Arthritis following combined vaccine against diphtheria, poliomyelitis, and tetanus toxoid

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ABSTRACT
We describe 2 cases of arthritis following immunization against diphtheria, poliomyelitis and tetanus toxoid. One patient developed monoarthritis of the right knee after vaccination, that regressed following synovectomy. Five years later, the arthritis recurred after a booster vaccine injection. One day after immunization, another patient developed arthritis of the ankle that persisted for 3 days. It is difficult to know whether there is a coincidental or a causal relation between immunization and arthritis. Although our cases suggest that immunization against diphtheria, poliomyelitis and tetanus toxoid may cause arthritis, additional cases must be reported before studies aimed at confirming this possibility are considered.

Introduction
Joint complications following immunization are rare. They have been mostly reported after rubella vaccine (1-3). In the past years, several cases of arthritis following hepatitis B vaccination have been published (3-8), but a causal relationship between hepatitis B vaccination and the observed rheumatic manifestations cannot be easily established. We report on 2 cases of arthritis following immunization with a combined vaccine against diphtheria, poliomyelitis and tetanus toxoid.

Case 1
In 1992 a 17-year-old girl with no past medical history was given a booster injection of a combined vaccine against diphtheria, poliomyelitis and tetanus toxoid and, a few days later, an hepatitis B vaccine injection. Three or four weeks afterwards she developed arthritis of the right knee. Treatment with non-steroid anti-inflammatory drugs (NSAIDs) proved ineffective. The symptoms did not worsen after the second and the third injections of hepatitis B immunization. Four months after onset, the symptoms completely regressed following an arthroscopic synovectomy. Pathologic examination revealed aspecific synovitis. The patient was well between 1992 and 1997. In 1993 she was given a booster injection of the hepatitis B vaccine and experienced no complication. In June 1997 a booster injection of the combined vaccine against diphtheria, poliomyelitis and tetanus toxoid was performed. Twelve days later the arthritis of the right knee recurred. NSAIDs proved ineffective. The pain and arthritis were relieved by prednison, but recurred when therapy was tapered off.

She was referred in February 1998 to our unit. Physical examination showed arthritis of the right knee. The general examination was normal. Laboratory tests showed a normal erythrocyte sedimentation rate and C-reactive protein. The blood cell count, liver function tests, and serum creatinine were in the normal range. There were neither proteinuria nor hematuria. Urine culture and urethral swab were negative. The serum anti-streptolysines were in the normal range. Results of other serologies (brucellosis, lyme arthritis, hepatitis B and C, reactive arthritis) were negative. The research for antinuclear antibodies was moderately positive (80; normal < 80, indirect immunofluorescence on Hep-2000 cells) with no anti-ds-DNA. The patient was found to be HLA A1, A2, B8, B41, DRB1 03 and DRB1 13. Aspirated knee fluid was sterile and contained 80,000 leucocytes/mm³ with no crystals.

The patient was treated unsuccessfully with intra-articular steroids, and then by intra-articular osmic acid synovectomy. In April 1998 an arthroscopic synovectomy was performed. Pathologic examination showed hyperplasic aspecific synovitis. The evolution was favourable, with regression of the arthritis. There was no recurrence during the 11-month follow-up.

Case 2
A 22-year-old woman was given a booster injection of a combined vaccine against diphtheria, poliomyelitis and tetanus toxoid. One day after the injection she developed arthritis of the right ankle and fever (40°C). She was referred to our unit 2 days later. She had no relevant medical history, had not developed any symptom following past immuniza-
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The authors postulated that the immunization may have acted as a trigger for the development of the disease. In our two cases immunization may have been the etiologic factor for the arthritis: the delayed onset and evolution were suggestive, and no other causes could be found to explain the symptoms. Case 1 is particularly suggestive since the patient was well for several years, with recurrence of the arthritis following a new immunization. In this case the hepatitis B vaccine was another possible explanation for the arthritis, but the symptoms did not worsen after the second and third injections, and especially, there was no recurrence following a booster injection one year later. However, it is difficult to establish whether there was a coincidental or a causal relationship between the immunization and the observed rheumatic manifestations. Misdiagnosis also cannot be excluded, particularly in case 2. In cases of new observations of arthritis after combined vaccine against diphtheria, polioimmunization and tetanus toxoid, it might be of interest to study in vitro the reactivity of lymphocytes after stimulation with each vaccine by itself, in comparison with normal subjects, as was performed by Biasi et al. in a case of arthritis following hepatitis B immunization (8). Although our cases suggest that the combined vaccine against diphtheria, polioimmunization and tetanus toxoid may cause inflammatory joint symptoms in some patients, additional cases must be reported before studies aimed at confirming this possibility are considered. Consequently, in patients with the onset of arthritis from unknown origins, physicians should study their history with regard to recent immunization, including the combined vaccine against diphtheria, polioimmunization and tetanus toxoid, and notify possible cases to national reporting systems for the adverse effects of drugs.

References