focus score of one lymphocyte focus for 4 mm^2 salivary gland tissue. Additionally, thyroid function tests showed a raised thyroid stimulating hormone (11 mU/l), low free thyroxine 4 (13.0 pmol/l) with positive antithyroid microsomal antibodies and negative antithyroglobulin antibodies.

The clinical, serological, and histopathological manifestations fulfilled the European study group criteria for the diagnosis of SS. The patient was treated with artificial tears and thyroxine supplements that returned her thyroid function tests to normal.

Prevalence of neuropathy in patients with SS ranges from 10 to 50%.[2] Polyneuropathy can be the first clinical manifestation of SS and may even precede sicca symptoms in 40% of patients.[3] However, less frequently, cranial neuropathy can occur with a predisposition to involvement of the trigeminal nerve.[4] The vasculitic damage to vaso nervorum documented by pathological studies is associated with a higher incidence of serum anti-SS-A (Ro) antibodies.[5] The association of SS with autoimmune thyroid disease (AITD) is well recognised.[6 7] AITD and SS share similarities in the immunopathology in addition to their genetic linkage to the HLA-DR3/DR4 alleles.[7] Only nine cases of facial nerve involvement associated with SS have been described previously.[1 8–10]

This case illustrates how facial palsy disclosed the primary SS as an underlying systemic disorder. To our knowledge the combination Bell's palsy as presenting feature in a patient with SS, and hypothyroidism secondary to AITD has not been reported hitherto.

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α_1 Antitrypsin phenotypic variability is not associated with ANCA in southern Chinese

α_1 Antitrypsin (α_1AT) is a 52 kDa proteinase encoded by a gene locus Pi on chromosomal segment 14q32.1. It is a natural inhibitor of proteinase 3 (PR3), a neutrophil granular protein and a major autoantigen of antineutrophil cytoplasmic antibody (ANCA). The function of α_1AT is in turn restricted by myeloperoxidase (MPO), another autoantigen of ANCA. The interplay between the enzymes, inhibitors, and the autoantibodies is implicated in the dynamics of the vasculitic process,[1] resulting in a whole spectrum of clinical conditions ranging from systemic granulomatous diseases to kidney limited glomerulonephritis. There have been reports of the correlation of specific α_1AT alleles, notably Pi^Z, with ANCA.[2–4] These were largely studies of white subjects, which may not necessarily be extrapolated to all populations.

α_1AT variant phenotypes may have predisposed to PR3-ANCA, but the same association may not exist for MPO-ANCA. In populations with a low prevalence of α_1AT variant phenotypes, the pattern of ANCA could differ from that in white subjects where such variants prevail. We set out therefore to establish the distribution of α_1AT in patients with the two main forms of ANCA (anti-PR3 positive and anti-MPO positive). Blood samples of patients with vasculitis received at the immunology section of the Department of Pathology, Queen Mary Hospital, Hong Kong, were tested for ANCA by indirect immunofluoresence, followed by enzyme linked immunosorbent assays (ELISA) for anti-PR3 and anti-MPO. α_1AT phenotypes were determined by isoelectric focusing, the results of which were compared with those of healthy Chinese adults.

A total of 157 samples from ANCA+ (either anti-MPO or anti-PR3 positive by ELISA) patients were evaluated, 60 (38%) of which were positive for anti-PR3 and 97 (62%) for anti-MPO by ELISA. All were Chinese patients with a clinical diagnosis of vasculitis. The male to female ratio was 0.76 (0.94 for anti-PR3 positive and 0.67 for anti-MPO positive patients). The mean age of the two groups was 52.4 and 59.4 years, respectively. A total of 103 (66%) were homozygous M, 50 (32%) heterozygous M (for example, M1 M2), and 4 (3%) heterozygous for M and a variant allele. Tables 1 and 2 show the allelic and phenotypic frequencies. In the healthy controls (n=1085), 717 (66.1%) were homozygous for an M phenotype. Allelic variants were rare, accounting for only 0.7% of all alleles. The α_1AT deficiency variant Pi^Z was absent in both the study group and the healthy control group. There was no significant difference in the proportion of homozygous and heterozygous M phenotypes between the normal and the ANCA+ group (exact χ^2 test, p=0.56) and between anti-PR3 and anti-MPO (exact χ^2 test, p=0.80). ANCA+ patients had a higher proportion of variant alleles, but this did not reach significance (1.26% *v* 0.70%; exact χ^2 test, p=0.10).

The rarity of the Pi^Z allele in oriental[5] and black populations[6] has been previously reported, a finding which is confirmed for Chinese patients in this study. We found no association of α_1AT variant phenotypes with ANCA in Chinese patients. It is interesting to note the higher number of anti-MPO positive patients in the study group. In a separate study the anti-MPO to anti-PR3 ratio in Chinese patients diagnosed over a defined period was 1.4:1 (the reverse of the situation in white populations, where PR3-ANCA positive Wegener's granulomatosis is much more common).[7] Even for the Chinese patients who tested positive for PR3-ANCA, the positive predictive value for Wegener's granulomatosis was less than 25%. The low prevalence of α_1AT variant phenotypes may be one factor behind the uncommon presence of anti-PR3 in Chinese people. We conclude that α_1AT does not have a significant role in ANCA

Table 1 α_1 Antitrypsin phenotypes in ANCA (anti-PR3* or anti-MPO*) positive patients*

Phenotypes	*All ANCA+ No (%)*	*Anti-PR3+ No (%)*	*Anti-MPO+ No (%)*
Homozygous M			
M1 M1	99(63)	36(60)	63(65)
M2 M2	4(3)	2(3)	2(2)
M3 M3	0(0)	0(0)	0(0)
M4 M4	0(0)	0(0)	0(0)
Heterozygous M			
M1 M2	48(31)	20(33)	28(29)
M1 M3	0(0)	0(0)	0(0)
M2 M3	2(1)	0(0.0)	2(2)
Other heterozygous			
M1 S	2(1)	1(2)	1(1)
M2 S	0(0)	0(0)	0(0)
M1 other	2(1)	1(2)	1(1)
M2 other	0(0)	0(0)	0(0)
Total	157(100)	60(100)	97(100)

*ANCA = antineutrophil cytoplasmic antibody; PR3 = proteinase 3; MPO = myeloperoxidase.

Table 2 α_1 Antitrypsin alleles in ANCA (anti-PR3* or anti-MPO*) positive patients*

Allele	*All ANCA+ No (%)*	*Anti-PR3+ No (%)*	*Anti-MPO+ No (%)*
M1	250(80)	94(78)	156(80)
M2	58(18)	24(20)	34(18)
M3	2(1)	0(0)	2(1)
M4	0(0)	0(0)	0(0)
S	2(1)	1(1)	1(0.5)
Z	0(0)	0(0)	0(0)
Other	2(1)	1(1)	1(0.5)
Total	314(100)	120(100)	194(100)

*ANCA = antineutrophil cytoplasmic antibody; PR3 = proteinase 3; MPO = myeloperoxidase.

associated diseases in southern Chinese among whom anti-MPO predominate.

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A case of cholesterol embolism with ANCA treated with corticosteroid and cyclophosphamide

We report a case of a patient with cholesterol embolism who showed positive for both myeloperoxidase antineutrophil cytoplasmic antibody (MPO-ANCA) and proteinase 3 antineutrophil cytoplasmic antibody (PR3-ANCA) and who was treated with prednisolone (PSL) and cyclophosphamide.

A 50 year old man underwent cardiac catheterisation for back pain. The examination disclosed 90% stenosis of the right coronary artery and a saccular aneurysm in the thoracic aorta. The patient underwent percutaneous transluminal coronary angioplasty and the aneurysm was wrapped with an artificial blood vessel. Postoperatively, the patient had a fever, pleural effusion, abdominal pain, and increased white blood cell (WBC) count, C reactive protein (CRP), and serum creatinine. Cultures of blood and pleural effusion exudate were negative. PSL 15 mg/day was started. However, acute progression of renal failure required haemodialysis.

The patient was transferred to our hospital. Physical examination showed a temperature of 38.0°C and blood pressure of 178/98 mmHg. Cyanosis was noted in both heels and all toes with necrosis and ulcers at the tips of the fifth toes. He had an increased erythrocyte sedimentation rate (ESR) of 82 mm/1st h. Anaemia was noted with a red blood cell count of 2500×10^9/l, while the patient's WBC count was high at 12×10^9/l. His platelet count (304×10^9/l) was within the normal range. Biochemistry showed high levels of blood urea nitrogen (10.0 mmol/l of urea), creatinine (710 μmol/l), and CRP (11.3 mg/l). Complements components were within normal ranges. PR3-ANCA and MPO-ANCA were high at 82E and 29E, respectively.

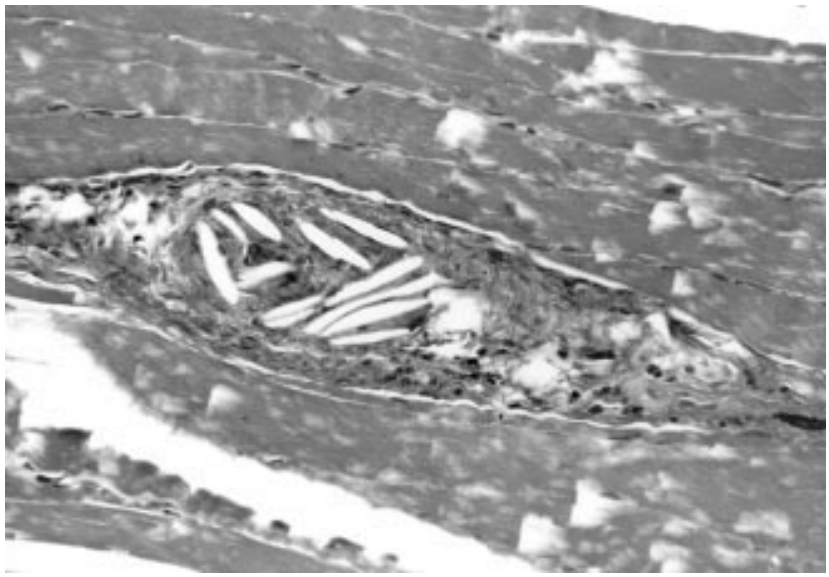

Figure 1 Skin biopsy specimen showing cholesterol embolism in arterioles within subcutaneous tissues (haematoxylin and eosin, × 400).

After admission to hospital, circulatory disturbance in his toes worsened. A diagnosis of ANCA associated vasculitis was made based on systemic inflammatory findings and high levels of WBC, CRP, PR3-ANCA, and MPO-ANCA. High dose steroid treatment was started. Biopsies of the right heel skin and thigh quadriceps showed cholesterol embolism (fig 1). However, PSL treatment was continued together with three courses of cyclophosphamide pulse treatment because of persistent fever and high ANCA values. The treatment reduced the fever and toe necrosis, and the ulcers improved. ANCA gradually decreased to normal. The PSL dosage was reduced to 15 mg/day and the patient was discharged.

Cholesterol embolism predominantly affects elderly men with a history of hypertension, atherosclerotic vascular diseases, and renal insufficiency at the time of diagnosis. At least 31% of patients had a preceding history of anticoagulant use or the antecedent performance of a vascular procedure affecting the arterial circulation.[1] The presence of these cholesterol embolisms within the vascular lumen triggers a characteristic localised inflammatory and endothelial vascular reaction. The inflammatory changes resulting from cholesterol embolism may be responsible for many of the systemic manifestations such as fever, weight loss, myalgias, leucocytosis, eosinophilia, and a raised ESR. Thus cholesterol embolism is referred to as both vasculitis look-alikes[2] and pseudovasculitic syndrome.[3] The prognosis is poor, particularly in the presence of acute renal failure.[4]

Three ANCA positive cases[5 6] of cholesterol embolism have been described. Peat and Mathieson reported an ANCA positive patient with dyspnoea and haemoptysis after acute deterioration of renal function.[5] Cyclophosphamide and PSL improved the symptoms, but cyclophosphamide was discontinued and the PSL dose was reduced because renal and skin biopsies showed cholesterol embolisms. Subsequently, the patient died of intractable cardiac failure.

Kaplan-Pavlovcic *et al* reported two cases of renal failure with positive MPO-ANCA.[6] The details are unknown for one patient. The other patient was treated with corticosteroid alone. This patient required haemodialysis and amputation of the toes. Although their treatment did not result in the improvement of vasculitis, the combination of PSL and cyclophosphamide was effective in our patient with ANCA.

This result suggests that active treatment with corticosteroid and cyclophosphamide should be considered in ANCA positive cases of cholesterol embolism.

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