in malignant neoplasm.

Rongioletti & Rebora (7) recently published a classification of reactive angiomatoses where they attempted to establish a relationship between different variants of histopathological patterns with precipitant factors. They included reactive angioendotheliomatosis, acroangiodermatitis (pseudo-Kaposi sarcoma), diffuse dermal angiomatosis, intravascular histiocytosis, glomeruloid angioendotheliomatosis and angiopericytomatosis (angiomatosis with cryoproteins).

The clinical presentation of our case with cold exposure is very similar to that described by Porras-Luque et al. (8). Nevertheless, in our case the absence of cryoprecipitates revealed typical features of angioendotheliomatosis without glomeruloid pattern.

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