

Post nCoV-2 limping Child: Report of two cases and a rapid Review

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Case Report

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Abstract

Background: Identification of the etiology of acute limping in children is challenging. Both benign and life-threatening disorders can present with limp. However, among atraumatic conditions, benign conditions including toxic synovitis and post infectious arthritis are the most common causes of this dilemma.

Case Presentation: During the recent COVID-19 pandemic in Kerman, South East of Iran; two pediatric patients referred to the Rheumatology clinic with new onset gait disturbance. One 8 years old boy and the other 6 years old girl who presented with hip joint pain and limping. Both of them had joint effusion jackknife of mild respiratory symptoms and fever. Altogether, precise history taking and accurate physical examination, alongside radiological investigations and positive laboratory results for coronavirus infection emphasized the diagnosis of post Coronavirus arthritis. They treated with rest and Non-Steroidal Anti-Inflammatory Drugs (NSAID) successfully, and followed at least for one month later.

Conclusions: Here, we described the first report of post n-CoV-2 arthritis in the world in two Iranian pediatric patients, who presented with limp. Contrary to preliminary phantasms, this may indicate that the Corona virus has some rheumatogenic specifications.

Background

Limp is a deviation from a normal age-appropriate gait pattern as a result of a variety conditions (1). Acute atraumatic limp is a common cause of presentation to pediatric rheumatology and emergency departments with an incidence rate of near 1.8 per 1000 children, a male to female ratio of 1.7:1, and median age of 4.4 years, as has been previously reported in a large cohort of children (2). Although, the toxic synovitis is the most common diagnosis; in some cases the limp can occur as a manifestation of a serious or life-threatening condition (3).

Generally, a child develops a mature gait pattern about age three years and it consists of stance and swing phases (4). Deviation from normal gait can be classified as antalgic and non-antalgic gaits. An antalgic gait results from pain in an affected limb, resulted in a shortened stance phase. In contrast, several types of limp are associated with non-antalgic gait and most of them do not need urgent evaluation and treatment (5, 6). However, evaluation of a limping child should begin with a thorough history taken from both child and parents. The age of the child at onset of the limp, and the presence of pain, fever and systemic symptoms, alongside the duration of limp can reduce and narrow the differential diagnosis. A complete and systematic physical examination also should be performed in this situation. The main differential diagnosis that considered in a patient is determinative of necessitous laboratory and imaging evaluations (4, 7). However, the viral infections are a well-recognized cause of acute arthralgia and arthritis with a large number of causative agents. A careful consideration of epidemiological, clinical and serological properties is so needful to making the correct diagnosis. Studies have suggested a viral tendency to arthritis for some viruses including Parvovirus B19, Hepatitis B and C,

Human Immunodeficiency Virus (HIV) and some other viruses (8-10), but as yet there have been no reports of novel Coronavirus rheumatogenicity.

Here in, we reported two cases of gait disturbance following n-CoV-2 infection, that both of them were treated in our pediatric rheumatology department in Kerman University, Iran.

Case Presentations

Case-1. An 8 years old healthy boy referred to the pediatric rheumatology center of Kerman University, in the South East of Iran due to left side lower extremity gait disturbance and limping. He experienced this condition from three weeks ago, without a history of trauma and vigorous activity. Although, he had a history of mild respiratory tract infection including low grade fever and cough about one week before refusal to walk. During this time, he had several visit by an orthopedist and due to lack of Kocher criteria, having a normal pelvic radiograph and laboratory test results had been treated with Ibuprofen, albeit with an insufficient dose. However, due to the duration of limp for three weeks, he referred to our center. The patient did not have fever at the time of visit. In a complete and systematic examination, he had an antalgic gait at left side as a difficulty in weight bearing. He had also, pain and limitation in the range of flexion, internal and external rotation movements in left hip with a positive FABER Test, alongside a less pain and restriction in contralateral hip joint examination. There were no evidence of some other contributory findings and red flags including organomegaly, lymphadenopathy, skin lesions, neurological deficits and other occasions. Nevertheless, he underwent Laboratory and Radiological studies as diagnostic assessments for his prolonged limp. Laboratory evaluation revealed a peripheral white blood cell (WBC) count of 910^9 /L with an Absolute Neutrophil count (ANC) of 3.2×10^9 /L and an Absolute Lymphocyte count (ALC) of 10^9 /L, without any atypical lymph and blast cells. The platelet count was 312000/ μ L and Red Blood Cells (RBC) count was 5.8×10^6 / μ L, with a hemoglobin of 15.5 g/dl, and MCV of 76.8 fl. The Erythrocyte Sediment Rate and C - reactive protein were 3mm/h and 3.5mg/L respectively. The laboratory test results were demonstrated in Table 1. Considering the new pandemic of COVID-19 and due to precede symptoms of fever and cough; the serological investigation for both IgM and IgG of nCoV-2 infection were requested, with a high level of IgM (3.4 with a 1.1 cut off) at first, alongside a high IgG level (3.8 with a 1.1 cut off) in the second occasion one week later. Anyway, the nasopharyngeal swab for coronavirus Polymerase Chain Reaction (PCR) assay was not sent due to latency evaluation from precede symptoms and his parent's refusal. There were no evidence of marked joint space widening, reactive bone changes, fatty changes and other pathologic findings including any asymmetry in hip X-Ray, and also the Chest radiograph was normal. He underwent both hip joints ultrasound study with a result of 7mm effusion in left side. Thereafter, a Magnetic resonance imaging (MRI) as complementary facility showed a moderate joint effusion at left hip articulation and a minimal joint effusion at right side hip joint, while the bone marrow signal intensity was intact (Figure 1). Treatment was planned by rest and prescription of Naproxen 250mg twice a day. The patient consequently recovered near one week later, without effect on either hip movement restriction or gait pattern and mobility.

Case-2. A 6 years old girl who had experienced a high grade fever (up to 39°C) for two days near one week ago without additional symptoms, referred with left side lower extremity limp to the pediatric rheumatology center of Kerman University . She complained of polyarthralgia in several joints including both knees and wrists with a predominant left lower limb pain in groin region and knee. She was result of a consanguineous marriage from a repeated cesarean section with a birth weight of 2.7 Kg. The patient has a history of limping three years ago, which led to hospitalization and aspiration of right hip joint fluid. She had been treated as septic arthritis by an orthopedist, although its accuracy seems questionable. She also had a history of right side hydronephrosis that has improved gradually. She has only an older sister in a healthful condition. Her mother was a nurse and worked in a hospital as a center of coronavirus in the Southeast of Iran. However, on a complete examination, at the time of visit; she did not have fever and her vital signs were in normal ranges. She had lack of weight bearing in left lower limb with an antalgic gait. She had no evidence of muscle involvement, but there was some limitations in the range of movement of left hip joint, alongside scant tenderness in both wrists examination. Laboratory evaluation revealed a peripheral WBC count of 9.68×10^9 /L with an ANC of 5.69×10^9 /L and an ALC of 10^9 /L without any atypical lymph and blast cells. The platelet count was 511000/ μ L and RBC was 4.11×10^6 / μ L, with a hemoglobin of 11.9 g/dl, and MCV of 82 fl. The Erythrocyte Sediment Rate and C - reactive protein were 39mm/h and 12mg/L respectively. Serological investigation for both IgM and IgG of nCoV-2 infection revealed a mild increase IgM level (1.2 with a 1.1 cut off), without increasing in the IgG level in two occasions one weeks apart. The patient candidate for Coronavirus molecular study and the nasopharyngeal swab for coronavirus PCR assay was sent with a positive result in both patient and her mother too. The laboratory data are presented in Table 1. Her hip X-Ray was normal; but for evaluation of joint effusion, the parents refused for MRI due to social phobia and fear of coronavirus infection. However, the hip ultrasound showed the evidence of mild joint effusion in both hip joints especially in anterior part of left hip joint (Figure 2). Finally, the patient was diagnosed as post coronavirus limp and successfully treated with Ibuprofen 40mg/kg/day three times a day. She completely recovered clinically within 4 days and both laboratory and ultrasound findings changed to normal, and patient could walk and play normally. She followed at least for 45 days later, without any subsequent sign or sequel.

Discussion And Conclusion

So far, studies have shown that children appear to represent 2.4% of reported cases of COVID-19. The overall severity of COVID-19 in children was reported to be significantly milder than in adults (11). As COVID-19 continues to spread, there is growing evidence that children may be vulnerable to another rare or even a serious complication of disease. They might be experienced hospitalization with the risk of superinfection and bacterial colonization (12). Case reports have appeared describing the pediatric patients with unusual presentations of Kawasaki s disease, toxic shock syndrome, acute abdominal conditions, and encephalopathy, macrophage activation syndrome, along with other reports of patients with fever, elevated inflammatory markers, and multisystem involvement as a new entity called childhood multisystem inflammatory syndrome (13).

However, reports of viral arthritis in this pandemics are lacking in both pediatric and adult patients. Albeit, the viral infections are a well-recognized cause of acute arthralgia and arthritis with a large number of causative agents. The diagnosis of this condition can be difficult for clinicians to confirm. In addition, to clinical features that point the clinicians to a specific virus, serological testing may be requested based on both clinical and epidemiological data. Accurate data regarding the incidence and prevalence of virally induced arthritis are lacking. Studies have suggested a viral etiology in about 1% of cases of acute arthritis. Worldwide, Parvovirus B-19, Hepatitis-B and C. HIV and the alpha viruses are among the most important causes of virally induced arthritis (14).

The pathogenesis of post viral arthritis is complex, because they often do not meet the classical definition criteria of reactive arthritis, and there being some viral infections (rubella, varicella zoster, herpes simplex virus, cytomegal virus, etc.) during which the virus can be isolated in synovial fluid (15). With other viral infections (hepatitis-B, adenovirus type-7) in synovial fluid antigen-antibody immune complexes were isolated, highlighting a possible role of these in the pathogenesis of virally induced arthritis (15-17). Generally, post infectious arthritis involves the lower limb joints especially ankles and knees and can cause limping occurrence (18, 19). However, it is important to maintain that in about 50% of cases, the etiologic agent cannot be isolated, and in 25% of children with post infectious arthritis, the infection is asymptomatic in history (15).

Our patients had no history of falling or other traumatic process. Also, both of them had no evidence of serious and life threatening condition like septic arthritis, osteomyelitis, malignancies and other causes. Both of them had a preliminary mild symptoms of upper respiratory infection including fever and cough about seven days earlier to limp. The first case referred with a prolonged duration of limp for three weeks, and the second one had the additional polyarthralgia in this period. The IgM and IgG levels against nCoV-2 were significantly higher than normal first and after 1 week, respectively. Although, his parents refused to do the nasopharyngeal sampling; due to latency visit and evaluation from precede symptoms, the molecular evaluation was of little value. The patient was considered as a reactive arthritis and gave a good response to the NSAID treatment, and of course, with 40 days follow up, he was completely fine and had no other problem. In the second patient, the results were positive for both serological and molecular tests. In addition, in her mother, has a positive PCR test and experienced mild symptoms. These two patients are symbols of the coronavirus arthrogenicity; what has been seen a lot with other viral infections, but so far has not been reported after nCoV-2 infection. At this days, we see some other cases of coronavirus related arthralgia, which suggesting more consideration to pediatricians. Further reports will help clarify the corona virus arthrogenicity.

Abbreviations

NSAID: Non-Steroidal Anti-Inflammatory Drugs

HIV: Human Immunodeficiency Virus

WBC: White blood cell

ANC: Absolute Neutrophil count

ALC: Absolute Lymphocyte count

RBC: Red Blood Cells

MRI: Magnetic resonance imaging

PCR: Polymerase Chain Reaction

Declarations

Ethics approval and consent to participate

Informed consent was received from all patients before starting the work and the study had been approved by the ethics committee of Kerman University of Medical Sciences (Code: IR.KMU.AH.REC.1399.029).

Consent for publication

Written informed consent for publication of their clinical details was obtained from the patient/parent of the patient.

Availability of data and materials

All data generated or analysed during this study are included in this published article [and its supplementary information files].

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

All authors involved in searching process and data collection. The first and corresponding authors designed the body of article and wrote the results and conclusions.

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Tables

Table 1- The Laboratory finding of both patients at the time of limp. The acute phase reactant of both patient were in normal range after 1 week.

Laboratory Test	Case-1	Case-2
WBC(5-14.5)10 ³ /μL	9.3	9.7
RBC(3.9-5.3)10 ⁶ / μL	6.16	4.11
ANC	3255	5600
ALC	5700	2650
Hb(11.5-15.5 g/dl)	15.9	11.9
MCV(75-87 fl)	75.6	82
Platelet(172-450)10 ³ / μL	310	511
ESR(0-15 mm/h)	7	39
CRP(0-10 mg/l)	13	12
PBS for blast	Negative	Negative
BUN	10	7
Cr (0.5-1 mg/dl)	0.5	0.6
AST (5-60 IU/ml)	24	23
ALT (6-50 IU/ml)	17	12
ALP (180-1200 IU/ml)	558	339
Ferritin(11-92 ng/ml)	-	49.30
LDH (<746 U/L)	385	409
Uric Acid (3-6.4 mg/dl)	2.1	-
Wright Agglutination Test	Negative	Negative
2ME	Negative	Negative
Coombs Wright	Negative	Negative
ASO-Titer (up to 200 IU/ml)	62	31
ANA (IU/ml)	Negative (0.2)	Negative
RF (+, -)	+	Negative
Coronavirus IgM (<1.1)	3.4	1.2
Coronavirus IgG (<1.1)	3.8	0.35
Coronavirus PCR	-	+

Figures

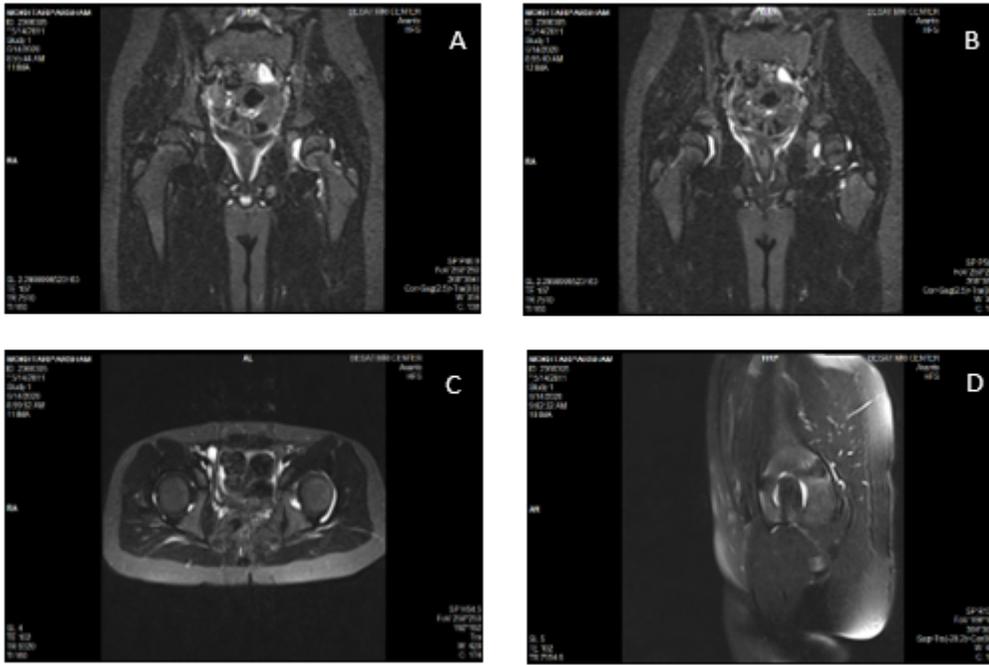


Figure 1

STIR sequencing MRI of both hip joints. A- B: Coronal view. C: Axial view. D. Sagittal view. Both hip joint effusion, especially in left side.



Figure 2

Ultrasound of both hip joints. Mild bilateral hip joint effusion, especially in anterior synovial space of left side.