CASE REPORT
NORTH BENGAL MEDICAL COLLEGE JOURNAL [2022], VOL., 8, No. 1 : 32-37

A Rare Combination of Systemic Onset Juvenile Idiopathic Arthritis (SOJIA) with Ventricular Septal Defect (VSD): A Case Report

*Syed Mohammad MonowarAli

ARTICLE INFO

Article history:
Received: 10 December 2021
Accepted: 31 December 2021

Online:
www.nbmc.ac.bd

Keywords:
Juvenile idiopathic arthritis, Systemic-onset Juvenile idiopathic arthritis, ventricular septal defect

ABSTRACT

Juvenile idiopathic arthritis (JIA) is an umbrella term for a family of heterogeneous childhood arthritis of unknown cause. It is defined by the presence of inflammatory arthritis with a duration of ≥6 weeks in children <16 years of age. Systemic-onset JIA (SOJIA) is a distinct subset of JIA, characterized by the presence of systemic inflammation as extra-articular features. This case of SOJIA who presented with recurrent bouts of fever and deforming arthritis along with ventricular septal defect, a rare association of SOJIA.

[1.] *Professor, Department of Medicine, Shaheed M Monsur Ali Medical College, Sirajganj, Bangladesh*

***Corresponding author:** ✉syedmonowaraliapu@gmail.com

INTRODUCTION

Juvenile idiopathic arthritis (JIA)is a common chronic childhood disease and the most common childhood rheumatic disease.[1] The incidence and prevalence vary widely, with lower rates in Asian populations and higher among those of European background(Incidence ranges from <1per 100,000 children in Japan to 23 per 100,000 in Norway).[2] Various terms were in practice to classify children with persistent arthritis, until the integrated term "juvenile idiopathic arthritis " was first introduced by the International League of Associations for Rheumatology (ILAR), to describe the heterogeneous group of disorders of unknown etiology characterized by arthritis lasting ≥6weeks in children <16 years of age. The ILAR classification was formed by expert consensus in 1995, with revisions in 1997 and 2001.[3]

Systemic-onset JIA (SOJIA), formerly known as Still's disease, accounts for 10% to 20% of all JIAs. It has unique characteristics that include fever, specific rash, lymphadenopathy, organomegaly, serositis and significantly elevated inflammatory markers in addition to arthritis.[1]It may begin in young children during the first or second year of life, although cases are distributed throughout childhood. The fever of SOJIA is usually quotidian or double-quotidian, which means temperature returns to base line on a daily basis. The temperature swings can often become dramatic, may behave like remittent fever with changes up to 4^0C within four hours.[4,5] The rash can assume any pattern, often urticarial, macular and salmon pink in colour, can occur on any part of the trunk or extremities, typically spares the face. Sometimes it appears during temperature peak, with a predilection for axilla and waist.[1,4] ILAR defines SOJIA as, "arthritis in one or more joints with or preceded by fever of at least 2 weeks duration that is documented to be daily ("quotidian") for at least 3 days and accompanied by one or more of the following: 1. evanescent (nonfixed) erythematous rash 2. generalized lymph node enlargement 3. hepatomegaly and/or splenomegaly 4. Serositis (pleural/ pericardial involvement/ abdominal pain). Exclusions: psoriasis/or history of psoriasis,

arthritis in an HLA-B27 positive male, ankylosing spondylitis, enteritis related arthritis and other arthritis and extra-articular features related to spondyloarthritis, the presence of IgM rheumatoid factor on at least two occasions at least 3 months apart.[3] Other systemic features include headaches, and sore throat. Pericarditis and pericardial effusions are the most common organ system manifestations, occurring in 30-40% of patients. Myocarditis is a rare complication that can cause arrhythmias and heart failure.[4]

Recent research has identified biologic differences of SOJIA from other JIA subcategories, including prominent involvement of components of the innate immune system (in particular, inflammatory cytokines IL-1, IL-6, and IL-18, neutrophils and monocytes/macrophages), suggesting that SOJIA is closer to the auto-inflammatory pole of the disease spectrum compared with the autoimmune pole.[6, 7]

There are no diagnostic tests for SOJIA. Actually it is a diagnosis of exclusion, although there are characteristic patterns of laboratory abnormalities, including high inflammatory markers (e.g., elevated serum ferritin in 70% cases), significant leukocytosis with neutrophilia, thrombocytosis and anemia. Liver transaminases and coagulation screen may be abnormal in severe cases.[4]

Treatment of SOJIA depends on the extent of organ involvement (especially arthritis) and the severity of systemic inflammation. American College of Rheumatology (ACR), recommends treatment of SOJIA after categorizing it into two sub-groups: 1. systemic arthritis with active systemic features (and without active arthritis) and 2. systemic arthritis with active arthritis (and without active systemic features).[8] In general, treatment of SOJIA begins with nonsteroidal anti-inflammatory drugs (NSAIDs), which alone maybe effective for many children. Second line agents, such as glucocorticoids or methotrexate, are used if NSAIDs are ineffective. Biologic agents, such as monoclonal antibodies to interleukin-1 (IL-1) or IL-6, appear effective in reducing clinical symptoms in patients with disease refractory to conventional therapy.[4]

This presenting case is a unique one, as I didn't find any case report of SOJIA with congenital heart disease, during our extensive and diligent MEDLINE/Pub search. The peculiar combination of SOJIA with VSD may thus be considered as first ever case report in Bangladesh nevertheless, if not on a subcontinent or global basis.

The Case

Master Ovi, a 12-year-old boy with short stature and micrognathia from a non-consanguineous parent, got admitted into the department of medicine, Shaheed M Monsur Ali Medical College Hospital (SMMAMC&H), Sirajganj, Bangladesh on October, 2021 with the complaints of high fever, prostration and pain, swelling and deformity of few large joints (bilateral wrists, knees, left elbow) and pain in right groin with limping. He has had a history of fever, pain and swelling of the mentioned joints, which first appeared eight years back (Figure 1)

Figure 1: The case (boy) with apparent knee (bilateral) and elbow (left) deformity

That initial episode ended with subsidence of fever but persistence of joint symptoms at a lower intensity. Since then he experienced multiple episodes of fever and aggravation of joint symptoms and gradual development of deformity. He didn't give any history of inflammatory back or neck pain, neither any history of red itchy eye, blurred vision, bloody diarrhoea, scaly skin rash or inflammation of small hand-feet joints. He was treated with different NSAIDs and corticosteroids, of and on for all these years and methotrexate for few months initially.

His general examination revealed, stunted growth (height 132 cm), raised temperature (103^0F), micrognathia, severe anemia, bilateral cervical lymphadenopathy, leg oedema and engorged neck vein. Examination of abdomen revealed hepato-splenomegaly. Cardiovascular system examination revealed displaced apex and a pansystolic murmur. Auscultation of lung revealed bilateral basal crepitation. In locomotor system examination he showed grade: IV tenderness of knees and wrists, grade: II of left elbow with movement restriction of all those joints. Hip joint examination was normal on the left side but restricted flexion, abduction and external rotation with grade: III tenderness on the right side. Gait was antalgic with less time spent on the right-side during walking.

Investigation revealed: haemoglobin: 7.3 gm/dl, total count leukocyte: 14,000/mm^3, Neutrophil: 81%, ESR: 120 mm in 1^{st} hour, peripheral blood film (PBF): normocytic normochromic anaemia, serum ferritin: 1500 ng/ml (marked raised), anti-nuclear antibody (ANA): negative, anti-cyclic citrullinated peptide(anti-CCP): negative, X-Ray chest postero-anterior view: shows cardiomegaly (right ventricular type) with fullness of pulmonary conus (Figure 2), X-Ray pelvis with both hip joints AP view: shows deformity of femoral head with narrowing of joint space (Figure 3), ultrasonography of whole abdomen: hepato-splenomegaly, echocardiography: sub-aortic ventricular septal defect (VSD) with moderate pulmonary hypertension (Figure 4).

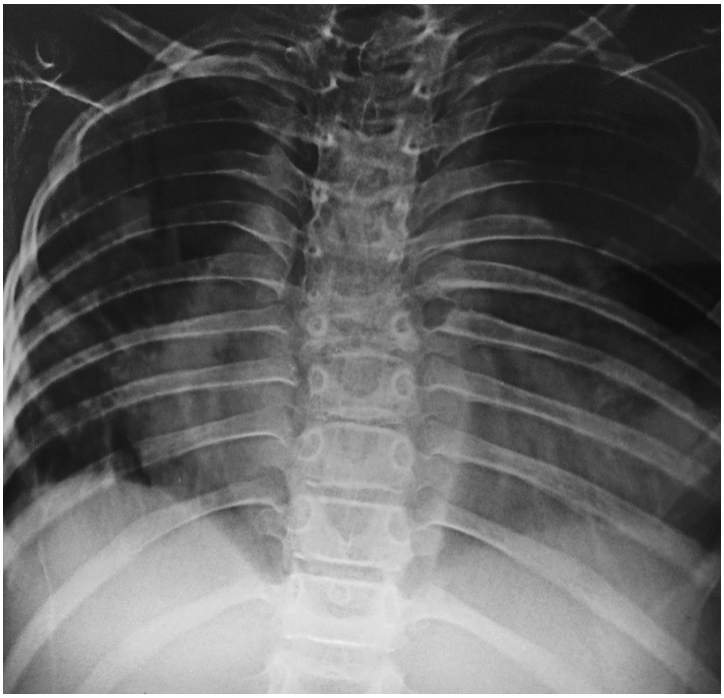

Figure2: X Ray chest PA view showing cardiomegaly (right ventricular type)

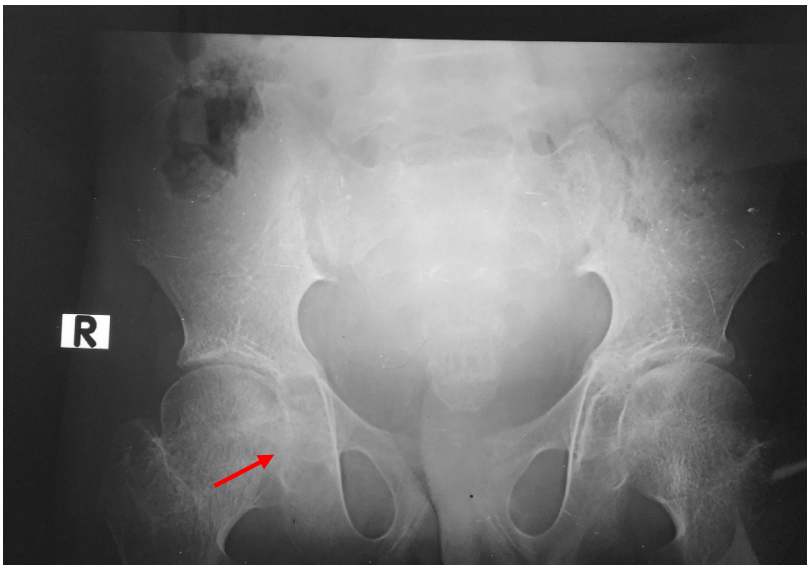

Figure3: X-Ray pelvis with both hip joints AP view showing deformity of femoral head (right) with narrowing of lower and medial joint space (Arrow).

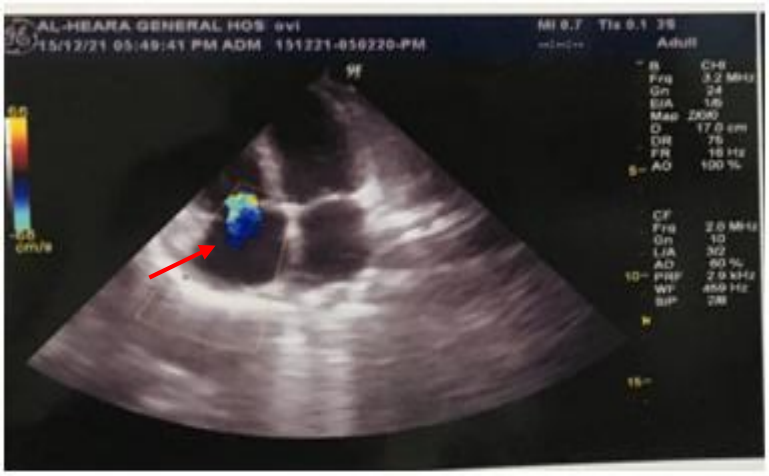

Figure 4: Doppler echocardiography showing subaortic VSD (Arrow)

During stay at our hospital, he was prescribed naproxen (250 mg, twice daily), tramadol (25 mg, twice daily), prednisolone (20 mg/day), methotrexate (MTX,10mg/week), calcium (1 gm/day) and vitamin D(400 IU/day) and frusemide (20 mg twice daily). Intra-articular steroid (triamcinolone acetonide 20mg each joint) was given in both knees. After seven days his joint symptoms improved significantly and fever subsided completely. He was discharged after 15 days with advice to continue MTX indefinitely, naproxen for 2 weeks and prednisolone, in a tapered schedule to discontinue in 6 weeks. He was on regular physiotherapy (as per our advice), on regular follow-up, in our weekly rheumatology out-patient department (OPD) SMMAMC&H and continuing his health reasonably well.

DISCUSSION

Systemic-onset JIA (SOJIA), a relatively common form of JIA, differs from other JIAs, in respect to its systemic involvement, absence of serologic markers, and relatively early age of onset and gender neutrality. Unlike the pauciarticular and

polyarticular subtypes of JIA, the arthritis of SOJIA may begin in the hips and progress very rapidly, causing severe damage and dysfunction as well as loss of growth prospective in younger patients. Micrognathia and cervical spine fusion are commonly present in children with chronic SOJIA.[4] According to the classification criteria proposed by the International League of Associations for Rheumatology (ILAR), clinical presentation of this case qualifies him as a case of SOJIA.[3]Regardless of having most of the typical clinical feature of SOJIA since his early childhood, the diagnosis was not confirmed before his admission in our hospital, and neither did he get standard treatment. We labeled him as a case of"chronic SOJIA", based on growth retardation and deforming arthritis of right hip and other large joints of upper and lower extremities and micrognathia, although his cervical spine was spared.

Fever is the most common initial presentation according to many authors.[1,4,9,10] Arthralgia/ arthritis are the second most common presentation.[1,4] Tajkia et al.[9]reported two cases: both had fever as their presenting complaint, one of them had no musculoskeletal complaints, the another had arthralgia at presentation. Hepatomegaly, splenomegaly, rash and lympha-denopathy are other common presentation.[1,4] This case presented with all those typical clinical features of SOJIA (high spiking quotidian fever, deforming arthritis, lymphadenopathy and hepato-splenomegaly) except the rash. Serositis is another characteristic but a less common feature of SOJIA.[1,4,11] The presented case had ascites but no abdominal pain or tenderness. This (ascites) can better be explained by congestive cardiac failure (CCF) consequent upon ventricular septal defect (VSD). This patient had echocardiographic proven VSD with CCF. VSD in association with SOJIA was a unique feature of the presented case. After extensive internet search I found one case of JIA with congenital heart disease.[12] That Iranian boy had echocardiographic evidence of patent ductus arteriosus (PDA); he was diagnosed as a case of JIA with DiGeorge syndrome. Predictors of poor articular outcome in SOJIA include systemic features for 6 months after onset, thrombo-cytosis, and the presence of polyarthritis with hip involvement and cervical spine fusion.[1,11] This identifies the case as having poor prognosis.

Nonsteroidal anti-inflammatory drugs (NSAIDs) and/or intra-articular steroid (IAS) injections are the first-line treatment for most JIAs including SOJIA.[1] Initially this patient was treated our case with NSAIDs, IAS, systemic steroid (oral prednisolone 20 mg/day) and methotrexate (10mg/week). As the boy had poor prognostic factors, the treatment we offered might not be enough. The newer biologics that inhibit IL-6 (tocilizumab) and IL-1 (anakinra, canakinumab, and rilonacept) and TNF inhibitors would have been better options.[1,11] Clearly, cost (and less availability) of those newer agents prohibited their use in this case.

CONCLUSION

Systemic Onset Juvenile Idiopathic Arthritis (SOJIA) is a disease of exclusion. We were careful to exclude other potential differentials (Kawasaki's disease, lymphoma, leukaemias, Infections) by detailed history taking, meticulous clinical examination and some rational investigations. Delay in diagnosis and sub-optimal management of this boy with poor prognostic factors accounted for his growth retardation, joint deformity and recurring systemic inflammation. Financial constraints prohibited his further management with newer agents. A customized (but somewhat sub-optimal), management plan, which we offered may hopefully alleviate his suffering to some extent.

***Acknowledgement*:** Author is grateful to the patient for his cordial cooperation.

Conflicts of interest: None

REFERENCES

1. Joyce j, Hsu TC, Lee, Christy I, Sandborg. Clinical Features and Treatment of Juvenile Idiopathic Arthritis. Firestone and Kelley's Textbook of Rheumatology. 11th ed. Philadelphia, USA: Elsevier Sunders; 2021. p. 1911-1930.
2. Oberle EJ, Harris JG, Verbsky JW. Polyarticular juvenile idiopathic arthritis - epidemiology and management approaches. Clin Epidemiol. 2014; 6: 379-393. DOI: 10.2147/CLEP.S53168. PMID: 25368531; PMCID: PMC4216020.

3. Petty RE, Southwood TR, Manners P, Baum J, Glass DN, GoldenbergJ, et al.International League of Associations for Rheumatology classification of juvenile idio-pathic arthritis: second revision, Edmonton,2001. J Rheumatol. 2004; 31(2): 390–392. PMID: 14760812.
4. Mandl LA, Goldenberg DL, Romain PA. Clinical manifestations and diagnosis of adult Still's disease. 2014; UpToDate 20.3.
5. Bywaters EG. Still's disease in the adult. Ann Rheum Dis. 1971; 30(2): 121-133. DOI: 10.1136/ard.30.2.121. PMID: 5315135; PMCID: PMC1005739.
6. Ombrello MJ, Arthur VL, Remmers EF, Hinks A, Takmazidou I, Grom AA,et al. Genetic architecture distinguishes systemic juvenile idiopathic arthritis from other forms of juvenile idiopathic arthritis: clinical and therapeutic implications. Ann Rheum Dis.2017; 76(5): 906–913.
7. Mellins ED, Macaubas C, Grom AA. Pathogenesis of systemic juvenile idiopathic arthritis: some answers, more questions. Nat Rev Rheumatol.2011; 7(7): 416–426.
8. Beukelman T, Patkar NM, Kenneth G, Saag KG, Rinehart ST, Cron RQ, et al.2011 American College of Rheumatology Recommendations for the Treatment of JIA: initiation and Safety Monitoring of Therapeutic Agents for the Treatment of Arthritis and Systemic Features. Arthritis Care Res (Hoboken). 2011; 63(4): 465–482. DOI: 10.1002/acr.20460. PMID: 21452260; PMCID: PMC3222233.
9. Tajkia G, Amin SK, Rima S, Halder S, Hannan F. Systemic Onset Juvenile Idiopathic Arthritis (sJIA) or Still's Disease: A Diagnostic Challenge; while Presented as Fever of Unknown Origin. 2 Cases. Anwer Khan Mod Med Coll J. 2019; 10(1): 84-88.DOI: https://doi.org/10.3329/akmmcj.v10i1.43667.
10. Alzyoud RM,Alsuweiti MO,Almaaitah HQ, Aladaileh BN, Alnoubani MK, Alwahadneh AM. Juvenile idiopathic arthritis in Jordan: single center experience. Pediatric Rheumatol. 2021; 19(90):1-9.DOI: 10.1186/s1 2969-021-00572-8.
11. Ringold S,Weiss PF, Beukelman T, DeWitt EM, Ilowite NT, Kimura Y, et al. 2013 update of the 2011 American College of Rheumatology Recommendations for the Treatment of Juvenile Idiopathic Arthritis: Recommendations for the Medical Therapy of Children With Systemic Juvenile Idiopathic Arthritis and Tuberculosis Screening Among Children Receiving Biologic Medications. Arthritis Care Res. 2013; 65(10): 1551–1563: DOI:10.1002/acr.22087.
12. Salehzadeh F, Bagheri A. Association of Juvenile Idiopathic Arthritis and Digeorge Syndrome; a Case Report. Iran J Pediatr.2014; 24(3): 334-336. PMID: 25562032; PMCID: PMC4276593.