Immunisation triggering rheumatoid arthritis?

Sir, We read with interest the article by Turner-Stokes and Isenberg on immunisation of patients with rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE).1 Isolated reports of the onset of SLE following immunisation have occurred,2 but we are unaware of similar cases in RA. We have recently observed a patient who developed RA three weeks after a second dose of tetanus toxoid. A 34 year old woman received two doses of tetanus toxoid in November and December 1986. A week after the second dose she developed severe pain with erythema and induration measuring 10 cm in diameter at the site of injection over the left deltoid muscle. This severe local reaction lasted 10 days. A few days after the erythema and induration started to fade the patient developed a symmetrical inflammatory polyarthritis involving the proximal interphalangeal, metacarpophalangeal, wrist, elbow, shoulder, knee, and the metatarsophalangeal joints. The arthritis was severe with early morning stiffness lasting several hours. There was no past history of arthritis, inflammatory bowel disease, iritis, back pain, psoriasis, or recent infection and no family history of inflammatory arthritis.

Investigations in March 1987 showed haemoglobin 149 g/l, white cell count 8×10⁹/l, platelet count 307×10⁹/l, erythrocyte sedimentation rate (ESR) 17 mm/h, C reactive protein 120 mg/l (normal range (NR) <60), albumin 45 g/l, globulin 33 g/l (NR 18–32), antinuclear antibodies negative and Igm rheumatoid factor positive (titre 1/32). An x-ray examination of her hands and feet showed periarticular osteoporosis.

She was treated with bed rest, splintage of the inflamed joints, and non-steroidal anti-inflammatory drugs. The response was incomplete and in December 1987 treatment was started with sulphasalazine. Her arthritis responded and by March 1988 her early morning stiffness was minimal and her joints were quiescent. Her haemoglobin was 152 g/l, ESR 7 mm/h, C reactive protein 60 mg/l, and serum albumin and globulin were 49 and 27 g/l respectively. Her IgM rheumatoid factor remained positive (titre 1/64).

Our patient satisfied the American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis.3 She had a severe local reaction after the second dose of the toxoid; a not uncommon side effect, and the incidence of which increases with the age of the subject, and is more common in women. Those who develop severe reactions frequently have high titres of the circulating antitoxin.4 It could well be that the B cell proliferation that followed the vaccination might have precipitated the onset of RA in our patient, who might have been genetically predisposed. Although one cannot draw too many conclusions from one isolated case, there was a strong temporal relation between the introduction of the vaccination and the development of the severe local reaction, and the onset of RA.

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References


Lymphoma chemotherapy as remission inducing treatment in rheumatoid arthritis

Sir, I read with interest the article by Cohen et al on the
response of a patient with rheumatoid arthritis, IgA deficiency, and overlap connective tissue disease to chemotherapy for co-existent Hodgkin's disease. This case report illustrates that progressive rheumatoid disease may be arrested by vigorous chemotherapy even when previous conventional treatment has failed to produce a significant reduction in disease activity. We reported a similar patient with rheumatoid arthritis who developed non-Hodgkin's lymphoma and was treated with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone). Our patient enjoyed a complete remission, with evidence of radiological improvement, for about 18 months and received no more drug treatment before the disease returned. Cohen's case had a flare of disease after three years.

The drawback to this form of treatment is undoubtedly the near certainty of side effects. Cohen's patient developed myelosuppression, as a result of which cyclophosphamide was substituted for nitrogen mustard. No mention was made of any other toxic effects. Our patient developed alopecia (temporary) and felt unwell for a few days after each course of treatment, but apart from this suffered no untoward side affects.

These case reports would appear to indicate that selected rheumatoid patients who have failed to respond to conventional second line antirheumatic drug treatment might benefit likewise and should not perhaps be denied the chance of a prolonged remission merely because they have not been dealt the 'lymphoma passport' to effective treatment.

Thus it may be worth exploring the feasibility of treating severe but otherwise uncomplicated rheumatoid arthritis with similar drugs. Though somewhat daunting, their side effects are not far removed from those of conventional second line drugs on which patients remain at risk for prolonged periods. Of course we do not know the actual likelihood of malignancy developing as a result of chemotherapy induced immunosuppression, and this would have to be explained to patients beforehand. But the possibility exists that a carefully thought out and administered chemotherapy protocol, for carefully selected patients, may be the logical next step forward in much the same way as already attempted in some centres with total lymphoid irradiation.

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Canal-like structures in menisci

Sr., In your issue of September 1987 Drs Bird and Sweet draw attention to the canal-like structures that can be recognised when the menisci of young calves and of young humans are examined by scanning electron microscopy. These canals appear to be identical with those described by Virchow (1858). The concept of 'cellular pathology', formulated by Rudolph Virchow, rested heavily on arguments adduced from studies of the mesenchyme and, in particular, from observations of cartilaginous tissues. It is therefore perhaps not surprising that he recognised and illustrated a 'system of tubes' anastomosing within the fibrocartilages of the knee. There appeared to be no blood vessels but an arrangement of canals that he illustrated with great clarity. The mechanism by which the fibrocartilages derive their nutrition is still not well understood, and Virchow was not able to explain how these structures were able to sustain their metabolic activities remote from an active capillary network.

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References

Skin test responsiveness to Mycobacterium tuberculosis, HLA-DR4, and rheumatoid arthritis

Sr., Tuberculin tests on 84 Spanish patients with leprosy showed a significant association between large sized responses and HLA-DR4. This HLA type is associated with rheumatoid arthritis, and a role for mycobacterial antigens has been suggested both in this disease and in experimental adjuvant arthritis of rats. Thus skin test responsiveness to tuberculin in rheumatoid arthritis may provide a clue to its aetiology.

We carried out skin testing in 19 HLA-DR4 female patients with rheumatoid arthritis and in 19 DR4 and 17 non-DR4 female controls, with exactly the same new tuberculin (ultrasonicate preparation) as that used to test the patients with leprosy. The study subjects were recruited from a large population of HLA-DR typed women involved in a case-control study of the relation

References