First attack of rheumatic fever in an adult: the case for greater awareness

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Abstract

A 40 year old white woman presenting with rash, fever, and migratory polyarthralgia developed a symmetrical polyarthropathy and remained unwell for 10 weeks. Fulfilment of the revised Jones criteria reinforced the clinical diagnosis of rheumatic fever. Antistreptococcal antibodies peaked four to six weeks into the illness and declined thereafter.

Rheumatic fever is a childhood disease now rare in this country. Attacks in adult life are usually recurrences of rheumatic fever in childhood. First attacks in adults were rare even when the disease was common. Currently there is concern that after many years of decline recent American outbreaks herald its resurgence.

Case report

We report the case of a 40 year old housewife who presented with a three week history of a widespread evanescent maculopapular rash, fever, and migratory polyarthralgia. The polyarthralgia progressed to a symmetrical polyarthropathy of the knees and proximal interphalangeal joints. The rash affected the face but spread well beyond photosensitive areas and was concurrent with daily fever up to 40°C. Symptoms consistent with a mild pharyngitis were noted, though there was neither erythema nor tonsillar enlargement. Modest cervical lymphadenopathy was the only other positive physical finding. A similar but milder illness had occurred 12 months previously. Antibiotics, antihistamines, and antipyretics had been given to little effect. There was no history of exposure to drugs or toxins.

Investigations showed haemoglobin 129 g/l, white cell count $11.5 \times 10^9/l$, neutrophils $9.5 \times 10^9/l$, erythrocyte sedimentation rate 70 mm/h, and C reactive protein 92 mg/l. Urea and electrolytes, liver function, urine examination, immunoglobulin electrophoresis, and C3, C4, and C1q were normal. Rheumatoid factor and antibodies to DNA, nRNP, Sm, Ro, and La were not detected. Serology was negative for Epstein-Barr virus, cytomegalovirus, rubella, parvovirus, *Yersinia enterocolitica*, *Treponema pallidum*, *Brucella abortus*, hepatitis A and B, *Borrelia burgdorferi*, toxoplasma and toxocara, as well as common respiratory pathogens. Throat swabs, stool cultures, urine cultures for mycobacteria, Mantoux test, and repeated blood cultures were negative. Electrocardiography and echocardiography were also normal. Antistreptococcal antibodies were significantly

The Jones criteria (revised) for guidance in the diagnosis of rheumatic fever¹

Major manifestations	Minor manifestations
Carditis	Previous rheumatic fever or rheumatic heart disease
Polyarthritits	Arthralgia
Chorea	Fever
Erythema marginatum	Prolonged P-R interval
Subcutaneous nodules	Acute phase reactants

Supporting evidence of streptococcal infection

Increased titre of antistreptococcal antibodies, such as antistreptolysin O or others
Positive throat culture for group A streptococcus
Recent scarlet fever

The presence of two major criteria, or of one major and two minor criteria, indicates a high probability of acute rheumatic fever, if supported by evidence of preceding group A streptococcal infection.

raised, however, peaking at four to six weeks after onset and declining thereafter. The highest titres reached were antistreptolysin O 1920 units (normal 160-240), DNase B 1920 units (160-240), and antihyaluronidase 1024 units (up to 256). A separate laboratory confirmed the antistreptolysin O titre.

These results indicate recent streptococcal infection, which is the proviso attached to the two major and two minor criteria required by the revised Jones criteria (table).¹ This patient had a major criterion, polyarthritits, and two minor criteria, fever and an acute phase reaction (C reactive protein, erythrocyte sedimentation rate, etc). The illness lasted about 10 weeks. The symptoms were treated effectively with naproxen 500 mg twice a day or aspirin 2.4 g daily, though raised transaminases were associated with the latter. The duration was consistent with rheumatic fever. A first attack of rheumatic fever in an adult of 40 is extremely rare. The clinical and laboratory evidence in this case strongly supports a diagnosis of rheumatic fever. At the time there was no evidence of an outbreak of streptococcal pharyngitis or rheumatic fever in the community. After two years of oral penicillin prophylaxis the patient remains well and has shown neither clinical nor laboratory evidence to suggest a chronic rheumatic disorder or an alternative explanation for the original illness.

Discussion

The message of this case is that despite its rarity rheumatic fever should be remembered in the differential diagnosis of fever of unknown origin with joint, cardiac, or renal abnormalities, whatever the patient's age.

Although our patient had a first attack of rheumatic fever aged 40, it is still regarded as predominantly a childhood disease and there is

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Accepted for publication
30 January 1990

no clear trend towards an older age group being affected despite its decline in both Europe and North America. It remains, however, a major cause of morbidity and mortality in poorer countries. The estimated incidence in India is between 200 and 1200 per 100 000 a year (age adjusted, 5–17 year olds),² compared with an incidence in the United States during the seventies of between 0.23 and 1.88 per 100 000 a year.^{3–4} Recent American experience illustrates the need for vigilance, however. The outbreak of rheumatic fever in Utah during 1985–1986 represented an incidence of 18 per 100 000 in a prosperous state where the victims were almost all white subjects from families with socio-economic advantages.⁵ There did not seem to be an increase in streptococcal pharyngitis or carriage in the community, though there were no data to establish whether changes in serotype prevalence might have been responsible. Other outbreaks in North America have occurred in Ohio⁶ and in military recruits.^{7–8} The explanation for this apparent resurgence of rheumatic fever in America is uncertain and there is little evidence as yet to suggest a similar increase of the disease in the United Kingdom.

Detection of any such resurgence will require increased vigilance and recognition of milder disease, especially in the adult. Our patient's illness consisted of fever, rash, and polyarthritides without carditis and might be distinguished from the classical childhood expression of the disease by the term 'poststreptococcal arthropathy'. The advantage of this terminology is that it includes within it cases of polyarthritides with evidence of antecedent streptococcal infection which did not fulfil the revised Jones criteria.¹ This is crucial if expression of the disease is different in adults. These arguments are supported by McDonald's report of six young Mexican-American adults with articular involvement of the lower limbs of a few days' duration⁹ and an early sixties series from a United Kingdom tertiary referral centre.¹⁰ Of 14 patients presenting with rheumatic fever at this referral centre, 13 had polyarthritides, nine had fever, and only five evidence of carditis. Only two patients were undergoing their first attack of rheumatic fever, the rest having established rheumatic heart disease. Most revealing were the patients excluded from the series, four of whom did not fulfil the revised Jones criteria and a further three in whom 'acute rheumatoid arthritis could not be excluded'. On clinical grounds our patient appeared more likely to have adult onset Still's disease than either rheumatic fever or systemic lupus erythematosus, which were the three principal differential diagnoses.

The striking similarity between rheumatic fever and other autoimmune joint diseases, exemplified by our case, suggests a possible role for the group A streptococcus in the pathogenesis of chronic inflammatory arthropathies. There is certainly overwhelming evidence that group A streptococci cause by an autoimmune mechanism, a multisystem disorder, rheumatic

fever, and an organ specific disease, post-streptococcal glomerulonephritis, and moreover that there are 'rheumatogenic' and 'nephritogenic' strains of the organism.¹¹ Antigenic cross reactivity between various human tissues and microbial components is thought to be responsible. Cross reactive sites have been identified within the group A specific polysaccharides,¹² the protoplast membrane,¹³ and M proteins.¹⁴ Only recently non-cross reacting immunogenic fragments of M proteins have been synthesised, offering the possibility of safe and effective vaccines.¹⁵

An understanding of susceptibility to rheumatic fever is also recent and followed Patarroyo's discovery of the B cell alloantigen that he called 883.¹⁶ It is similar to the later identified 83S19.23¹⁷ and seems to identify 70–75% of patients with rheumatic fever from different regions of the world and just 17% of controls. Patients with the B cell alloantigen 256.S10 seem not to have carditis, and this may be a marker of milder disease.¹⁷ Susceptibility thus appears not to be linked to the HLA loci.

The new information and observations above suggest that the role of group A streptococci in initiating chronic arthropathies merits further investigation. We hope this case and the discussion will serve as a timely reminder that rheumatic fever and the group A streptococcus should not be forgotten.

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