Patient with Arthritis and Down's Syndrome: A Dilemma to Distinguish, Juvenile Idiopathic Arthritis or Arthropathy of the Syndrome?

Artritli ve Down Sendromlu Hasta: Ayırt Edilmesi Gereken Bir İkilem, Juvenil İdiopatik Artrit mi, Yoksa Sendromun Artropatisi mi?

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ABSTRACT

Objective: There is data suggesting that the prevalance of arthritis is higher in children with Down syndrome (DS). In this case report we aimed to increase the awareness by discussing clinical features and course of the arthropathy in a patient with DS to facilitate more appropriate and timely diagnosis of arthritis in these patients.

Case: A 12 year-old girl with DS was diagnosed rheumatoid factor negative polyarthritis-type Juvenile idiopathic arthritis (JIA) according to modified diagnostic criteria of the International League of the Association for Rheumatology after one year the symptom onset. The patient was treated with methotrexate (MTX) 7,5 mg weekly, folic acid 5 mg/per week, prednisolone 5 mg daily, and naproksen 20 mg/kg per day. Six months after the initiation of the MTX therapy, all joint pain and swelling had resolved, erythrocyte sedimentation rate and C-reactive protein were within the normal ranges, indicating the achievement of clinical remission. The patient received rehabilitation programme consisting of hydrotherapy and physical therapy in our hospital. After comprehensive rehabilitation programme, patient exhibited gradual improvement regarding the functional status.

Conclusion: Healthcare professionals should be aware of the increased risk of arthropathy in patients with DS. Although DS arthropathy was encountered higher than JIA in the general population, it is yet an overlooked condition that might lead disability and functional impairment in children with DS.

Keywords: Down Syndrome, Juvenile idiopathic arthritis, pediatric arthritis

ÖZET

Amaç: Down sendromlu (DS) çocuklarda artrit prevalansının yüksek olduğunu düşündüren veriler mevcuttur. Bu olgu sunumunda, DS'lu bir hastada artropatinin seyri ve klinik özelliklerini tartışarak farkındalığı arttırmayı ve böylece bu hastalardaki artrit tanısının daha doğru ve zamanında konabilmesini amaçladık.

Olgu: DS'lu 12 yaşında bayan hastaya semptom başlangıcından bir yıl sonra Uluslararası Romatoloji Birliğinin modifiye tanı kriterlerine göre, romatoid faktör negatif poliartikuler tip Juvenil idiopatik artrit (JIA) tanısı konuldu. Hasta haftada bir 7,5 mg methotrexate (MTX), haftada bir 5 mg folik asit, günlük 5 mg prednizolon ve günlük 20 mg/kg naproksen ile tedavi edildi. MTX tedavisinin başlangıcından 6 ay sonra klinik remisyona ulaşıldığını gösterir şekilde, tüm eklemlerdeki ağrı ve şişlik gerilemişti, eritrosit sedimantasyon hızı ve C-reaktif protein değerleri normal sınırlarda idi. Hastaya hastanemizde hidroterapi

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ve fizik tedaviyi içeren rehabilitasyon programı uygulandı. Kapsamlı rehabilitasyon programı sonrası, hastanın fonksiyonel durumunda giderek artan bir iyileşme gözlendi.

Sonuçlar: Sağlık profesyonelleri DS'lu hastalarda artmış artropati riskine karşı uyanık olmalıdır. DS artropatisi ile genel populasyondaki JIA'dan daha fazla karşılaşılmasına rağmen, DS artropatisi hala DS'lu çocuklarda özürlülük ve fonksiyonel yetersizliğe neden olabilen, gözden kaçan bir durumdur.

Anahtar sözcükler: Down Sendromu, Juvenil idiopatik artrit, pediatrik artrit

Introduction

Juvenile idiopathic arthritis (JIA) is the most common cause of chronic joint inflammation in childhood, which is defined as an arthritis developing in patients aged 16 years or younger with no known cause, so other disorders need to be ruled out for the diagnosis (1). Down's syndrome (DS) is a disorder associated with trisomy of the chromosome 21 and characterized by an increased incidence of autoimmune diseases (2). However, there is limited information about the association of the rheumatic diseases with DS (3). It is unknown whether arthritis in DS patients represents JIA or a unique arthropathy when genetic and immunologic abnormalities associated with DS are taken into consideration (4).

There are only few reports in the literature demonstrating the association of DS with JIA until now (3-8). Increased awareness of arthritis in DS patients may facilitate earlier diagnosis. The lack of professional awareness of this condition and inconsistent surveillance for arthritis increases the time for diagnosis. Delayed diagnosis of patient can lead to permanent joint damage which could be avoided with early treatment. With this case report, we aimed to increase the awareness by discussing clinical features and course of the arthropathy in a patient with DS to facilitate more appropriate and timely diagnosis of arthritis in DS patient.

Case report

A 12 year-old girl with DS had a 5 year history of symptoms in her joint. She was 7 years old when she had pain and swelling in her left knee. She also had pain and swelling of the wrist and small joints of the hands, which lasted for months. In a clinic elsewhere; the patient was diagnosed as JIA and began to receive treatment with prednisolone 5 mg daily and non-steroidal anti-inflammatory drugs when she was 8 years old. Partial response was achieved with this treatment. In the subsequent year she developed deformities in the wrists and the small joints of the hands.

She was referred to our hospital when she was 10 years old. Examination of the musculoskeletal system revealed bilateral synovitis of proximal interphalangeal joints, limited motion of bilateral elbows, wrists, metacarpophalangeal joints, proximal interphalangeal joints. There were pain and swelling in the proximal interphalangeal joints of the hands. She had full range of motion in her lower extremities. The patient reported morning stiffness lasting for one hour or longer. She had no occular involvement, had normal range of motion of the neck and neurologic examination revealed no pathology. The patient also had mild mental motor retardation with typical stigmata of DS.

On admission to our hospital, she had 12 painful joints and 15 swollen joints. Of her laboratory examination; complete blood count was normal, serologic investigation was negative for rheumatoid factor (RF) and antinuclear antibodies (ANA). C-reactive protein (CRP) was 6.1 mg/dl (normal ranges, <0.5 mg/dl). Also erythrocyte sedimentation rate (ESR) was 46 mm/h. HLA typing was negative for HLA B27 and additionally C3 and C4 were normal. Finally her chromosome analysis revealed 47xx, + 21 karyotype.

In consistent with physical examination, radiographs revealed typical features of advanced disease; soft tissue swelling, bilateral radiocarpal and carpometacarpal joint space narrowing, periarticular osteoporosis, demineralized carpal bones, erosions in carpal bones (Figure 1). Cervical, thoracic and lumbosacral spine x-rays were reported as normal.

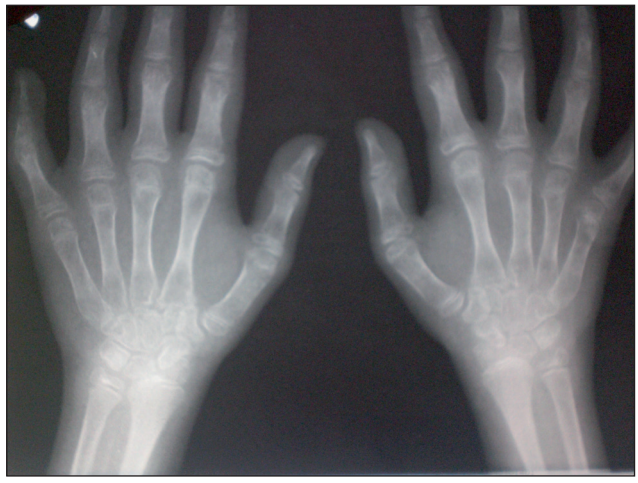

Figure 1. Bilateral hand x-ray.

She was also dependent in activities of daily living such as feeding, hygiene and dressing. Functional ability was assessed by the Turkish version of The Childhood Health Assessment Questionnaire (CHAQ), which is a reliable and valid tool for the functional ability in daily living activities of children with JIA (11). On admission to our rehabilitation unit her CHAQ disability index score was 0.58 ±64.

On the basis of these findings, RF negative polyarthritis-type JIA was diagnosed in accordance with the modified diagnostic criteria of the International League of the Association for Rheumatology (12). The patient was treated with methotrexate (MTX) 7,5 mg weekly, folic acid 5 mg/per week, prednisolone 5 mg daily, and naproksen 20 mg/kg per day. Six months after the initiation of the MTX therapy, all joint pain and swelling had resolved, ESR and CRP were within the normal ranges, indicating the achievement of clinical remission (tender joint count 0, swollen joint count 0). A resolution of clinical signs of active inflammation was achieved six months after the initiation of MTX.

The patient received rehabilitation programme consisting of hydrotherapy and physical therapy in our hospital. Hydrotherapy program was planned as five sessions a week of 20 minutes with warm water swirling in whirlpool tank for four weeks, for a total of 20 sessions. We recommended a static hand-wrist splint and active extension exercises. Static wrist splint and stretching exercises help to prevent and can gradually correct deformity. Moreover we added active and passive range of motion exercises for finger joints, preserving muscle power with squeezing a sponge and not alllowing excess load onto loose joints. The strengthening exercises were also performed for upper and lower extremity muscles using therabands. A postural exercise was also included in the exercise programme. At the end of 4 weeks; home based exercises programme was started. After comprehensive rehabilitation programme, patient exhibited gradual improvement regarding the functional status and her CHAQ disability index score decreased to 0.23 after 6 months.

Discussion

JIA is diagnosed by fulfilling criteria that include 6 weeks of persistent synovitis in one or more joints and excluding other causes of childhood arthritis. There are previous reports in the literature of patients with DS and JIA (3-8). Our patient with DS developed a symmetric inflammatory polyarthritis at the age of 7, affecting both small and large joints and sparing the back and sacroiliac joints. Her RF and HLA-B27 antigens were negative. Her symmetric polyarticular inflammatory arthritis showed a clinical response to medical therapy.

There is data suggesting that the prevalance of arthritis is higher in children with DS (9). Prevalence of DS arthropathy is 8.7/1000, more than 6 times higher than JIA in the general population (10). In a case series, seven DS patients with arthritis have been described which large joints were involved and associated with negative ANA and RF (3). However unlike JIA, systemic features were absent. Researcher recommended a new condition to be named as arthropathy of DS since the diagnosis of JIA is a diagnosis of exclusion. It is contraversial whether the "JIA like arthritis" in DS patients is actually "JIA" or "a unique arthropathy associated with DS".

Four previous reports described polyarticular JIA and assosiated DS briefly (5-8). All of these patients had cervical spine subluxation and this was the major emphasis of the disease reports, so specific details of the arthritis are somewhat limited. In general population, pauciarticular disease is the most frequent onset type, representing approximately half of the patients with JIA, polyarticular onset disease is seen in one third of patients. However, in a case series 71% of 21 patients with DS and arthritis presented with polyarticular disease (4). In a recent study it was reported that 57% had polyarticular disease, and 43% had oligoarticular disease at symptom onset, but later 54% with oligoarticular disease progressed to polyarticular disease (10). Moreover in this study the majority of patients had long delays before diagnosis. (4). Average delay from symptom onset to diagnosis was 2 years in another study with age at onset varied from 20 months to 12 years (10). In a recent case, the diagnostic delay of JIA was eight years for a patient with DS (13). In DS, the diagnosis of arthritis is usually delayed because the joints' symptoms are assumed to be related to the syndrome itself. Furthermore children with DS have unusual hand shapes and joint hypermobility which may lead to miss arthropathy. Also our patient was diagnosed one year after the symptom onset when she was 8 years old and had polyarticular disease onset.

In a case series, it was concluded that DS patients with arthritis frequently follow a progressive polyarticular course complicated by subluxations, and perhaps may have increased drug toxicity, but long-term follow-up and collaborative study are needed to determine whether the course of rheumatic diseases and complications of therapy in DS differ from those in the general population (4). Furthermore in another study, seventy-two percent DS patients with arthritis had an elevated ESR, almost half had development of joint subluxation and most of them required disease modifiying drugs (10). In our case, radiographic findings of affected joints showed rapid progression, deformities in multiple joints despite treatment and elevated inflammatory markers such as CRP and ESR, which revealed poor prognosis. A

comprehensive rehabilitation programme must be started early to restore loss of function and permanent handicap.

DS and JIA have been associated with ligament laxity, particularly the atlantoaxial ligament, which maintains the proper positioning of the cervical first and second vertebrae (14). Both DS and JIA can cause instability of the cervical spine (5). DS is also associated with a variety of skeletal abnormalities and an increased incidence of joint hypermobility (3). Four previous reports briefly described cervical spine subluxation which was indeed their major concern (5-8). Although stabilization of cervical spine is poor in these patients, our patient had normal cervical spine radiography with normal neurological findings. DS patients with JIA should be considered as having potential risk for the development of cervical subluxation.

Conclusion

Healthcare professionals should be aware of the increased risk of arthropathy in patients with DS. Although DS arthropathy was encountered higher than JIA in the general population, it is yet an overlooked condition that might lead disability and functional impairment in children with DS.

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