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Case Report

Chronic arthropathy in Down's syndrome: Case report and literature review

Down's Syndrome (DS) is associated with an increased incidence of autoimmune diseases and it association with chronic arthropathyhas been described. This clinical condition has been described as Chronicarthropathy in Down Syndrome (A-DS) since 1984. We report acase of DS and polyarticulararthritis successfully treated with anti-tumor necrosis factor-alfa after immunosuppressant therapy. In this case we emphasize the importance to perform musculoskeletal clinic screening in every patient affected by DS. In fact, a precocious diagnosis of A-DS and an early treatment could prevent future functional limitations especially in this category of patients which present a worse prognosis.

Keywords: Down's syndrome • juvenile idiopathic arthritis • down's arthropaty • late diagnosis

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Introduction

Chronic arthropathy in Down Syndrome (A-DS) was first described in 1984 [1]. To date, the literature available about the clinical and radiological characteristics of this condition is scanty, despite its incidence being 3 to 6 times greater than the incidence of Juvenile Idiopathic Arthritis (JIA) in the general population [2]. Patients with Down Syndrome (DS) are routinely checked for various autoimmune diseases (Diabetes, thyroiditis, celiac disease) but not for arthritis. For this reason, A-DS is rarely recognized at its onset leading to a considerable diagnostic and therapeutic delay resulting in permanent joint damage.

Case report

A3-year-old girl with DS was referred to our department for the presence of lameness, swelling and functional limitation of the hands for about 1 year. Furthermore, morning stiffness lasting about 1 hour has been reported. Family and physiological history were unremarkable. The presence of patent foramen oval was reported in the patient's previous medical history. Blood tests, performed about 1 month before admission, showed an increase in the patient's inflammatory indexes (ESR 45 mm/1h, CPR 1.08 mg/dl).

At physical examination, the patient showed good general conditions. Normal vital parameters, characteristic facies, no evidence of pathological findings at cardio-thoracic and abdominal examination. Erythematous rash on lower limbs was observed. The articular examination showed arthritis involving the ankle joints (Tibio-Tarsic (TT), sub-astragalic (SA)), knees, wrists, Metacarpal Phalangeal joints (MCP) and Proximal inter-phalangeal joints (IFP) of the hands. Knees flexed (about 30°). On suspicion of chronic juvenile idiopathic arthritis, routine blood tests (blood count with formula, ESR, CPR, transaminases, Creatinine, LDH, CK, IgA), anti-Transglutaminase IgA and anti-Endomysium antibodies, Thyroid screening (FT4, TSH, antibodies) tireoglobulin and anti-thyroperoxidase antibodies), Anti-Nuclear Antibodies (ANA) and Rheumatoid Factor (RF) were performed, all in the normal range except for an increase of the inflammatory indexes (ERS 70, CPR 1.5 mg/dl). An eye examination with a slit lamp (no uveitis) was also carried out.

She started treatment with Naproxen 250 mg/day with partial benefit. After about 50 days, therapy with Methotrexate (MTX) SC (10 mg/m^2/week), Folic Acid (5 mg) and Prednisone (20 mg/day, progressively reduced over 3 weeks) started with benefit. After 1 month the patient showed good general condition. Absence of signs of arthritis except for slight pain in the wrists. No morning stiffness. Blood tests were normal.

At the inspection visit, after 3 months the patient presented no signs of arthritis but reported morning stiffness lasting about 20 minutes and feeling easily tired. Blood tests showed a slight increase in transaminases (AST 58 U/L, ALT 86 U/L). For this reason, it was decided to increase the dosage of folic acid (5 mg after 24 hours from MTX and 5 mg after 48 hours).

After 3 months, at the next checkup, the patient reported worsening morning stiffness (about 1 hour) and on physical examination there were signs of arthritis in the wrists, the MCPs and IFP of the hands, knees and ankles (TT,SA). Blood tests showed increases of inflammatory indexes (ERS 35 mm/1h, CPR 1.8 mg/dl and transaminases (AST 61 U/L, ALT 94 U/L).

Due to the persistence of symptoms, despite the therapy, and the patient's intolerance to the drug, we decided to discontinue MTX and start anti-TNF α therapy (Adalimumab 20 mg/m^2). At the check after 3 months the patient appeared in good general condition. General and articular physical examination were negative, blood tests normal, but slight knee flexion and bone enlargement in the ankles persisted as a permanent joint damage.

Discussion

Since 1981 authors have tried to evaluate the possible association between arthritis and DS. Only some years later Yancey et al. firstly described juvenile idiopathic arthritis-like arthropathy in patients with DS defining this clinical condition as Arthropathy of Down Syndrome (A-DS) [1,3,4].

Several case reports have been presented in literature and since the 1990 many authors tried to identify the exactly clinical and radiological findings of A-DS [5]. In particular, in a very recent observational study performed on a sample of 503 affected by DS, Foley et al. found through a musculoskeletal clinic screening that the 7% of patients presented inflammatory arthritis suggesting an A-DS prevalence of 20/1000 patients [6].

This prevalence resulted higher than the previous analysis underlining [7] that also if A-DS has been described in literature it remains under-reported and/or misdiagnosed. Moreover, our case presented a polyarticular arthritis that is the pattern of the disease most commonly observed also in the 33/503 patients considered in the retrospective study previously mentioned [6].

Other retrospective chart review, recently published, underlines also the existence of a consistent delay in diagnosis of A-DS. In this analysis authors observed that almost of 30% patients of the cohort presented, already at the diagnosis, erosive bone changes. This finding is probably due to the delay in recognizing the A-DS, resulted in 19-month average delay [8,9].

To date, in 2019, Foley et al. identified undiagnosed cases of A-DS and documented time to diagnosis. They also described clinical, laboratory and radiological features of A-DS at diagnosis. They studied 521 patients with DS and identified 33 children with A-DS. For this, they observed a significant delay of diagnosis (1.2 years). About clinical findings they showed that most cases presented erosive polyarticular-rheumatoid factor-negative arthritis, with predilection for small joints of the hands and wrists. As our patients, all children with A-DS had a negative ANA measurement [10].

Conclusion

A-DS is a more aggressive disease at onset and over the course of the disease compared to JIA. Even if we based on only 10 month-follow up, our patient is in a good control of disease with anti-TNFα therapy. We report this case to emphasize the importance to perform musculoskeletal clinic screening in every patient affected by DS. This screening could guarantee a precocious diagnosis of A-DS and an early treatment preventing future functional limitations especially in this category of patients which present a poorly toleration to the classical therapies (corticosteroids, DMARDs and biologics) and a worse prognosis.

Conflict of Interest

The authors declared no conflicts.

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Author's Note

Informed consent was obtained from his parents.

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