CASE REPORTS

Raynaud’s phenomenon and positive antinuclear antibodies in a malignancy

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Abstract
Both Raynaud’s phenomenon and the presence of antinuclear antibodies are uncommon features of malignant disease and the association of both with a malignancy extremely rare. The case is reported of a 78 year old woman who presented with Raynaud’s phenomenon and positive antinuclear antibodies related to adenocarcinoma of unknown primary site.

Raynaud’s phenomenon is a vascular disorder characterised by episodes of abnormal digital vasospasm in the hands and sometimes in the feet. These episodes occur in response to cold or emotional stress and produce one or more colour changes. The most common sequence is an initial pallor followed by cyanosis and rubor, but incomplete episodes are more common.1 The prevalence in the general population has been estimated as 4–10%.2 Raynaud’s phenomenon as an isolated condition is classified as primary, and secondary when an underlying cause can be identified.1 The presence of antinuclear antibodies in these diseases was often associated with connective tissue diseases3 and only in rare cases with malignancies.4 We report a patient with Raynaud’s phenomenon and a high antinuclear antibody titre related to neoplasia.

Case report
A 78 year old woman presented with a two month history of gradual loss of weight and episodes of coldness, pallor and paraesthesia in all fingers of her hands followed by rubor with warming. She denied taking any drugs or smoking and did not have any signs or symptoms suggestive of connective tissue disease. On examination she looked well. Her fingers were not affected and the peripheral pulses were all palpable. There was no evidence of a cervical rib or carpal tunnel. Blood pressure was 140/70 mmHg. The rest of the clinical examination was unremarkable.

Laboratory tests showed white blood cell count 7.8×10⁹/l, haemoglobin 149 g/l, platelet count 282×10⁹/l, erythrocyte sedimentation rate 13 mm/h, total protein 64.1 g/l, gammaglobulin 8.8 g/l, alkaline phosphatase 137 IU (normal <92). Results of urine analysis, complement profile, hepatitis B surface antigen, smooth muscle, antimitochondrial and anti-centromere antibodies, cryoglobulins, cold agglutinins, rheumatoid factor, and screening test for syphilis were all normal or negative. The test for antinuclear antibodies was positive with a titre of 1/2560 in a speckled pattern. An ultrasonographic study of the abdomen disclosed several hyperechogenic areas within the liver. A percutaneous needle biopsy was carried out and microscopical examination showed infiltration by moderately differentiated adenocarcinoma. Her primary malignant disease remained undiagnosed despite further examinations. Treatment was suggested for her symptoms and the patient was discharged; her Raynaud’s phenomenon did not worsen. She died four months later. A necropsy was not allowed.

Discussion
Raynaud’s phenomenon is generally classified as primary when no associated condition explains its presence and secondary when accompanied by one of several disorders.1 Raynaud’s phenomenon secondary to neoplasia has rarely been reported,4–8 except when related to chemotherapeutic treatment.9 The most common histological variant found was adenocarcinoma, usually in an advanced stage. The vascular symptoms may be poor, as in our patient, but typically onset is acute, bilateral with persistent ischaemic manifestations that often progress to digital necrosis.4–8 Sometimes Raynaud’s phenomenon may improve after tumour treatment.7–8

The presence of antinuclear antibodies is common in connective tissue diseases, but they have been associated with malignancies, also. Moreover, it has been suggested that malignant disease should be suspected in patients with a positive antinuclear antibody test in whom there is no evidence of connective tissue disease or drugs taken associated with antinuclear antibody induction.10–12 These antibodies are probably an epiphomenon and are usually detected in a low titre.4 12 The speckled pattern found in the case reported here has often been found associated with malignancies and it seems to be related to novel specific antigenic determinants.4 13

The association of Raynaud’s phenomenon and a positive antinuclear antibody test is common in connective tissue diseases, such as scleroderma and systemic lupus erythematosus, but extremely rare in malignant diseases.5

In this patient, with metastatic adenocarcinoma of unknown primary site, there was no evidence of any signs or symptoms of aetiological factors that might explain the
presence of antinuclear antibodies and Raynaud's phenomenon. Thus we believe that these features were both related to her malignant disease. Thus the possibility of a malignancy should be borne in mind when there is sudden development of Raynaud's phenomenon or a positive antinuclear antibody test, or both, in the absence of any other disorder.

Raynaud's phenomenon and positive antinuclear antibodies in a malignancy.

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