Juvenile Idiopathic Arthritis: Review of the Literature and Case Report

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ABSTRACT

Juvenile idiopathic arthritis (JIA), previously known as juvenile chronic arthritis or juvenile rheumatoid arthritis, is a chronic disease of childhood with a spectrum of joint involvement and associated systemic involvement. The cause of JIA is poorly understood, and no drugs can cure the disease currently. Pediatric dentists should be familiar with the symptoms, complications, and oral manifestations of JIA to help manage the disease and provide quality care to these patients. The purpose of this case report is to review the condition and to describe the case of an adolescent with polyarticular juvenile rheumatoid arthritis, focusing on specific recommendations for dental management. (J Dent Child 2013;80(1):25-30)

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Juvenile idiopathic arthritis (**JIA**) is the most common chronic rheumatic disease of childhood and an important cause of short- and long-term disability.[1] Juvenile arthritis is a heterogeneous group of diseases of unknown etiology, many of which are clinically and genetically distinct from chronic arthritis in adults (Table).[2] The term JIA has replaced previous terms such as juvenile chronic arthritis or juvenile rheumatoid arthritis to more accurately identify homogeneous groups of children with distinct clinical features. The International League of Associations for Rheumatology, which has provided the most recent classification, identifies 7 subtypes of JIA with specific exclusion and inclusion criteria.[2]

JIA patients experience a myriad of symptoms, including lethargy, reduced physical activity, poor appetite, and flu-like symptoms. Although the initial manifestation of JIA is variable, the cardinal clinical features include persistent swelling of one or more joints, limited range of motion of the joints, and pain during movement lasting at least 6 weeks[1]. Onset of JIA is usually before 16 years of age.[1]

In the most severe cases of JIA, the patients may exhibit marked retrognathia, open bite, microgenia, and "bird-like" facies. Females are much more frequently affected with almost all types of JIA than males.[1,3,4] The worldwide prevalence of JIA varies between 16 to 150 people per 100,000, with the frequency of different subtypes of JIA varying with location and ethnicity.[5]

The purpose of this case report is to review the condition and describe the case of an adolescent with polyarticular juvenile rheumatoid arthritis, focusing on specific recommendations for dental management

CASE REPORT

A 14-year-old female (Figure 1) was referred to the Department of Pediatric and Preventive Dentistry at the V.S. Dental College and Hospital by the medical outpatient department at the KIMS Hospital with a chief complaint of throbbing pain in the permanent maxillary central incisors. A fall four months before led to complicated crown fractures of the permanent maxillary right and left central incisors for which no dental treatment was sought. The pain was persistent and subsided only when she took analgesics.

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She was diagnosed with JIA at 2 years of age. Her family history was noncontributory. The patient's height was 76.2 cm and her weight was 20 kg (44lbs), which was below the fifth percentile on the growth chart. She had a limping gait, could not walk or stand without support, and was completely dependent on an adult. She had been on a daily dose of systemic steroids (1mg prednisolone which was gradually tapered to 0.1mg over a period of two weeks) and non-steroidal anti-inflammatory drugs (NSAIDs) since she was diagnosed. She was taking an oral combination of ibuprofen 100mg and paracetamol 162.5mg/5ml every six to eight hours for her toothache. She did not have any drug allergies. She showed painful ankylosis of the elbow and knee, proptosis of the eye, and JIA-associated uveitis, an inflammation of the middle layer of the eye, which caused loss of vision. Due to long periods of illness, she had to attend a special education school, even though she had normal intelligence. The school helped her participate as fully and independently as possible in daily activities. This was the patient's first visit to the dentist.

The extraoral examination revealed brachycephaly, and a short and broad but symmetrical face. She had a straight facial profile and an orthognathic facial divergence. Then lips were incompetent. She also exhibited a flat nasal bridge with a large, bulbous tip and a small mouth (Figure 2). Examination of the temporomandibular joint (TMJ) revealed no tenderness, clicking or crepitation. There was a slight deviation of the mandible to the right. She had a 35-mm interincisal opening without any difficulties. The intraoral examination showed permanent dentition, with unerupted second molars and maxillary canines. The molar relation was Angle Class II subdivision 1. Anterior open bite, chronic generalized gingivitis, moderate deposition of calculus, and inflamed and edematous marginal gingiva were noted (Figure 3). There were also complicated crown fractures and extensive dental caries in the permanent maxillary right and left central incisors as well as incipient carious lesions on the permanent mandibular right and left first molars. The central incisors were tender to percussion due to acute exacerbation of chronic pulpitis. Because of the time elapsed between the dental trauma and seeking treatment, the pulpal tissue became necrotic and root canal treatment was indicated.

Due to frequent hospital visits, the patient developed phobia of the environment and became uncooperative for dental treatment. Therefore, the treatment was carried out under general

Table. ***International League of Associations for Rheumatology Classification, Inclusion, and Exclusion Criteria, Frequency, and Sex Distribution of Juvenile Idiopathic Arthritis*[2,3]**

Classification	Inclusion criteria	Exclusion criteria	Frequency (%)	Sex ratio (F:M)
Systemic arthritis	Onset age: throughout childhood No. of joints affected: variable Systemic features: quotidian fever +≥1 of the following: erythematous rash, myalgias, lymphadenopathy, hepatosplenomegaly or serositis	N/A	4-17	1:1
Oligoarthritis	Onset age: early childhood, peak 2-4 ys No. of joints affected: persistent: ≤4; extended: ≥4 joints after the first 6 mos	Psoriasis/family history human histocompatibility leukocyte antigen B27 Rheumatoid factor: positive Males >6 ys	27-56	3:1
Rheumatoid factor: positive Polyarthritic	Onset age: late childhood, adolescence No. of joints affected: ≥5 joints Serological test: immunoglobulin M Rheumatoid factor: positive	Immunoglobulin M rheumatoid factor: negative	2-7	2:1
Rheumatoid factor: negative Polyarthritis	Onset age: biphasic distribution, early peak 2-4 ys, later peak 6-12 ys No. of joints affected: ≥5 joints Serological test: immunoglobulin M Rheumatoid factor: negative	Immunoglobulin M rheumatoid factor: positive	11-28	2:1
Enthesitis-related arthritis	Onset age: late childhood or adolescence No. of joints affected: variable, usually ≤4 Other diagnosis: enthesitis	N/A	3-11	2:1
Psoriatic arthritis	Onset age: biphasic distribution, early peak at 2-4 ys, late peak at 9-11 ys No. of joints affected: variable, usually ≤4 Other diagnosis: psoriatic rash, family history of psoriasis, dactylitis	N/A	2-11	3:1
Undifferentiated arthritis	Onset age: N/A Patients who do not satisfy inclusion criteria for any other category	N/A	11-21	No known sex predilection

**** A child is diagnosed with a specific subtype of juvenile idiopathic arthritis if he or she falls into one of the categories listed here.***

Figure 1: 14-year-old female with juvenile idiopathic arthritis.

anaesthesia and amoxicillin 20mg/kg body weight t.i.d for seven days was prescribed because of the pulpal necrosis. The patient did not receive a steroid boost perioperatively because she did not have adrenal insufficiency. The treatment included dental prophylaxis, root canal treatment on the maxillary central incisors, followed by a composite build-up, pit and fissure sealants on the maxillary right and left first molars, occlusal composite on the mandibular right and left first molars, and application of topical 1.23% acidulated phosphate fluoride. The patient's recovery was uneventful. Her weekly follow-up for a month revealed good oral hygiene, no eating difficulties, and no dental symptoms. Oral hygiene instructions were repeatedly reinforced to the patient and her parent on each visit.

DISCUSSION

JIA PATHOGENESIS

Inflammation of the synovium, a thin layer of tissue only a few cells thick which lines the joints and tendon sheaths, is a key pathological feature of JIA.[3] The exact trigger and factors that allow the inflammation to become chronic, however, are not clearly understood. The prevailing view is that both inherited and environmental factors are important and that an autoimmune reaction precipitates a cascade of inflammatory changes.[3]

Once an immune response is initiated and inflammation in the joint is triggered, B lymphocytes produce immunoglobulins. In some subsets of JIA, rheumatoid factors of the immunoglobulin G (IgG) and immunoglobulin M (IgM) classes are deposited in the sublining layer of the synovium.[6,7] This response subsequently activates the serum complement cascade and recruits the phagocytic arm of the immune response, which further exacerbates the inflammation of the synovium, leading to edema, vasodilation, and infiltration of activated T cells.[6,7]

Early and intermediate molecular mediators of inflammation have been identified in the synovium of some JIA patients, including tumor necrosis factor alpha, interleukins 1, 6, 8, and 15, transforming growth-factor beta, fibroblast growth factor, and platelet-derived growth factor.[8,9] All these factors contribute to the breakdown of collagen and the proteoglycan matrix of articular cartilage. Once the inflammation is established, the synovium thickens, the cartilage and the underlying bone begins to disintegrate, and evidence of joint destruction occurs.[10-12] Genetic factors and specific gene loci are important in the pathogenesis of JIA.[13] Several genes, including at least one in the human histocompatibility leukocyte antigen (HLA) region, affects susceptibility to JIA. Different subsets of JIA, however, are associated with different HLA and non-HLA regions, which likely account for the heterogeneity of the disease. In predisposed children, environmental triggers, such as exposure to sunlight or cigarette smoke, drugs, and infection, may precipitate the development of JIA.[3]

CLINICAL PRESENTATION

JIA is a clinically diverse spectrum of diseases, and many children will have spontaneous remission. At least one third of patients, however, have either ongoing active disease into adulthood or will have significant morbidity from sequelae of previous inflammation. The long-term effects of JIA are joint damage that may require joint replacement, visual loss, osteoporosis, psychosocial morbidity, and unemployment due to the chronicity of the disease.[3] Common differential diagnosis of systemic JIA includes infections (septicemia, infective endocarditis, brucellosis, typhoid fever leishmaniasis, and viral infections), malignancy (leukemia, lymphoma, and neuroblastoma), rheumatic fever, connective tissue disease (systemic lupus erythematosus, Kawasaki disease), inflammatory bowel disease, Castleman's disease, and auto-inflammatory syndrome.[3]

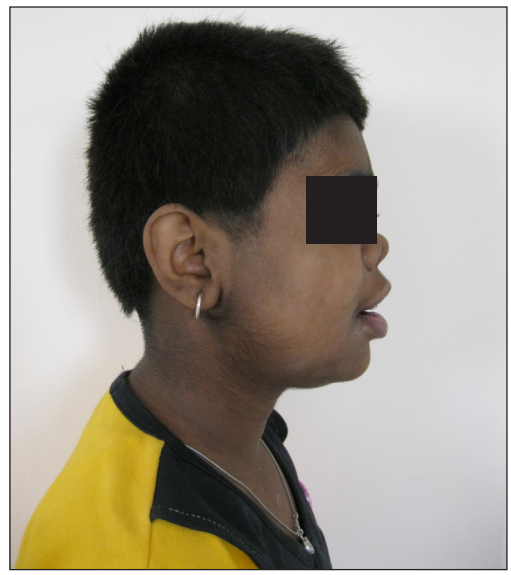

Figure 2: Profile photo showing a flat nasal bridge with a large, bulbous nose tip and incompetent lips.

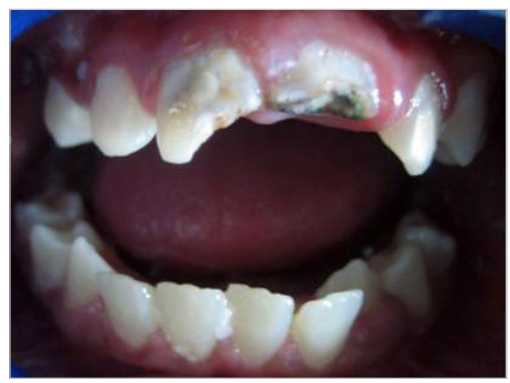

Figure 3: Intraoral photo showing complicated crown fractures and caries in the maxillary central incisors, poor oral hygiene and generalized gingivitis.

TREATMENT

Management of JIA is based on a combination of pharmacological interventions, physical and occupational therapy, and psychological support. Among the pharmacological treatments used in JIA patients are NSAIDs, intra-articular steroids (triamcinalone hexacetonide), systemic steroids (prednisone), disease-modifying antirheumatic drugs (**DMARDs**, such as methotrexate), and biological medications (etanercept, anti-IL-1 or anti-IL-6 drugs).[13]

NSAIDs have been the mainstay of the treatment of this disease for decades; however, only a few, such as naproxen, ibuprofen, and indomethacin, are approved for use with children. They are generally well-tolerated and have few side effects.[3] Intra-articular steroid injections with triamcinolone hexacetonide are frequently needed at the onset and during the course of the disease.[3] For monoarticular or oligoarticular arthritis, they may be used with or with-out NSAIDs.[3] These steroids are effective rapidly and help prevent deformities.[4] Moderate- or high-dose systemic corticosteroid therapy is reserved for patients with systemic JIA whose disease is not well-controlled by NSAIDs.[3] Corticosteroids are used very selectively because of their potentially toxic effects such as growth arrest and retardation, cataracts, osteoporosis, compromised immunity, atherosclerosis, hyperglycemia, Cushingoid appearance, acne, adrenal insufficiency, and osteopenia.[3]

There have been major changes in the management of JIA over the last 10 years. In particular, DMARDs have become the second line treatment of choice for persistent active arthritis because of its steroid-sparing activity and ability to minimize growth failure.[14] Improvement is usually seen after 6 to 12 weeks, and supplementation with folic acid helps prevent the occurrence of liver-enzyme abnormalities that can occur as a result of methotrexate treatment.[15,16] However, methotrexate in pediatric rheumatology is used in smaller doses and for longer periods of time when compared with pediatric oncology, for example.

The introduction of biological medications has also provided an important new therapeutic option for the treatment of JIA patients who are resistant to antirheumatic agents. Etanercept (0.4 mg/kg, given subcutaneously 2x weekly) is very effective for patients who have polyarticular disease and are resistant or intolerant to methotrexate.[17] Because JIA patients take combinations of potent immunosuppressives, including methotrexate, biological medications, and steroids, they are at constant risk for infection and bacteremia.[18] Systemic features of sepsis may be altered by immunosuppression, thus a child with well-controlled JIA whose condition flares up for no apparent reason should be examined to rule out an odontogenic infection.

PROGNOSIS AND OUTCOMES

Many of the reports of poor disease outcome and disability reflect the treatment of decades ago. Contemporary therapies, such as early and aggressive use of methotrexate and other immunosuppressives, have resulted in improved outcomes.

JIA in children has a negative effect on bone and joint development.[19,20] Local growth disturbances take place at the sites of inflammation and result in either overgrowth (possibly related to inflammation-induced increased vascularization and growth-factor release) or undergrowth, secondary to growth-center damage or premature fusion of epiphyseal plates of the juxta-articular bone extremities. Anomalies in the growth and morphogenesis of skeletal segments also result from irregular traction on growing structures.[3,6] Micrognathia, unequal leg length, and developmental anomalies of the hip are examples of possible results of these processes.[21-23]

JIA AND ORAL HEALTH

Oral inflammation and infections contribute to the overall inflammatory response of the body, which makes optimal oral hygiene for patients with JIA mandatory.[23] In addition to that, the anti-inflammatory and analgesic medications taken by these patients may camouflage an infection.[24] JIA may lead to malocclusion and increased dental caries due to poor oral hygiene and use of potentially sucrose-rich medications. Poor oral hygiene may be a result of upper-limb involvement, which may affect the patient's ability to perform fine-motor movements required for efficient tooth-brushing and flossing. Although used in small doses in JIA, methotrexate may lead to stomatitis or oral ulceration.

Cyclosporine may cause gingival hyperplasia, blood dyscrasia, renal impairment, and hypertension.[25] Patients with JIA who have decreased levels of Calcium, phosphate, potassium, lysozyme, and immunoglobuin A, have more salivary abnormalities than healthy controls.[26]

OROFACIAL FINDINGS ASSOCIATED WITH JIA

Orofacial findings in JIA include limited range of motion of the TMJ with progressive open bite and retrognathia. Reports of TMJ involvement in JIA range from 17% to 87%.[22] Approximately 45% of cases may be diagnosed from radiographic changes on an orthopantogram.[27,28] TMJ involvement is not uncommon but it may be subclinical. JIA patients with TMJ involvement may complain of morning stiffness of the joint, trismus, reduced interincisal opening, reduced ability to translate, and possible clicking or crepitation.[28] Pathologic changes within the condylar head, such as progressive loss of the posterior vertical dimension from progressive condylar resorption, are thought to adversely affect the growth potential of the region.[5]

Micrognathia and retrognathia, which are less common nowadays because of the current management of the disease, usually occur in children with severe refractory

disease or those who received care late in the course of their disease.[29] Radiographic changes may include shortening of the mandibular body and ramus, flattening of the condyles, and increased antegonial notching.[27] JIA patients also typically present with posterior or downwards mandibular rotation, a steep mandibular plane and mandibular retrognathia.[27-32] Associated with the mandibular changes are an increased vertical growth of the anterior face and anterior open bite.[33]

DENTAL CARE FOR PATIENTS WITH JIA

Dental evaluations/screenings must be included in the initial team assessment of these patients because poor oral health is a risk factor for systemic infection, especially when the patient is immunocompromised through the use of corticosteroids or DMARDs. For patients who are taking long term-term corticosteroids, delayed wound healing and increased risk of infection may impact the delivery of dental care because of the risk of adrenocortical insufficiency when any surgery or stressful treatment is planned.[34] Steroid coverage prior to invasive dental treatment may be needed for those at risk of adrenal crisis. The use of regular daily exercises has been proposed to improve the range of movement of the TMJ and, hence, facilitate oral hygiene maintenance. Good oral health is, therefore, important to minimize complications of the disease.[35]

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