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- Loeliger A E, Kruize A A, Bijlsma J W J, Derksen R H W M. Arthritis in hyperimmunoglobulinaemia D. *Ann Rheum Dis* 1993; 52: 81.
- Prieur A M, Griscelli Cl. Aspect nosologique des formes systémiques d'arthrite juvénile à début très précoce. A propos de dix-sept observations. *Ann Pédiatr* 1983; 30: 565-9.
- Hiemstra I, Vossen J M, Van Der Meer J W M, Weemaes C M R, Out T A, Zegers B J M. Clinical and immunological studies in patients with increased serum IgD level. *J Clin Immunol* 1989; 9: 393-400.
- Haraldson A, Weemaes C M R, De Boer A W, Bakkeren J A J M, Stoelinga G B A. Immunological studies in the hyperimmunoglobulin D syndrome. *J Clin Immunol* 1992; 12: 424-8.
- Prieur A M, Ansell B M, Bardfeld R, et al. Is onset type evaluated during the first three months of disease satisfactory for defining the sub-groups of juvenile chronic arthritis? A EULAR cooperative study (1983-1986). *Clin Exp Rheumatol* 1990; 8: 321-5.
- Van der Meer J W M, Vossen J M, Radl J, et al. Hyperimmunoglobulinaemia D and periodic fever: a new syndrome. *Lancet* 1984; i: 1087-90.

Buerger's disease and antiphospholipid syndrome

Sir: Casellas *et al* reported a patient in whom arterial occlusions were found in association with anticardiolipin antibodies.¹ The authors discussed the diagnosis of Buerger's disease (thromboangiitis obliterans) and the relation with the antiphospholipid syndrome.

Buerger's disease is an uncommon vasculitis of unknown cause, in which tobacco is implicated. Diagnosis is difficult because clinical, anatomopathological, and arteriographic features are not specific. Cell mediated sensitivity to collagen was reported to be helpful in diagnosis,² but was not specific.³ Several diagnostic criteria have been proposed.⁴ Adar and Mozes suggested that positive and negative criteria might be used for diagnosis.^{2,5} Thus these authors considered that other causes of arterial occlusions, such as coagulation disorders, systemic diseases, or embolism, rule out the diagnosis of Buerger's disease.²

The patient described by Casellas *et al* presented with repetitive intrauterine fetal deaths, mild thrombopenia, and a significant level of anticardiolipin antibodies without evidence of systemic lupus erythematosus. A diagnosis of primary antiphospholipid syndrome could be made. The major arterial lesions of the patient were in agreement with those now well recognised in the antiphospholipid syndrome.⁶⁻¹⁰ The range of histopathological changes seen in antiphospholipid arterial vasculopathy is quite different from changes in Buerger's disease.¹⁰ The acute lesions of Buerger's disease are associated with an intense mixed cell inflammatory infiltrate. This is not present in patients with antiphospholipid vasculopathy, in whom thrombosis appears at various stages of thrombus organisation, and not vasculitis.⁹

We conclude that the patient described by Casellas *et al*, even if she fulfilled the criteria

of probable Buerger's disease according to McPherson, should not be considered to have this disease. The negative criteria of Adar and Mozes should be taken into account, thus preventing overdiagnosis of Buerger's disease and avoiding the risk of misdiagnosis of a more common and curable disease and delay of urgent specific treatment.

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- Casellas M, Pérez A, Cabero L, Segura A, Puig de Morales E, Selva O'Callaghan R. Buerger's disease and antiphospholipid antibodies in pregnancy. *Ann Rheum Dis* 1993; 52: 247-8.
- Adar R, Papa M Z, Halpern Z, et al. Cellular sensitivity to collagen in thromboangiitis obliterans. *N Engl J Med* 1983; 308: 1113-6.
- Smolen J S, Weidinger P, Menzel E J. Sensitivity to collagen in thromboangiitis obliterans. *N Engl J Med* 1983; 309: 857-8.
- McPherson J R, Juergens J L, Gifford R W. Thromboangiitis obliterans and atherosclerosis obliterans. Clinical and prognostic differences. *Ann Intern Med* 1963; 59: 288-96.
- Mozes M, Cahansky G, Doitsch V, Adar R. The association of atherosclerosis and Buerger's disease: a clinical and radiological study. *J Cardiovasc Surg* 1970; 11: 52-9.
- Jindal B K, Martin M F R, Gayner A. Gangrene developing after minor surgery in a patient with undiagnosed systemic lupus erythematosus and lupus anticoagulant. *Ann Rheum Dis* 1983; 42: 347-9.
- Asherson R A, Harris E N, Gharavi A E, et al. Arterial occlusions associated with antibodies to cardiolipin [Abstract]. *Arthritis Rheum* 1985; 28: S89.
- Asherson R A, Derksen R H W M, Harris E N, et al. Large vessel occlusion and gangrene in systemic lupus erythematosus and "lupus-like" disease. A report of six cases. *J Rheumatol* 1986; 13: 740-7.
- Lie J T. Vasculopathy in the antiphospholipid syndrome: thrombosis or vasculitis, or both? *J Rheumatol* 1989; 16: 713-5.
- Alarcón-Segovia D, Cardiel M H, Reyes E. Antiphospholipid arterial vasculopathy. *J Rheumatol* 1989; 16: 762-7.

AUTHORS' REPLY: Puéchal *et al* suggest that the patient we described recently in the *Annals*¹ had primary antiphospholipid syndrome (PAS) rather than Buerger's disease.

The authors adduce histological differences between these two conditions: in Buerger's disease the primary lesion is vasculitis, whereas in PAS it is thrombosis. Although correct, this fact does not exclude, in our opinion, a possible association: it is theoretically possible that vasculitis, by causing endothelial cell damage, might have triggered the reaction of antiphospholipid antibodies with negatively charged phospholipids on these cells, as described by Alarcón-Segovia *et al*.²

Puéchal also suggests, based on the negative criteria of Adar and Mozes,³ that diagnosis of another associated disease should exclude Buerger's disease. The paper published by Adar was designed to examine the 'possible relationship between Buerger's disease and atherosclerosis by clinical and radiological analysis of young patients with ischaemic disease of the lower extremities'. Patients with evidence of embolism, trauma, or collagen disease were excluded from the study group, but, in our opinion, these diseases were not defined as negative criteria for the diagnosis of Buerger's disease. A clinical diagnosis of Buerger's disease was

made by Adar when, in addition to ischaemic manifestations in the legs, two or more of the following systemic manifestations were present: migrating phlebitis; vasospastic elements—such as Raynaud-like phenomena—in hands or legs, or both; and ischaemic manifestations in the arms.

Although there were grounds for diagnosing Buerger's disease in our patient in accordance with McPherson, we did in fact point out in our paper that the clinical picture might be attributed entirely to PAS. However, given the possible association, we tested 13 patients diagnosed in our hospital as having Buerger's disease over the past three years for the presence of antiphospholipid antibodies; these were absent in all cases. Although this suggests that these two conditions are not related, further studies are needed to confirm this. Otherwise there will be a risk of failing to establish a possible, though unlikely, association between two conditions of as yet unknown cause.

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- Alarcón-Segovia D, Cardiel M H, Reyes E. Antiphospholipid arterial vasculopathy. *J Rheumatol* 1989; 16: 762-7.
- Mozes M, Cahansky G, Doitsch V, Adar R. The association of atherosclerosis and Buerger's disease: a clinical and radiological study. *J Cardiovasc Surg* 1970; 11: 52-9.

LETTERS TO THE EDITOR

Erythema induratum and pulmonary tuberculosis

Sir: Erythema induratum, first described by Bazin in 1861,¹ is an uncommon inflammatory skin disease pathologically characterised by nodular vasculitis.² Erythema induratum occurs mainly in women and features recurrent, painful, subcutaneous nodules generally found on the lower legs, which usually deteriorate in winter.² A direct correlation with *Mycobacterium tuberculosis* infection has been found. Rarely, however, an active tuberculous focus has been reported.³ On the other hand, it is well known that mycobacterial infections can be associated with raised titres of rheumatoid factor (RF).⁴ Recently, we studied a woman with erythema induratum who had high levels of RF and active pulmonary tuberculosis. After specific chemotherapy the skin lesions disappeared and RF fell to normal.

A 35 year old woman was referred to the rheumatology unit of this hospital because of

a two year history of recurrent painful violet erythema nodular lesions associated with high levels of RF (latex; range 1048–2000 U/ml). She denied asthenia, weight loss, fever, and had no respiratory or articular complaints.

On physical examination many scattered, painful, tender and slightly raised violet subcutaneous nodules were found on the posterior aspects of both calves. The patient was afebrile. Results of cardiopulmonary and abdominal explorations were unremarkable. White blood cell and platelet count were normal. The haemoglobin was 126 g/l and erythrocyte sedimentation rate 18 mm/1st h. Urea nitrogen, creatinine, glucose, bilirubin, aspartate transaminase, alkaline phosphatase, cholesterol, triglycerides, calcium, and phosphorus were all normal. A positive purified protein derivative skin test, antinuclear antibodies, cryoglobulins, and serum complement (C3 and C4) were unremarkable. Serum RF determined by turbidimetric immunoassay was 2048 U/ml (Quantex RF plus—latex; WHO units). Rheumatoid factor determined by haemagglutination on slide (modified Waaler-Rose procedure) was 256 U/ml (Celarkit AR; Biokit SA, Spain; WHO units).

Chest films showed a fibroproductive pattern affecting both upper lung lobes without paratracheal or perihiliary adenopathies. Microscopic examination of three sputum specimens stained by Ziehl-Neelsen's method disclosed no acid-fast bacilli. A wedge biopsy of one skin nodule was performed and pathological examination disclosed a granulomatous panniculitis consistent with erythema induratum (figure). Ziehl-Neelsen and auramine-rhodamine stains were negative. Sputum cultures in Löwenstein-Jensen medium grew *M tuberculosis*.

Specific daily treatment with rifampicin 600 mg, isoniazid 300 mg, and pyrazinamide 1500 mg was started and continued for two months. Rifampicin and isoniazid was continued for four more months at the same dose. The two Mantoux tuberculin skin tests (5 tuberculin units of purified protein derivative) performed while the patient was receiving chemotherapy were negative. At the end of the first, third, and sixth months of treatment, RF had decreased to 600, 200, and 44.2 U/ml respectively. The patient remained asymptomatic, and skin lesions healed leaving a pigmented scar.

Erythema induratum, included in the tuberculids, is not a 'true' manifestation of skin tuberculosis because acid-fast bacilli are not

found.² Although *M tuberculosis* has occasionally been isolated when erythema induratum coincides, most authors support its aetiological role.³ Nodular vasculitis is a form of multifactorial lobular panniculitis that may coexist with a tuberculous focus (erythema induratum of Bazin) or may not (nodular vasculitis erythema induratum complex). Throughout the two year follow up of our patient no nodule became ulcerated and the lesions healed with specific chemotherapy.

Rheumatoid factors in low titres are found in a small percentage of young adults. A high prevalence of RF is also found in patients with chronic infections, such as syphilis, leprosy, and tuberculosis. These observations have suggested that extensive or persistent exposure to antigens and immune complex formation induces the synthesis of RF.⁴ *M tuberculosis* antigens can induce the production of RF, and several reports have demonstrated the autoimmunogen capacity of some proteins of this microorganism, particularly heat shock protein 60.⁵

Immune complexes seen to have an important pathogenic role in nodular vasculitis.⁶ They have been found in patients with Henoch-Schönlein purpura associated with active tuberculous infection.⁷ It should be pointed out that in our patient autoimmune diseases with increased RF levels, such as rheumatoid arthritis, Sjögren's syndrome, cryoglobulinaemia, and autoimmune liver disease, were excluded. Moreover, after treatment was started RF progressively fell to nearly normal values.

The persistent negativity of the Mantoux skin test deserves a special mention. It is unlikely that the patient had disseminated tuberculosis or any other immunosuppressive condition. A negative Mantoux skin test has been described in patients with erythema induratum.² There is no doubt about the importance of the skin biopsy as it allows histological demonstration of erythema induratum and helps to establish the differential diagnosis with erythema nodosum, syphilis, foreign body granuloma, and skin tuberculosis.^{8,9} Finally, we strongly believe that the finding of erythema induratum should prompt a diagnostic search for pulmonary or extrapulmonary involvement of tuberculous infection.

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- 1 Feiwel M, Munro D D. Diagnosis and treatment of erythema induratum (Bazin). *BMJ* 1965; **i**: 109–11.
- 2 Bondi E E, Lazarus G S. Panniculitis. In: Fitzpatrick T B, Eisen A Z, Wolff K, Freedberg I N, Austen K F, eds. *Dermatology in general medicine*, 3rd ed. New York: McGraw-Hill, 1987: 140–1.
- 3 Hassoun P M, Shepherd K E, Flotte T T, Kazemi H. Erythema induratum and active pulmonary tuberculosis. *Am J Med* 1988; **84**: 784–5.
- 4 Bartfield H. Distribution of rheumatoid factor activity in non-rheumatoid states. *Ann NY Acad Sci* 1969; **168**: 30–8.
- 5 Rook G, Lydyard P, Stanford J. Mycobacteria

and rheumatoid arthritis. *Arthritis Rheum* 1990; **33**: 431–5.

- 6 Parish W E, Rhodes M D. Bacterial antigens and aggregated gamma-globulin in the lesions of nodular vasculitis. *Br J Dermatol* 1967; **79**: 131–47.
- 7 Pacheco A, Mateos P, Medina J, Guisasola L, Carrillo F, Pérez-Oleiza J. Tuberculosis pulmonar y púrpura de Schönlein-Henoch. *Rev Clin Esp* 1987; **180**: 515.
- 8 Niemi K M, Forstrom L, Hannuksela M, Mustakallio K K, Salo O P. Nodules on the legs. A clinical, histological and immunohistological study of 82 patients representing different types of nodular panniculitis. *Acta Derm Venereol (Stockh)* 1977; **57**: 145–54.
- 9 Harahap M. Tuberculosis of the skin. *Int J Dermatol* 1983; **22**: 524–45.

CREST syndrome with pericardial but not peripheral calcinosis

Sir: The CREST subgroup of systemic sclerosis is a mild or slowly progressive form of the disease characterised by calcinosis, Raynaud's phenomenon, oesophageal dysfunction, sclerodactyly, and telangiectasia.¹ Anticentromere antibodies detected on the Hep-2 substrate appear highly selective for this group of patients.² In the Johns Hopkins series calcinosis was present in all patients with CREST, being peripheral or around joints in the majority.¹ Patients with CREST do develop internal organ manifestations but usually only in the second and third decades of their disease.³ We describe a patient with the CREST syndrome who presented with dyspnoea due to calcific pericarditis without peripheral calcinosis.

A 65 year old white female smoker presented to her general practitioner with shortness of breath in August 1989. He detected an expiratory wheeze and prescribed amoxycillin. Her pulse was 160 beats/min, and she was referred to a cardiologist. She was in atrial flutter with 2:1 block and had signs of 'mild congestive heart failure'. The jugular venous pressure was raised 9 cm. A chest radiograph showed a cardiothoracic ratio of 58% with upper lobe venous diversion. She was anticoagulated and cardioverted but atrial flutter recurred, and her ventricular rate was controlled with verapamil, digoxin, and a diuretic. The patient had a six year history of Raynaud's phenomenon and was noted to have facial telangiectasia and mild sclerodactyly. Further investigation showed a positive anticentromere antibody and negative antinuclear and Scl-70 (topoisomerase 1) antibodies. A barium study showed markedly reduced oesophageal motility. A diagnosis of CREST syndrome was made, though no calcinosis had been detected either clinically or radiologically. She gained symptomatic relief from wearing heated gloves and using cisapride, having been intolerant of H₂ blockers.

Although there was improvement in her dyspnoea, the jugular venous pressure remained raised. In March 1991 she reported increasing shortness of breath on exertion and swelling of the legs. Her jugular venous pressure was 8 cm raised with a positive Kussmaul's sign and pulsus paradoxus of 30 mmHg. A lateral chest radiograph showed marked pericardial calcification (figure) that had not been apparent on previous postero-anterior views. There was no history of tuberculosis or tuberculous contacts. The possibility of an operation to relieve her tamponade was discussed, but the patient refused.

Nodular panniculitis. Some granulomata show caseous central necrosis (haematoxylin and eosin).