Correspondence

Influence of trauma on initiation of Reiter’s syndrome and ankylosing spondylitis

Sir, we read with interest the papers by Wisnieski and Jacoby et al., studying the influence of trauma on initiation of Reiter’s syndrome and ankylosing spondylitis. These authors found only a few incidents on this association. We would like to point out that traumatic initiation of ankylosing spondylitis, although infrequent, has been reported by several European authors, including Forester et al., Louyot et al., Ott et al., Doury and Pattin, and Arnaud. In the case of Reiter’s syndrome Doury et al. in 1974, Gaglielmino in 1977, Noer in 1966, and Bernard et al. in 1964 reported this phenomenon. We have seen three such cases in men which we summarise briefly here. None of these patients presented any signs of ankylosing spondylitis or Reiter’s syndrome before trauma.

Case No 1

Patient No 1 born 1 December 1951 suffered trauma to the base of the left fifth metacarpal causing 10 minutes of severe pain on 3 December 1979. Pain recurred on the evening of the accident, gradually becoming more severe. After two days there developed local signs of inflammation, and after three days urethritis. Urethral smears and culture were negative. After 10 days he developed inflammatory pains of the cervical and lower thoracic spine, and after 30 days bilateral sacroiliac pain developed, worse on the right: scintigraphy confirmed bilateral sacroiliitis with right sided predominance. X-rays were normal. The sedimentation rate was 80 mm in the first hour. The patient was HLA-B27 positive. Spinal pain resolved after one month of non-steroidal anti-inflammatory drug therapy; pain in the left hand persisted for six months. To the best of our knowledge this patient has not had any further episodes of inflammatory pain.

Case No 2

Patient No 2 born 7 November 1961 had a motorcycle accident on 13 December 1982, sustaining 16 fractures (pelvis, left tibia, right and left forearms) and dislocation of the left knee. Surgical recovery was good, and weight could be borne by the end of February. Nevertheless, pain persisted after this initial improvement, and after three months there was worsening of inflammatory pain in the left knee and both hips. After three and a half months he developed conjunctivitis and sterile urethritis. After four months there appeared local signs of inflammation of the right hip (local redness, and warmth) accompanied by fever and chills. Three days later he developed arthritis of his left tibiotalar joint, both hips, right elbow, and left shoulder, together with inflammatory pain in the cervical region. X-rays showed bilateral sacroiliitis, which had not been present at the time of the accident; the sedimentation rate was 50 mm in the first hour. The patient was HLA-B27 positive. On treatment with non-steroidal anti-inflammatory drugs there was a very gradual resolution of pain, with complete recovery only after one and a half years.

Case No 3

Patient No 3 born on 1 May 1951 suffered a slight injury to his right wrist on 16 August 1975, causing mechanical pain which was not improved by immobilisation in a cast. After 15 days the pain became inflammatory and then bilateral; after 21 days there was conjunctivitis and arthritis of both knees and the cervical spine. X-rays were normal. The sedimentation rate was 70 mm in the first hour. The patient was HLA-B27 positive. The past history included two episodes of urethritis in 1974, resolving after three days of antibiotics. On non-steroidal anti-inflammatory drugs the pain in the knee settled within one month and in the wrist within two months. The patient subsequently had two recurrences of arthritis: in 1977 inflammatory pain involved his spine, without radiological abnormalities, and in 1982 both iliac crests, both wrists, and the lumbar spine were affected, with radiological evidence for sacroiliitis. These two episodes each lasted seven days.

Discussion

These three cases appear to be examples of Reiter’s syndrome provoked by trauma. We hope that others will report similar experiences and thus allow an assessment of the role of trauma in the genesis or initiation of Reiter’s syndrome and a comparison with the situation in rheumatoid arthritis and ankylosing spondylitis.

The medicolegal implications have been studied by European authors. Like Jacoby, these authors separate two entities: (a) Usually (18% for Forester, 4% for Jacoby) disease was already present, as shown by radiographs taken immediately after trauma, but was clinically non-apparent, and trauma triggered the symptoms which led to diagnosis. (b) Less often (3–5% for both Forester and Jacoby) ankylosing spondylitis develops ab initio as a result of trauma.

During 10 years we observed five patients whose ankylosing spondylitis appeared to be generated (three cases) or unmasked (two cases) by trauma. Contrary to Jacoby’s work the causative trauma was twice minimal. It affected peripheral joints in three cases. Inflammatory episodes involved preferentially the traumatised joints throughout the whole course of the disease.

Wisnieski proposed a hypothesis of an antigen-antibody reaction after trauma in genetically predisposed patients.
New antigens might be exposed through the trauma, leading to the development of autoimmune phenomena. This hypothesis is supported by other studies,\(^1\)\(^2\) which tend to indicate that ankylosing spondylitis is a reactive arthritis following infection with various gram-negative organisms. Cross reactivity between infecting organisms and self components could be involved. The reason why some individuals develop Reiter’s syndrome and others ankylosing spondylitis remains a mystery. It will be informative to seek differences in the genetic map of HLA-B27 positive patients which give rise to either disease.

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References


Mepacrine induced hepatitis

Sir. When mepacrine was introduced in 1930 as an antimalarial it was frequently noted to cause yellow discolouration of the skin. It rarely caused jaundice and fatal hepatitis, introducing the possibility of serious confusion with the common skin discoloration.\(^2\)\(^3\) Hepatitis due to mepacrine therapy has not been reported during therapy of connective tissue disorders. In view of this we describe such a case.

A 37-year-old woman presented with an 18-month history of malaise, mouth ulcers, and arthralgias. From the age of 18 she had a persistent telangiectatic facial rash, similar to that of systemic lupus erythematosus, and from the age of 25 she had recurrent migraine and frequent episodes of bronchitis with asthma. Skin tests to common allergens were negative, but there was a strong family history of atopic disease. Full blood count and complement levels were normal, the erythrocyte sedimentation rate was 4 mm/1st h, and rheumatoid factor and antinuclear antibody tests were negative. Parotid scintigraphy studies and labial salivary gland biopsy were normal, and skin biopsy did not show immunoglobulin deposition. She was considered to have an undifferentiated connective tissue disorder and received trials of hydroxychloroquine and chloroquine without benefit. After she complained of nausea and blurred vision the chloroquine was stopped.

Liver function tests were normal, and mepacrine was substituted at a dose of 100 mg daily, increasing after two weeks to 300 mg daily. The patient was warned of the possibility of skin yellowing. Six weeks later she reported that her skin and eyes had abruptly turned yellow accompanied by feelings of lethargy, loss of appetite, itching and tender cervical lymphadenopathy. She was instructed to stop the mepacrine, but four weeks later her urine contained urobilinogen, her γ-glutamyltransferase was 264 IU/l (normal (n)<65 IU/l), alanine transaminase 210 IU/l (n<45 IU/l), aspartate transaminase 107 IU/l (n<41 IU/l), and alkaline phosphatase 160 IU/l (n<105 IU/l). However, the bilirubin (5 μmol/l) was normal, indicating that she was not jaundiced. An absolute eosinophil count of 680/mm\(^3\) (0·68×10\(^{9}\)/l) was noted. Serological tests for hepatitis A and B and cytomegalovirus were negative. Further investigations were considered unnecessary as the liver function tests gradually improved and after two months were normal. The skin and sclera remained yellow for two months after mepacrine was stopped.

In this patient the systemic symptoms, scleral yellowing, and urinary urobilinogen suggested hepatitis. The liver function tests supported this diagnosis, but the normal bilirubin indicated that the yellow discolouration was due to mepacrine. Mepacrine hepatitis associated with therapeutic doses is an idiosyncratic, unpredictable reaction similar to that caused by halothane. In addition to eosinophilia and lymphadenopathy, fever, rashes, and arthralgias may occur, features commonly found in the connective tissue diseases. Liver histology is similar to viral hepatitis\(^2\) or acute massive necrosis may result. The precise pharmacokinetics of mepacrine are not known but, like its fellow 4-aminoquinoline, chloroquine, it has an unusually large volume of distribution being widely distributed and bound in liver, lungs, spleen, adrenal, skin, and leucocytes.\(^3\) The long half life of mepacrine presents a particular hazard in cases of sensitivity.

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