Case report

Chronic Q fever with mixed cryoglobulinaemia

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SUMMARY A 47 year old woman presented with a six month history of vasculitic rash, splenomegaly, and cardiac murmurs. Investigations showed the presence of mixed cryoglobulinaemia and raised titres to *Coxiella burnetii* consistent with chronic Q fever infection. The patient was treated with tetracycline (1 g four times a day).

Key words: subacute bacterial endocarditis, *Coxiella burnetii*, vasculitis.

Case report

A 47 year old woman presented with a six month history of an intermittent vasculitic rash occurring in crops and confined to her lower limbs. This rash had first occurred two weeks after an acute febrile flu-like illness in February 1987. The lesions took between 10 and 14 days to disappear and recurrence appeared to be related to increased physical exercise.

Specific questioning showed a history of Raynaud's disease, generalised malaise, night sweats, and arthralgia affecting elbows and wrists.

On examination her pulse was collapsing and cardiac murmurs were noted consistent with aortic stenosis and regurgitation. There was moderate hepatosplenomegaly, and fading purpuric lesions were present on the lower limbs. There was no evidence of finger clubbing or splinter haemorrhages.

Investigations showed haemoglobin 117 g/l, normochromic normocytic film, white cell count $4.9 \times 10^9/l$, erythrocyte sedimentation rate 35 mm/first hour, and C reactive protein 20 IU/l (normal value <10). Liver function tests showed a mild increase in globulins with raised IgG and IgA concentrations. Serum electrophoresis was normal. Six sets of blood cultures were performed, all of which failed to grow any organisms. A skin biopsy of a fresh lesion showed capillaritis with C3 deposition around vessels in the capillary dermis.

Cardiac ultrasound showed a bright aortic valve echo consistent with calcification, with no evidence of vegetations. This was repeated at an interval of one week and no change noted.

Complement levels showed a slight decrease in C4 to 190 mg/l (normal range 200–550).

In view of the strong clinical suspicion that this was subacute bacterial endocarditis in the presence of negative blood cultures a full atypical organism screen was performed. This showed raised titres to *Coxiella burnetii* with a phase 1 antibody of 1/4096 and a phase 2 antibody of 1/131 073. A cryoprecipitate of polyclonal IgG and IgA with an IgMx which showed definite restriction was also detected—that is, a mixed cryoglobulinaemia.

She was treated with tetracycline (1 g four times a day). Within one week she felt better, and the spleen had decreased in size. The C reactive protein fell from 20 to 15 IU/l and the erythrocyte sedimentation rate fell from 35 to 19 mm in the first hour.

Discussion

This case shows the importance of looking for atypical organisms in cases of suspected subacute bacterial endocarditis, which are culture negative even when there is no obvious risk factor¹—this woman lived in a small town, consumed only pasteurised dairy products, and had no farms or animals in her vicinity.

The existence of Raynaud's disease, vasculitis, and splenomegaly could be explained by Q fever or mixed essential cryoglobulinaemia,^{2,3} and indeed it

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was questioned whether the monoclonal IgM in the cryoprecipitate might have caused a false positive result in the complement fixation test for Q fever. This was resolved by testing against a wide range of organisms and evaluating specific antibody to *C burnetii* in the serum supernatant after the cryoglobulin had been removed. Titres showed phase 1 antibody levels of 1/2048 and phase 2 levels of 1/65 000. Antibody was also detected in the cryoprecipitate but at much lower levels, thus confirming the diagnosis of chronic Q fever.

Short of testing for seroconversion after inoculation of cardiac tissue into guinea pigs, a diagnosis of Q fever endocarditis is made serologically.

Titres to phase 1 antibody of greater than 1/200 are diagnostic of chronic Q fever⁴ and at one time were thought always to be associated with endocarditis. Evidence presented by Ellis *et al* in 1983⁵ and by Palmer and Young in 1982⁶ suggests that chronic infection with *C burnetii* can occur in other organs—for example, the liver, without coexistent endocarditis. In this case, however, evidence of a valvular abnormality and strongly positive titres to phase 1 antibody suggest that this patient does indeed have endocarditis.

The Public Health Laboratory study of Q fever infection 1975–1981 found that on average five to 10 years elapsed between the occurrence of acute Q fever and the presentation with endocarditis in chronic infection.⁶ There is no way of assessing the duration of infection in this case or whether the febrile illness in February was this patient's acute phase coxiella infection.

For how long should this patient receive tetracycline? Most authorities use the antibody titre to monitor response and continue treatment until titres are low. Treatment must often be continued for over

one year,⁷ and in cases of uncertainty about the effectiveness of eradication of infection by antibiotics this treatment has been combined with valve replacement.^{8,9} Reinfection has been reported, however, despite preoperative tetracycline treatment, and the liver is thought to be a possible nidus of infection.

Clinical response in this case can also be monitored by regular measurement of cryoglobulins.¹⁰ If Q fever endocarditis is stimulating the production of cryoglobulins successful treatment of the underlying condition should cause the level of cryoglobulin to fall.

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References

- 1 Fergusson R J, Shaw T R D, Kitchin A H, Matthews M B, Inglis J M, Peutherer T F R. Subclinical chronic Q fever. *Q J Med* 1985; **57**: 669–76.
- 2 Gorevic P, Kassab H J, Levo Y, *et al*. Mixed cryoglobulinaemia: clinical aspects and long-term follow-up in 40 patients. *Am J Med* 1980; **69**: 287–303.
- 3 Lightfoot R W Jr. Cryoglobulinaemias and other dysproteinemias. In: Kelley W N, Harris E D Jr, Ruddy S, Sledge C B, eds. *Textbook of rheumatology*. 2nd ed. Philadelphia: Saunders, 1985: 1337–439.
- 4 Anonymous. Chronic Q fever [Editorial]. *J Infect* 1984; **8**: 1–4.
- 5 Ellis M E, Smith C L, Moffat M A J. Chronic or fatal Q fever infection: a review of 16 patients seen in north east Scotland. *Q J Med* 1983; **52**: 54–66.
- 6 Palmer S R, Young S E J. Q fever endocarditis in England and Wales 1975–81. *Lancet* 1982; **ii**: 1448–9.
- 7 Geddes A M. Q fever. *Br Med J* 1983; **287**: 927–8.
- 8 Anonymous. Q fever endocarditis. [Editorial]. *Br Med J* 1976; **ii**: 960–1.
- 9 Turck N P G, Hewitt G, Turnberg L A, *et al*. Chronic Q fever. *Q J Med* 1976; **45**: 193–217.
- 10 Brouet J C, Clauvel J P, Danon F, Klein M, Seligmann M. Biologic and clinical significance of cryoglobulins. *Am J Med* 1974; **57**: 775–87.