Clinical case

Arthritis in a Down Syndrome Patient

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Abstract

We present the case of a 35-year-old patient with long-standing polyarthritis and Down syndrome. Both of these conditions share a clinical and radiological sign in common, namely, atlantoaxial subluxation, though probably due to different causes.

We discuss this rare combination of both conditions as well as challenges for treatment.

Keywords: Down syndrome. Rheumatoid arthritis.

Introduction

A number of musculoskeletal problems have been documented in persons with Down syndrome (DS): developmental abnormalities such as hypermobility and malformations of the spine (1); osteoarthritis, especially of the hip (2); cervical spine disorders such as atlantoaxial instability (3); hyperuricemia and gouty arthropathy (4). This paper describes the case of a person with a much less-common association of DS and rheumatoid polyarthritis (RP), of which only isolated cases have been reported, in addition to ours.

Clinical Case

The patient was a 35-year-old female with a history of penicillin allergy and repeated tonsil infections. She is employed in a non-institutional workshop setting. Family history was uneventful.

The patient was referred to the rheumatology outpatient clinic by the traumatology department with polyarticular pain.

She complained of longstanding pain in the left shoulder attributed to a fall some time ago, although this was not demonstrated. She also had pain, although less, in hands, knees, hips and cervical spine with progressively limited mobility in various joints, and walked with knees and hips in valgus. Previous treatment included analgesics and anti-inflammatory drugs and functional rehabilitation, with very little improvement.

Examination: Obesity with body mass index of 28.3, DS phenotypical features, asymmetrical breast size. Cardiac auscultation: Rhythmic, without murmurs. Pulmonary auscultation: Vesicular murmur. Abdomen: Soft and depressible, without visceromegaly. Musculoskeletal system: Numerous symptoms in the shoulders, and pain and limitation with movement of any kind. Hands: Signs of bilateral metacarpophalangeal (MCP) joint synovitis with pain and limited finger flexion and extension, and pressure pain in proximal interphalangeal (PIP) joints with ulnar deviation of the little fingers and swan-neck deformity in the third and fourth fingers of both hands (figure 1). Wrists: Pressure pain with flexion/extension and pronation/supination movements. Hips: Bilateral pain on forced abduction and rotation. Feet: Pressure pain in distal interphalangeal (DIP) and metatarsophalangeal (MTP) joints. Cervical spine: Pain on forced flexion/extension; both right and left lateral flexion and rotation.

Lab work: Hemogram: Hemoglobin 11.9 g/dL, MCHC 30.9 g/dL, leukocytes and rest of hemogram normal. Uric acid: 6.5 mg/dL, C-reactive protein 24 (0.01-6), ESR 71 (1-20). Tyrotropin 11.94 um/L (0.27-5). Rheumatoid factor (RF) 7.9 IU/mL (0.1-18). Antinuclear antibodies (ANA) and anti-ENA negative, anti-CCP antibodies normal. Complement C3 and C4 normal. TPO antimicrosomal antibodies 187.7 U/mL (0-35). Rest of tests were normal.

Radiology: Hands: Juxtaarticular osteoporosis, diminished joint space, subchondral cysts, destruction and subluxation of PIP joints. Longstanding erosion at ends of metacarpals, radial and ulnar side. Subchondral cysts in carpal bones (figure 2). Erosion and diminished joint space at bilateral humeral heads (figure 3). Anterior atlantoaxial subluxation in X-ray of cervical spine in flexion (figure 4).

The patient was diagnosed with seronegative rheumatoid arthritis and treated with synthetic antimalarial medication (hydroxychloroquine 200 mg/day) and Dezacor 7.5 mg/day, resulting in clinical and analytical improvement.

Discussion

Down syndrome (DS) is caused by the presence of a third chromosome 21. It involves a wide range of phenotypical expressions and various systemic and musculoskeletal problems, among other manifestations.

This patient had DS and, according to clinical and radiological findings, rheumatoid polyarthritis (RP), probably for several years. Although she was negative for rheumatoid factor and anti-CCP antibodies, she met 5 of the 7 American College of Rheumatology criteria for a firm diagnosis of this condition (5). RF has always been negative in the few published series of arthritis in DS (6). However, the recently discovered anti-CCP antibodies, which are the most specific for rheumatoid arthritis and are often used to label RF-negative patients as RP, have been found to be more prevalent in DS individuals, although not associated with clinical manifestations of the disease (7).

Padmakumar et al. (8) published an article on the scant relation between the two conditions, in which they identified only four DS children with arthritis over a period of 22 years in the British region of Mersey. Three of them were girls and all started with

Fig. 1. Signs of MCP joint synovitis, ulnar deviation of little fingers.

Fig. 2. Juxtaarticular osteoporosis, diminished MCP joint space, subchondral cysts in carpal bones and MCP tips, destruction and ulnar subluxation at fifth PIP joint.

Fig. 3. Erosion and loss of joint space in right shoulder.

Fig. 4. 3-mm anterior atlantoaxial subluxation.

oligoarticular manifestations that progressed to polyarthritis, particularly in the proximal interphalangeal joints of the hands. One of them was positive for antinuclear antibodies.

Perhaps more unusual is the association of DS and RP with atlantoaxial subluxation. In DS this atlantooccipital instability occurs in 21% to 63% of cases (9). Although the cause is not clearly known, it appears to be related to hyperlaxity of the transverse ligament of the atlas, which should hold the odontoid process of the axis level with the anterior arch of the atlas; however, it rarely causes neurological problems. The same abnormality manifests in 22-33% of RP cases (10) and here it is well known that the cause is synovial inflammation between the posterior side of the odontoid process and the transverse ligament, which is damaged by granulation tissue and increases the anterior atlantoaxial subluxation. In this case it causes pain and limited mobility of the cervical spine and often requires surgical repair. Our patient had a clinical picture of pain and stiffness of movement in the cervical spine with a radiological image of anterior atlantoaxial subluxation, although we are not yet able to determine which of the two conditions was the cause. Magnetic resonance imaging might have been helpful in differentiating them, but the family rejected it.

No treatment for RP in DS has been described and we feel it is a delicate issue because some of the commonly used therapies are risky and life-long treatment is likely to be required. We began treating the patient with synthetic antimalarials and oral steroids, although we think this is not the best long-term treatment because of the side effects of these two medications, especially their impact on visual acuity in the form of retinal pathology or cataracts, already common in DS individuals. We will probably turn to other slow-acting antirheumatic drugs if the disease progresses, such as methotrexate (bearing in mind the risk of leukemia) or leflunomide, although we have not found any cases published to date. We may consider using one of the anti-tumor necrosis factor drugs that work so well with rheumatoid arthritis.

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