Rapidly destructive knee arthropathy associated with hepatitis B

Sirs,

Hepatitis B (HBV) represents one of the major causes of liver disease. Polyarthritis is an established extrahepatic manifestation of acute HBV infection and is believed to be immune-complex mediated (1). The administration of recombinant hepatitis B surface vaccine may induce the onset of rheumatic diseases and one of the cases represents lytic bone lesion (2, 3). In this report, we present a rare case of HBV-associated arthropathy resembling Charcot joint after the local injection of steroid.

A 67-year-old male was admitted to a local clinic complaining of left anteromedial knee pain of unknown origin. He was diagnosed as having osteoarthritis of the knee (Fig.1 A). Conservative therapy was initiated since January 7, 2003, and he received steroid (dexamethasone 2 mg) injections into his knee joint 5 times (every 2 weeks) for that period and received rehabilitation. However, his knee pain continued to worsen over the next three months. Then, he came to our hospital on April 15, 2003.

Severe left knee pain was present at the initial examination at our department. Physical findings included mild swelling and warmth of the right knee joint, the ROM of the knee at -15˚ extension to 130˚ flexion, and an effusion was present. Plain radiograms at the time of admission showed a large bone defect in the medial tibia and slight narrowing of the articular gap (Fig. 1 B).

Synovial fluid specimen failed to reveal any pathogens including *E. coli, Staphylococcus aureus* and other bacteria. Serum hepatitis B surface antigen (HBsAg) and HBe antigen were positive, while antibodies for HBs, HBe and HCV were negative. Liver function was normal, and rheumatoid factor was negative.

Total knee arthroplasty was performed. Histological examination revealed tiny fragments of mature bone within villous synovial tissue in a pattern resembling that of Charcot joint (Fig. 1C, x100). However, the patient has never been diagnosed as having diabetes and never been exhibited abnormal neurological signs or symptoms. Immunohistochemical studies revealed massive expression of HBs antigen in synovial cells (Fig. 1 D, x 400, antibody against HBs antigen) comparing to the control (Fig. 1 E, x 400, antibody isotype control).

We described here a rare case, who developed rapidly destructive arthropathy with chronic infection of hepatitis B virus (HBV). At the best of our knowledge, there is no report showing the onset of arthritis followed by intra-articular steroid injections in HBV positive patients. It has been reported that HBV carrier patients treated with steroids for malignancies, nephritic syndrome, and arthritis develop fatal liver failure by reactivation of HBV followed by massive liver damage (4, 5). On the other hand, there are some reports showing that HBV could cause arthritis (6-8). The surface antigen of HBV has been found in synovial tissues with the use of direct immunofluorescence, supporting the concept that this synovitis is immune-complex mediated. In addition, the administration of recombinant hepatitis B surface vaccine may induce the onset of rheumatic diseases and one of the cases represents lytic bone lesion (2, 3, 9, 10). Therefore HBs antigen could cause not only arthritis but also lytic bone lesion.

In our case, steroid injections (only 5 times) might lead to advantages for viral replication owing to escape from host antiviral mechanism. And this reactivation of HBV probably led to the local replication of the virus following the high production of HBs antigens in his joint and rapid and massive destruction of the joint took place, resulting in the pathological appearance resembling that of Charcot joint. This case is rare in which the arthropathy associated with HBV reactivation has shown rapidly destructive arthropathy resembling that of Charcot joint. Joints with over-expression of HBs antigens and Charcot joint may have mutual triggering factors that skew the bone lysis of affected joints. Immunological factors trigger bone "hyperremodeling" which has been pointed out by Cathebras *et al*. might be one of the mutual triggering factors that skew the bone lysis of affected joints (3). Further clinical and experimental studies should be performed to elucidate the factors and pathogenesis of this bone lytic process.

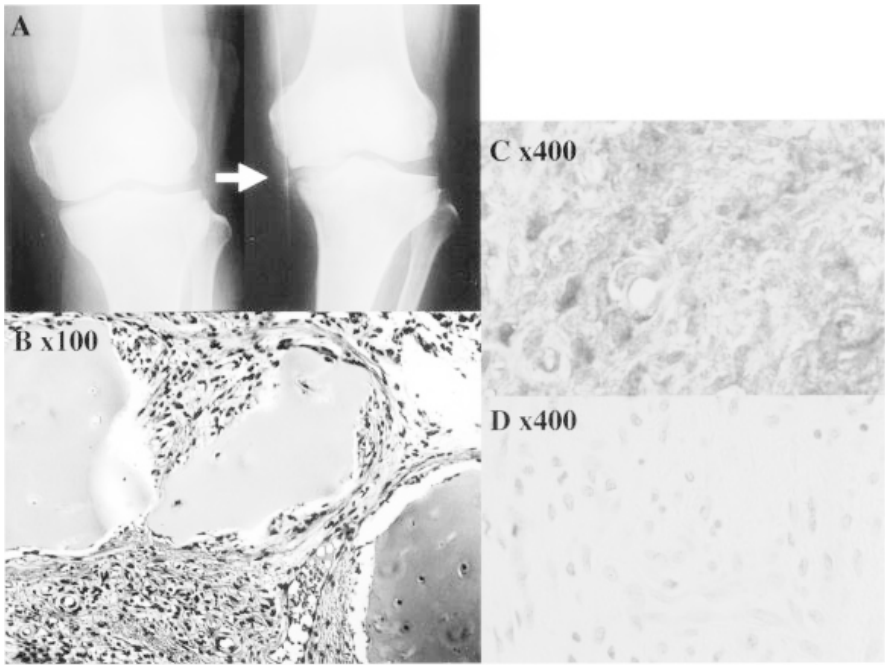

Fig. 1. Rapidly destructive knee arthropathy associated with hepatitis B. (**A**, left) Plain radiograms of the knee (January 7, 2003). Mild OA change was noted. (**A**, right) April 15, 2003, Massive destruction of the joint was noted (arrow). (**B**) Histological examination of the affected joint showed tiny fragments of mature bone within villous synovial tissue in a pattern resembling that of Charcot joint (x100). (**C**) Immunohistochemical studies with antir-HBs antibody showing massive expression of HBs antigen in synovial cells (x 400). (**D**) Antibody isotype control (x 400).

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Tophus in the odontoid process of C2

Sirs,

A cocktail party consultation by a healthy looking colleague, MD, disclosed that a malignant-suspect lytic lesion had been found in the dens of C2. He had had recurrent but self-resolving arthritis attacks of his 1st MTP joints. Twenty years later he developed severe neck pain and a lytic change in the dens of the axis, which was considered to be rheumatoid or metastatic. MRI and CT disclosed a punch-lesion with overhanging edges compatible with a tophus. Due to a risk of pathological atlanto-axial fracture, he was advised against contact sports, to purchase a neck support to his car and to use a soft cervical collar when necessary.

Gout is characterized by hyperuricemia leading at the age of 30-40 years to recurrent acute arthritis attacks caused by intra-articular precipitation of urate to insoluble needle-like strongly birefringent crystals. They evoke a vigorous host response dominated by accumulation, activation and rupture from within of neutrophils. Painful involvement of the 1st MTP joint, podagra, is very typical. In untreated patients arthritis becomes chronic after 10-20 years and tophi develop in soft tissues and as punch-like defects in bone. Gout is common in highly educated professionals. We describe a colleague, who in a cocktail party told about an erosion in the dens of his second cervical vertebra, which had been suspected to represent a malignant change.

This 69-year-old colleague had a history of mild hypertension and hyperlipidemia. Diuretics were not used. He had a long history of recurrent acute episodes of extremely painful, but self-limited attacks of his 1st MTP joints. Serum uric acid concentrations had been 0.45–0.55 mol/l (ref. 0.16-0.45 mmol/l in men). Attacks had been treated with indomethacin. Allopurinol caused skin eruptions so he took probenecid during symptomatic periods "on demand" with good results. At the time for the visit he had neck pain and torticollis to left without radicular symptoms or paresthesiae.

X-ray, CT and MRI findings were typical to a tophus (Fig. 1) (1, 2). A malignant metastatic change and rheumatoid arthritis were excluded clinically and by the test of time. He now uses probenecid regularly. The odontoid lesions have not changed and the patient is in good general health over five years afterwards.

The low temperature of the 1st MTP joint favours precipitation of soluble urate from supersaturated solutions (3). Nidus formation, perhaps as a result of microtrauma and osteoarthritis, is important for the initiation of the attack. Indeed, the 1st MTP joint is one of the predilection sites for osteoarthritis, the "poor man's gout". In Finland real gout occurs in the elbow of fishermen ("fisherman's gout"), who during extremely cold winter times strain their elbow joint when drilling holes to ice for bait fishing. A typical patient warms himself, not with Italian wines, but with strong spirits of good domestic brand. Baltic herring, small whitefish and other similar rich sources of urate are used for meals (4).

We believe, although needle aspiration and polarized light microscopic examinations had not been done, that there is no other disease with this clinical course able to explain symptoms of our patient. We found only three previous reports of tophaceous involvement of the dens (5-8). Tophi in the lumbar (9) and cervical spine (10) in the absence of peripheral tophi have been earlier described but our patient is the first reported case of tophaceous involvement of the dens without peripheral tophi.

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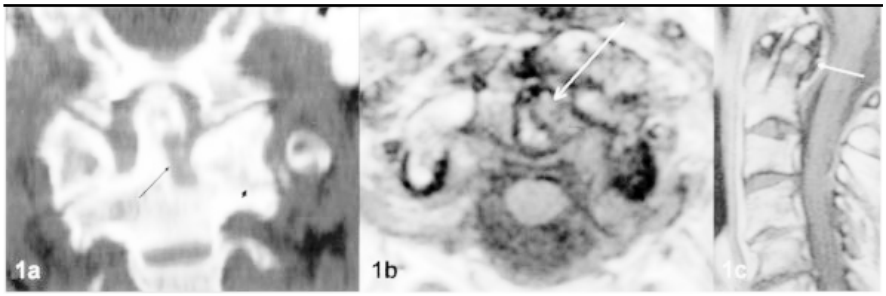

Fig. 1. CT (**a**) disclosed a punched-out lesion (**long thin arrow**) of the dens of C2 with an overhanging edge of the cortex at the base of it, surrounded by a thin sclerotic wall. There was osteoarthrosis (**small thick arrow**) in the left atlanto-axial joint. MRI (**b**, **c**) disclosed a periodontoid soft-tissue mass (**arrows**) with an associated sharply delineated erosion of the dens with tophus characteristics.