ed to catastrophic APS (CAPS). The precipitating factors for CAPS are debatable.

Since 1968, when the patient was 16, a bleeding tendency attributed to a decreased activity of coagulation factors II and V and the presence of inhibitors to factor IX had been apparent. The factor V deficiency was not further defined. The patient has been regularly taking the antifibrinolytic agent cyclocapron during menses.

Her diagnosis of PAPS was established in 1989 (age 37 years), based on the following clinical and laboratory criteria: a history of one stillbirth and one foetal loss, livedo reticularis and highly increased IgG aCL (1). A mild decline in renal function was noted in 1992, followed by moderate hypertension in 1994.

In April 1996, SLE was diagnosed due to Coombs positive haemolytic anaemia, thrombocytopenia, positive ANA and anti-dsDNA antibodies, renal affection (creatinine 263 mmol/L) with haematuria and proteinuria, arthritis and arthralgias (2). Echocardiography showed hypertensive myocardial changes and aortic and mitral valve lesions. Treatment with a high dose of methylprednisolone was instituted with rapid improvement. The dose was gradually tapered to the maintenance dose of 8 mg o.d. Renal biopsy was abandoned because of haemorrhagic diathesis. However, upon steroid therapy the bleeding disorders vanished and treatment with the antifibrinolytic was withdrawn.

The patient was readmitted to our hospital in April 1997 because of rapidly progressive renal insufficiency (creatinine 470 mmol/L on admission) and congestive heart failure. The results of immunoserological tests were as follows: highly positive IgG aCL, positive LA and ANA, negative anti-ENA and anti-dsDNA, positive direct and indirect Coombs test, normal C3 and slightly lowered C4 complement component. Echocardiography revealed pericarditis, dilated and poorly contractile left ventricle and haemodynamically significant aortic stenosis and regurgitation. Despite aggressive treatment, including haemodialysis, she died a few days later. Heart rupture found on autopsy was considered the direct cause of death.

Pathomorphologic changes were consistent with CAPS. Additionally, in several organs, including the kidneys, signs of chronic thrombotic microangiopathy were seen (3). Glomerulonephritis was estimated as WHO class IIA (4). No overt vasculitic lesions or granular vascular immune complex deposits, typical of SLE, were noted.

In analysing the clinical course, three points deserve to be noted. First, the patient had concomitant bleeding disorders and APS for a long period of time. A paradoxical bleeding tendency in patients with antiphospholipid antibodies has already been reported (5, 6). Second, despite the fact that the patient later fulfilled the ARA diagnostic criteria for SLE (secondary APS), post-mortem histomorphological changes suggested that a thrombotic tendency related to APS was the major cause of renal and heart failure. Anticoagulant therapy was not introduced for the treatment of APS due to the patient's haemorrhagic diathesis.

Third, it is not clear why upon steroid treatment the bleeding disorders disappeared and the thrombotic tendency escalated. It may be speculated that decreased activity of coagulation factors II, V and IX were secondary to the autoantibodies directed towards them, and that steroids suppressed their production (7). Additionally, it is also possible that the deficiency of factor V was due to patient's pseudohomozygosis for activated protein C resistance (APC-R), which paradoxically predisposed to thrombosis (8).

The ultimate precipitating factor for CAPS was most probably infection, as in the majority of such cases (9, 10). In fact, autopsy confirmed bilateral pneumonia, already suspected clinically. This clinical case illustrates the complexity of haemostatic disorders that may coexist in patients with secondary APS, and the potential danger of steroid therapy in such circumstances.

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A case of Takayasu's arteritis with parenchymal pulmonary involvement associated with spondylarthropathy

Sirs,

We report a case of a woman affected by Takayasu's arteritis (TA) with pulmonary parenchymal involvement and spondylarthropathy (SpA). The association of TA with SpA has been already reported, but pulmonary involvement was found in only one of these patients (1). Although the large and medium branches of the pulmonary arteries may be affected in TA (2), pulmonary parenchymal involvement, caused by vasculitis of the small and medium vessels, is very rare (3).

A 17-year old Caucasian female presented in June 1999 with a twelve-month history of arthralgia of her knees, shoulders and bilateral buttock pain. There was tenderness over her sacroiliac and sterno-costal joints. ESR was 57 mm/1sthour, CRP 2.4 mg/dl; antinuclear antibodies, rheumatoid factor and-HLA-B27 were negative. Radiographs showed grade-3 bilateral sacroiliitis (4) and erosive pubitis. Other causes of SpA were excluded and her condition was classified as undifferentiated spondylarthropathy (4). She was started on sulphasalazine 1 g *bid*.

At her periodic review (August 2001) she reported no joint symptoms, but mild exertional dyspnoea and remitting neck pain. On examination radial pulses were absent, BP was undetectable in her upper limbs and a right carotid bruit was audible; ESR was 33 mm/1sthour, CRP 2.1 mg/dl. Arteriography demonstrated stenosis of the brachio-

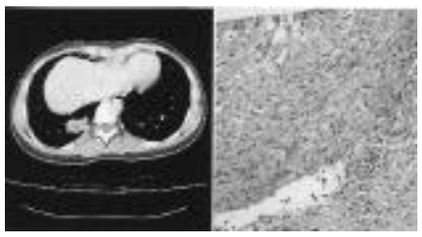

Fig. 1. (**Left**) Contrast-enhanced thoracic CT scan showing a 3 cm diameter mass with a low-density central area in the right posterior basal segment, adjacent to the parietal pleura. (**Right**) Lung biopsy specimen showing an organized thrombus with prominent endovascular recanalisation associated with a granulomatous process within the arterial wall,including multinucleated giant cells, mononuclear infiltration and local periarteritis (hematoxylin-eosin, 20x).

cephalic trunk and total occlusion of the left common carotid and left subclavian artery, with collaterals from the left suprascapular and intercostal arteries. Pulmonary artery pressure was normal on echocardiogram. A consolidation found on chest X-ray was confirmed on thoracic CT scan as a 3 cm diameter mass in the right posterior basal segment (Fig. 1). A needle biopsy showed an organized thrombus with prominent endovascular recanalisation and a granulomatous process within the arterial wall (Fig. 1). The diagnosis of TA with pulmonary parenchymal involvement in the pulseless phase was made (2, 3, 5).

The patient underwent surgical revascularisation with by-pass and was started on prednisone (1 mg/kg), methotrexate (10 mg/m^2/week)and low-dose aspirin. In January 2002 the pulmonary lesion was reduced on CT; at present she continues therapy with methotrexate and aspirin and remains asymptomatic with no signs of active disease (6).

A few cases of TA associated with SpA have been described previously; in these cases both sexes were affected, ages ranged from 15 to 55 years, most patients were HLA-B27 positive; inflammatory bowel disease was reported in two cases (7,8),and the diagnosis of SpA always preceded that of TA. The few reported cases are insufficient to establish a clear link between TA and SpA but they point to common etiological factor(s) and patho genetic mechanisms (i.e. molecular mimicry based on antigenic homologies between the aorta and bone entheses (9, 10)). Also, aortitis or aortic valve disease in SpA and articular manifestations in TA may be an expression of the link between the two disease.

The only case of SpA associated with TA and pulmonary involvement (1) was similar to our patient in terms of age, sex and the diagnosis of SpA preceeding that of TA. In that case, pulmonary involvement manifested as pleuritic chest pain, fever, and pulmonary infarction documented by chest X-ray and ventilation/perfusion lung scan; in our patient it manifested as exertional dyspnoea and coin lesion on CT scan (Fig. 1). The biopsy of the lesion - not performed in the first case (1) showed histopathological features (Fig. 1) identical to those described as type B lesion by Lie (3) in his series of patients with isolated pulmonary TA. Organized thrombus with prominent recanalization and neoangiogenesis is specific for pulmonary TA, allowing histopathologic differentiation from other lesions such as those found in pulmonary hypertension, granulomatous diseases or vasculitides (3).

In conclusion,our case provides further evidence of the association of TA with SpA. This is the second report of such an association with pulmonary vasculitis and in our case the diagnosis of parenchymal involvement is supported by histopathological findings.

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Molecular cloning and sequence analysis of variant TNF-α transcripts do not indicate a significant role of gene polymorphism in collagen-induced arthritis

Sirs,

In rheumatoid arthritis (RA) tumor necrosis factor alpha (TNF-α) mediates significant proinflammatory events (1). The TNF-α gene is characterized by a variety of polymorphisms but these variations were rarely correlated with RA severity (2-4) The exact biological function and significance therefore remains unclear (5). We wished to study these variations in collagen-induced arthritis (CIA) because inbred animals models greatly facilitate genetic experimentation.

RNA was obtained with a standard Trizol procedure from Dark Agouti rats with severe CIA (n = 8) from previous experiments (6). Investigated tissues included synovium form arthritis. normal joints and healthy spleens. cDNA synthesis was performed using 600 ng DNase treated RNA (Boehringer Mannheim, Germany) with a superscript reverse transcriptase kit (Life Technologies, France). PCR for the rat TNF-α propeptide was adapted from a previously described protocol (7). PCR products were isolated from an agarose gel, purified by electrolution and ligated into a pGEM-T vector (Promega, France). Colonies were screened by TNF-α PCR and cloned. DNA sequencing was performed with a conventional two-directional thermosequenase reaction (Promega) and bidirectional automated sequencing analyses (MWG Biotech, Germany). The sequences were registered at the NIH gene bank. To confirm the presence of intact RNA in inflamed tissue, ribonuclease protection assays (RPA) were performed as previously described (8).

RT-PCR yielded a fragment of 700 bp similar to previous reports (7). DNA sequencing confirmed two distinct cloned inserts (TNF3 and TNF5, NIH accession number AF269160 and AF269159). The 705 bp sized fragment and the open reading frame corresponded to previous results from rat