Klebsiella pneumoniae and acute anterior uveitis in ankylosing spondylitis

Acute anterior uveitis (AAU) is frequently associated with ankylosing spondylitis (AS). It is probably not a complication of AS as it may often manifest before the onset of the disease. Acute anterior uveitis also occurs in Reiter's disease, ulcerative colitis, and Crohn's disease. When sacroiliitis is present, all of these conditions are strongly associated with the HLA B27 antigen.[1] The incidence of HLA B27 in all individuals presenting to eye clinics with AAU is 58%.[2] Although infective agents are known to cause some forms of AAU, most cases are idiopathic or associated with diseases whose aetiology is unknown. We have reported evidence of a cross-reactivity among three Gram-negative micro-organisms—*Enterobacter aerogenes*, *Klebsiella pneumoniae*, and *Yersinia entercolitica*—and HLA B27 positive lymphocytes,[3] and have also found that *Kl pneumoniae* was found more frequently in AS patients with active disease than in controls or patients with inactive disease.[4] We now report, in detail, our findings relating to AAU in our group of patients with AS.

Patients, methods, and results

We have examined 190 patients with AS on 765 separate occasions. All patients fulfilled the New York criteria for AS.[5] Patients with early or possible ankylosing spondylitis were excluded from this study. Of the 155 patients tissue typed, 139 were positive for HLA B27 (90%). All patients with AAU were seen, the diagnosis confirmed, and treatment instituted by their ophthalmic physician. Faecal culture studies were carried out as described.[4] All episodes where patients or controls were taking antibiotics were excluded from the study. A total of 159 healthy hospital-associated controls provided one faecal sample each, and 93 patients with rheumatoid arthritis regularly attending a research clinic provided faecal samples on 250 visits. The interval between each visit was a minimum of three months. Fifty female physiotherapy students, on their first day of contact with a hospital environment, also provided single faecal samples.

The results are shown in the table. Three patients had two episodes of AAU during the study and each was counted separately. Positive cultures for *Kl pneumoniae* were found in 13 out of 17 episodes (76%). *Klebsiella/Enterobacter* spp were identified on 229 out of 763 occasions (30%), at which AAU was not found. The incidence in hospital controls, outpatients with rheumatoid arthritis, and female physiotherapy students was 33%, 20%, and 10% respectively. Many of the patients with AAU had positive cultures for klebsiella for some months before the development of AAU as well as at the time of assessment. Two cases were excluded because no cultures were available at the time of the AAU episode but previous cultures taken 9 and 12 weeks before gave positive results. One other case was excluded because no culture was available at the onset of AAU, although the culture result was positive when tested four weeks later and mild signs still present.

Comparison of positive and negative faecal cultures for Klebsiella/Enterobacter spp in AS patients with and without AAU, hospital controls, rheumatoid arthritis outpatients, and female physiotherapy students

	AS patients		Hospital controls	RA outpatients	Physiotherapy students
	With AAU	Without AAU			
Positive cultures	13	229	51	49	5
Negative cultures	4	536	106	201	45

χ^2 between AS patients with and without AAU = 16·86 ($P < 0·001$).

Comment

The cause of the joint and eye inflammation in HLA B27 positive individuals is unknown. An infective agent has been suspected, particularly in view of the evidence that reactive arthritis can occur after acute dysentery with salmonella, shigella, or *Yersinia enterocolitica* in HLA B27 positive individuals. *Kl pneumoniae* is only conditionally pathogenic and is commonly found in the gastrointestinal tract. Our finding that this organism is frequently associated with and often precedes AAU supports the hypothesis that many of the acute inflammatory episodes in HLA B27 positive patients whether acute peripheral arthritis, spinal disease, or eye inflammation are all responses to a common aetiological trigger. Whether this trigger is *Kl pneumoniae* remains to be seen.

Requests for reprints to RE.

[1] Brewerton, D A, *Arthritis and Rheumatism*, 1976, **19**, 656.
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[3] Ebringer, A, *et al*, in *HLA and Disease*, ed J Dausset and A Svejgaard, p 27. INSERM, Paris, 1976.
[4] Ebringer, R W, *et al*, *Annals of the Rheumatic Diseases*, 1978, **37**, 146.
[5] Bennet, P H, and Wood, P H N, in *Population Studies of the Rheumatic Diseases*, ed P H Bennet and P H N Wood, p 456. Amsterdam, Excerpta Medica Foundation, 1968.

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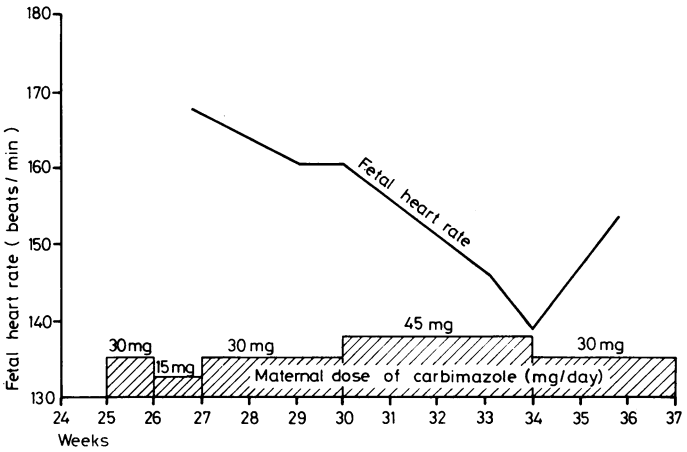
Prenatal treatment of fetal thyrotoxicosis

Fetal thyrotoxicosis may be predicted and diagnosed but there are few reported attempts to treat it before delivery.[1-3]

Case report

A 27-year-old woman presented 11 weeks advanced in her second pregnancy. At 24 years she had had a subtotal thyroidectomy for Graves's disease. Pretibial myxoedema developed within one year of the operation. During her first pregnancy at the age of 25 she was euthyroid. At 33 weeks' gestation she delivered spontaneously a boy of 1·83 kg (25th centile for gestational age). At birth this child was severely thyrotoxic, with a free thyroxine index (FTI) of 37·5 (reference range 3·2-12·5). He was treated successfully with oral carbimazole, digoxin, and diazepam. Puerperal maternal serum concentrations of long-acting thyroid stimulator (LATS) and LATS protector (LATSP) were 45 units/ml and 283 units/ml, respectively (fetal thyrotoxicosis invariably occurs when the total maternal serum LATS and LATSP concentrations exceed 20 units/ml[4]).

When first seen in her second pregnancy her FTI was 11·3 (reference range 3·2-12·3) and serum triiodothyronine concentration 8·2 nmol/l (5·3 ng/ml) (upper limit of normal in pregnancy 4·0 nmol/l). She therefore had T3 toxicosis. At 15 weeks oral propranolol 120 mg/day was started, and at 25 weeks oral carbimazole 10 mg eight-hourly. Her serum LATS and LATSP concentrations were 100 units/ml and 340 units/ml respectively. The fetal heart rate at 27 weeks was 168 beats/min (usual range 120-160). The dose of carbimazole was titrated against the fetal heart rate throughout the pregnancy (see figure). The propranolol was discontinued at 29 weeks.



Variations of fetal heart rate related to maternal daily dose of oral carbimazole.