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An Unusual Cause of Limping in Childhood: Lessons from H1N1 Influenza Case Series

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Abstract

Introduction: Identification of the etiology of limping and gait disturbances in children necessitates accurate physical examination and history taking. Although serious conditions such as septic arthritis and Guillain-Barre syndrome are usually prioritized in the differential diagnosis of limping, benign disorders such as benign acute childhood myositis (BACM) should not be discarded.
Case Presentation: During the recent H1N1 influenza pandemic in the fall and winter of 2015 - 2016 in Hamadan, Iran, three school children presented to our clinic with limping and abnormal gait. Precise history taking, in addition to accurate physical examination and simple laboratory tests, confirmed the diagnosis of myositis. The patients were discharged soon after complete recovery.
Conclusions: Based on the findings, in case a child suffers from calf pain or gait disturbances during influenza outbreak, the possibility of BACM should be considered before performing laboratory tests, radiological examinations, or other investigations.

Keywords: Limping, Children, Influenza, Myositis

1. Introduction

Limping or gait abnormality is one of the most common causes of children's admission to pediatric clinics and hospitals. Various etiologies have been proposed for limping in children, which can vary from medical emergencies such as septic arthritis to less important conditions such as transient synovitis (1, 2). To distinguish the cause of limping, careful history taking, physical examination, and various laboratory and radiographic studies, based on the clinical findings are required. For the evaluation of gait disturbances, physicians usually focus on the local signs and symptoms, while systemic or constitutional symptoms are important, as well (1, 2).

When a child suffers from calf pain or gait disturbances, one of the first diagnoses a physician should consider is benign acute childhood myositis (BACM). Lundberg A. reported the first case of abnormal gait, following viral infection among school children in 1957. He described the phenomenon as "myalgia cruris", which was later called BACM (3). Before confirming the diagnosis, serious conditions such as suppurative arthritis and neurological disorders including Guillain-Barre syndrome should be excluded through proper physical examinations. According to the literature, viruses associated with BACM include influenza, coxsackie virus, adenovirus, and parainfluenza viruses (4, 5).

There are helpful guidelines a clinician may follow to correctly diagnose myositis. Toe walking and wide-based gait are two common gait abnormalities associated with myositis (6, 7); in many children, these forms of walking are transient (8). Some patients with viral myositis suffer from rhabdomyolysis and consequently myoglubinuria. Although there are several etiologies for red-colored urine, the concurrence of red urine with muscle pain and limping may guide the diagnosis towards myoglobinuria and myositis.

Herein, we present three cases of gait disturbance due to myositis, following influenza H1N1 virus infection. All cases were examined at Besat hospital during the recent influenza outbreak in Hamadan, Iran in fall and winter of 2015 - 2016. Besat hospital is a teaching hospital and a referral center in West of Iran. The patients were first examined by pediatric residents, and all three cases were under observation by an infectious pediatric subspecialist.

2. Case Presentation

2.1. Case No. 1

A five-year-old boy was admitted to the hospital due to difficulty in walking and standing. The child had no history of vigorous activity. Neither the patient nor the family members had experienced such problems before. He had a history of high-grade fever, mild abdominal pain,

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anorexia, and sore throat five days prior to admission, which were completely recovered; however, he was unable to walk or stand a day before admission.

On physical examination, the patient's vital signs were normal. Erythema was detected in the throat, while deep tendon reflex (DTR) test and other neurological examinations were normal. Also, nerve conduction velocity (NCV) test, which was performed in accordance with neurological consultation, was totally normal. Afterwards, pediatric infectious disease consultation was requested. At the time, the patient had bilateral tenderness in calf muscles, tended to maintain his foot in plantar flexion, and apparently experienced pain on passive or active dorsiflexion. Chest X-ray results of the patient were normal; the laboratory data are presented in Table 1.

Considering the regional outbreak of influenza and featured clinical presentations, creatine phosphokinase (CPK) test and polymerase chain reaction (PCR) assay for influenza H1N1 were requested. CPK was measured to be 3200 (normal range: 24 - 229), and the nasopharyngeal swab for influenza H1N1 was positive. Finally, the patient was diagnosed with BACM and received symptomatic therapy. He completely recovered within 24 hours and was discharged from the hospital while being able to walk.

2.2. Case No. 2

A seven-year-old boy with walking disability was admitted to the hospital by his parents. The patient could not walk a day before admission and could only stand with assistance. He had a five-day history of fever, sore throat, rhinorrhea, and cough and had noticed dark-colored urine two days before admission. On examination, he had fever (axillary temperature of 38°C), moderate bilateral calf tenderness, and erythema in the throat. The remaining examinations, including DTR test and other neurological evaluations, were normal.

Based on the reasons mentioned in the first case, the possibility of myositis was raised and the necessary tests were requested. CPK was found to be 3000 (normal range: 24 - 229), and the nasopharyngeal swab for influenza H1N1 was positive. The patient's urinalysis results were as follows: specific gravity of urine: 1020; red blood cell (RBC): 0; white blood cell (WBC): 0; blood: 2+; bilirubin: negative. The reticulocyte percentage (number of reticulocytes compared to the total RBC count) was measured to be 0.1. Coombs test results were negative and glucose-6-phosphate dehydrogenase was in the normal range (total bilirubin: 1.3 and direct bilirubin: 0.4). Other laboratory test results are presented in Table 1.

To rule out hemoglobinuria, the plasma color was also investigated, which was found to be clear. Therefore, rhabdomyolysis following H1N1 influenza was confirmed. The patient was treated with appropriate intravenous fluids. After two days, he was able to walk on his own without difficulty. Urine analysis results changed to normal and the patient was discharged with no complications.

2.3. Case No. 3

The third case was a six-year-old boy who was admitted to the hospital due to his inability to walk normally. He obviously walked on toes (toe-walking gait) and had a history of fever, sore throat, cough, and myalgia of limbs, back, and shoulders six days prior to admission. He had also noticed high-colored urine, which had changed to normal a day before hospital admission. All the mentioned signs had recovered several days prior to admission, except coughing and mild bilateral calf tenderness. DTR test and other neurological examinations were normal.

The patient's chest X-ray was normal, urinalysis revealed normal results, and the nasopharyngeal swab for influenza H1N1 was positive. Other laboratory test results are demonstrated in Table 1. Upon admission, the patient was only treated with hydration and did not undergo any additional work-up. It took 48 hours for the signs and symptoms to completely recover, and the patient could walk normally without any sequels.

The nasopharyngeal swabs of all three patients for influenza H1N1 PCR assay were sent to Hamadan health center laboratory. Quantitative real-time PCR (QRT-PCR) was performed, using Roche LightCycler® 96 system. The routine protocol for detecting influenza virus was followed in our laboratory. Briefly, after extraction using the automatic extraction machine (Qiagen) and measuring RNA concentration by NanoDrop (Thermo), we screened the samples for flu types and finally determined the subtypes; all the used kits were in-vitro diagnostics kits (fast track diagnostics). In general, current molecular influenza virus tests are used in diagnostic testing facilities, where sophisticated equipments and highly trained technicians are available.

3. Discussion

Since 1957, when BACM was first described, no clear differentiation has been proposed between this complication and rhabdomyolysis (9). However, some researchers have attributed the term "benign myositis" to simple cases of muscle pain and inflammation, in combination with a rise in CPK level; the term "rhabdomyolysis" is used when myoglobinuria is added to this combination (10, 11). It should be emphasized that calf pain without a rise in CPK level is not myositis, but an uncommon symptom of viral infections such as influenza (12).

Table 1. Laboratory Data of BACM Cases

Laboratory Tests	WBC (cells/μL)	Hb (g/dL)	PLT (cells /μL)	ESR (mm/hr)	CRP Qualitative Test	H1N1PCR	CPK
Case 1	9300	11.9	270,000	50	++	+	3200
Case 2	12,500	12.3	321,000	NA	NA	+	3000
Case 3	11,500	12.0	325,000	42	++	+	2300

Abbreviations: CPK, Creatine phosphokinase; CRP, C-reactive protein; ESR, Erythrocyte sedimentation rate; Hb, Hemoglobin; NA, Not available; PLT, Platelet; WBC, White blood cell.

In this study, we described two cases of acute benign myositis and a case of rhabdomyolysis, presenting with acute limping. Most cases of BACM are assumed to be male, as confirmed in our patients (13). All three patients had a history of viral symptoms, although all the symptoms had recovered within less than a week before the onset of walking disturbances.

The differential diagnoses for a child with a complaint of difficult walking include trauma, infection (e.g., septic arthritis and osteomyelitis), juvenile rheumatoid arthritis, neuromuscular disorders, and malignancies (1, 14). Importantly, despite serious disorders considered in the differential diagnosis of limping, possibility of BACM should be assessed via thorough history taking, precise examinations, study of the local epidemiological pattern of influenza virus, and simple blood tests. Once the patient's condition is improved, he/she does not require additional follow-ups. Nevertheless, parents should be inquired about the history of red-colored urine and be informed to occasionally check the child's urine during illness (15).

In this regard, Swaminathan and colleagues presented the case of a four-year-old boy with acute onset transient toe walking, following H1N1 influenza in India (6). As mentioned earlier, there are different types of viruses which may cause myositis or rhabdomyolysis. In addition, Douvoyiannis et al. introduced the case of a seven-year-old boy diagnosed with rhabdomyolysis, associated with parainfluenza virus (10). Moreover, over a one-year period, Rajajee and colleagues reported 40 cases of myositis in whom Guillain-Barre syndrome was the most common referral diagnosis (5).

All the above-mentioned cases were suspected of Guillain-Barre syndrome and had been checked clinically by DTR test, which was found to be normal in all the patients. Also, in 2004, a study was performed on children with influenza, and the authors reported that 5.5% of the patients with influenza A virus and about 40% of patients with influenza B virus had myositis (12). Based on a study by Agyeman and colleagues, the duration of recovery is several days (16).

BACM is a mild phenomenon which can appear as an upsetting feature in patients. Therefore, it is the physician's responsibility to distinguish this benign complication from serious etiologies of limping in children. Given the fact that all the present cases were diagnosed during an influenza outbreak, we recommend that in addition to careful history taking and physical examination, regional epidemiology of viral diseases, especially influenza virus, be considered before laboratory tests, radiological examinations, or other investigations.

The importance of this case series lies in addressing one of the transient and disabling complications of influenza infection, which may be confused with serious disorders. Although three cases are clearly not adequate for making a final conclusion or recommendation, such studies could be the starting point for further large-scale research.

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Footnotes

Authors' Contribution: Iraj Sedighi and Shahla Nouri: substantial contributions to the conception/design of the study and acquisition of the data; Taravat Sadrosadat: drafting of the manuscript; Iraj Sedighi, Shahla Nouri, and Taravat Sadrosadat; final approval of the manuscript and agreement to be accountable for all aspects of the article.

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References

1. Naranje S, Kelly DM, Sawyer JR. A Systematic Approach to the Evaluation of a Limping Child. *Am Fam Physician*. 2015;**92**(10):908–16. [PubMed: 26554284].
2. Shah AP, Indra S, Kannikeshwaran N, Hartwig E, Kamat D. Diagnostic Approach to Limp in Children. *Pediatr Ann*. 2015;**44**(12):548-50–556. doi: 10.3928/00904481-20151112-01. [PubMed: 26678234].

3. Lundberg A. Myalgia cruris epidemica. *Acta Paediatr.* 1957;**46**(1):18–31. [PubMed: 13410584].
4. Havers FP, Campbell AJP. In: Nelson text book of pediatrics. Kliegman RM, editor. Philadelphia: Elsevier; 2016. pp. 2011–4.Influenza viruses.
5. Rajajee S, Ezhilarasi S, Rajarajan K. Benign acute childhood myositis. *Indian J Pediatr.* 2005;**72**(5):399–400. [PubMed: 15973022].
6. Swaminathan S, Jagadeesh A, Chandrasekaran V, Krishnamurthy S, Subramanian M. Acute onset transient toe walking in a 4 yr. Old boy due to h1n1 influenza a virus infection. *J Pediatric Care.* 2015.
7. Zafeiriou DI, Katzos G, Gombakis N, Kontopoulos EE, Tsantali C. Clinical features, laboratory findings and differential diagnosis of benign acute childhood myositis. *Acta Paediatr.* 2000;**89**(12):1493–4. [PubMed: 11195243].
8. Koliou M, Hadjiloizou S, Ourani S, Demosthenous A, Hadjidemetriou A. A case of benign acute childhood myositis associated with influenza A (H1N1) virus infection. *Clin Microbiol Infect.* 2010;**16**(2):193–5. doi: 10.1111/j.1469-0691.2009.03064.x. [PubMed: 19832721].
9. Belardi C, Roberge R, Kelly M, Serbin S. Myalgia cruris epidemica (benign acute childhood myositis) associated with a Mycoplasma pneumonia infection. *Ann Emerg Med.* 1987;**16**(5):579–81. [PubMed: 3565874].
10. Douvoyiannis M, Kielbasa JM, Chandrasekharan GM, Holmes CL, Gomez MR. Rhabdomyolysis associated with parainfluenza virus. *Case Rep Infect Dis.* 2013;**2013**:650965. doi: 10.1155/2013/650965. [PubMed: 23840985].
11. Gibson SB, Majersik JJ, Smith AG, Bromberg MB. Three cases of acute myositis in adults following influenza-like illness during the H1N1 pandemic. *J Neurosci Rural Pract.* 2013;**4**(1):51–4. doi: 10.4103/0976-3147.105614. [PubMed: 23546352].
12. Hu JJ, Kao CL, Lee PI, Chen CM, Lee CY, Lu CY, et al. Clinical features of influenza A and B in children and association with myositis. *J Microbiol Immunol Infect.* 2004;**37**(2):95–8. [PubMed: 15181490].
13. Noma S. [Acute myositis associated with influenza]. *Nihon Rinsho.* 2006;**64**(10):1921–3. [PubMed: 17037368].
14. Jain S, Kolber MR. A stiff-legged gait: benign acute childhood myositis. *CMAJ.* 2009;**181**(10):711–3. doi: 10.1503/cmaj.090781. [PubMed: 19825926].
15. Terlizzi V, Improta F, Raia V. Simple diagnosis of benign acute childhood myositis: Lessons from a case report. *J Pediatr Neurosci.* 2014;**9**(3):280–2. doi: 10.4103/1817-1745.147595. [PubMed: 25624939].
16. Agyeman P, Duppenthaler A, Heininger U, Aebi C. Influenza-associated myositis in children. *Infection.* 2004;**32**(4):199–203. doi: 10.1007/s15010-004-4003-2. [PubMed: 15293074].