**ORIGINAL ARTICLE** 



# From influenza to SARS-CoV-2: etiological evaluation of acute benign childhood myositis

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#### Abstract

Aim To present the etiological evaluation results of our acute benign childhood myositis cases.

**Materials and methods** Children, who were referred to pediatric neurology outpatient clinic in Maternity and Children's Hospital, with difficulty in walking and high creatinine kinase levels were evaluated. Viral and bacterial serological evaluation of children were performed by real-time polymerase chain reaction method.

**Results** Twenty-five children (21 M,4 F) included in the study. The most common complaints were walking difficulty and tenderness, pain on the gastrocnemius muscles. Their creatine kinase levels were between 216 and 8770 IU. Twenty-two children were hospitalized. Analgesic, intravenous fluid, antibiotic and/or antiviral drugs were given. The most common etiologies were influenza A and B. One children was diagnosed as suspected COVID-19 by the symptoms and the findings in thorax computerized tomography but the SARS-CoV-2 PCR and antibiody tests were negative.

**Conclusion** School-aged children admitted to hospital with walking difficulty generally after an upper respiratory tract infection with a moderate creatine kinase elevation should remind at first acute benign myositis. Resolution of the complaints in a short time and normalisation of the biochemical markers will prevent unnecessary tests. Endemic and pandemic infections may cause this entity as well.

Keywords Childhood · Acute benign myositis · Creatine kinase

# Introduction

Acute benign childhood myositis is often seen at schoolage. Walking difficulty and muscle pain are the most evident symptoms. It is a rapidly resolving disease. The most common cause is viral infections. Influenza type A and B viruses, especially type B, are frequently detected in the etiology. It is more common in boys than in girls. Differential diagnosis with Guillain–Barré syndrome (GBS) is important because patients suffer from difficulty in walking [1].

We would like to share our patient group that we evaluated etiologically. Acute benign myositis, which we usually experience seasonally after upper respiratory tract infections (URI), was also seen in a pediatric patient affected

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<sup>2</sup> Faculty of Medicine, Pediatrics Department, Giresun University, Giresun, Turkey by COVID-19 pandemic. Although the SARS-CoV-2 virus could not be confirmed serologically, this patient was presented because it was clinically compatible with COVID-19.

# **Patients and methods**

Children complaining of inability to walk and muscle pain, brought to Giresun University Faculty of Medicine, Maternity and Children's Hospital, Pediatric Neurology Department, with an increase in serum creatine kinase (CK) level between March 2019 and April 2020 were enrolled.

A respiratory panel test was used to detect the viral and bacterial agents by real time polymerase chain reaction (PCR) from the nasopharyngeal swab samples.

Respiratory panel included Influenza A, B, C, Rhinovirus, Coronavirus, Parainfluenza 1, 2, 3, 4, Human metapneumovirus A/B, Bocavirus, Respiratory syncytial virus A/B, Adenovirus, Enterovirus, Parechovirus, Mycoplasma Pneumonia, Chlamydia Pneumonia, Staphylococcus aureus, Streptococcus pneumonia, Haemophilus Influenza type B,

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Pneumocystis jirovecii, Boradatella spp, Moraxella catarrhalis, Klebsiella pneumonia and Legionella pneumophila. Also SARS-CoV-2 PCR and antibody tests were sent from a patient hospitalized during the COVID-19 pandemic.

Physical examinations of the patients were done by the pediatric neurologist. The Medical Research Counsil's (MRC) muscle strength scale was used. The scale proposed by the MRC uses the score of 0-5 (0: no contraction, 1: flicker or trace of contraction, 2: active movement, with gravity eliminated, 3: active movement against gravity, 4: active movement against gravity and resistance, 5: normal power).

#### **Statistical analysis**

All the continuous data were expressed as number and percentage and means. For categorical variables, we calculated the percentages of patients in each category.

### **Ethical issues**

All relevant ethical guidelines have been followed and ethics committee approval has been obtained.

## Results

Twenty-five children (21 M,4 F) were evaluated. Demographic and clinical data, and etiologies of our patients were given in Tables 1, 2, and 3. The majority of our patients complained of walking difficulty and calf pain. Mostly, findings of upper respiratory tract infection such as fever and cough, but rarely diarrhea were reported as prodromal findings.

 Table 1
 Demographical variables of patients and biochemical parameters

	Range	Mean	Percentage (%)
Number of patients	25		
Girl	4		16
Boy	21		84
Age (years)	2.5-16.7	6.9	
Fever (Celcius)	36.5–38	36.8	
Hospitalized patients	22		66
Hospital duration (days)	1–12	3.3	
First creatine kinase (CK) (IU)	216-8770	2898	
Control CK (2nd or 3rd day)	146-3376	779	
Final CK (within 1st week)	87–448	232	
ALT (mg/dl)	16–192	37.5	
AST (mg/dl)	30-318	126.4	
Sedimentation (mm/hour)	7–51	19.8	

Tabl	e 2	Presenting	complaints	and	physical	examination	findings	0
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Symptoms	Number of patients (N)	Percentage (%)
Fever	11	44
Cough	5	20
Upper respiratory tract infection	5	20
Diarrhea	2	8
Vomiting	1	4
Inability to walk	5	20
Difficulty walking	11	44
Pain at lower extremities	7	28
Pain of chest	1	4
No symptoms	1	4
Increased level of CK	7	28
Deep tendon reflex (DTR+)	25	100
Muscle strength (MRC)		
4(4+)/5	8	32
5/5	17	68
Treatment		
IV fluid	22	88
Antibiotics	9	36
Antiviral (oseltamivinir)	15	60
Analgesics	7	28

Muscle strengths of the patients were normal, or decreased slightly due to pain. Deep tendon reflexes (DTR) were normal. Twenty two patients were hospitalized and followed. Intravenous fluid, analgesics and antibiotics (mostly penicillin and cephalosporin group) and antiviral (oseltamivinir) treatment was given according to the patients' clinical

Table 3 Etiological evaluation

Detected organism	Number of patients (N)	Percent- age (%)
Influenza A	11	44
H1N1	11	44
Influenza B	7	28
S. pneumonia	5	20
M. pneumonia	2	8
M. catarrahalis	2	8
S. aureus	1	4
Enterovirus	1	4
Coronavirus HKU1h(HCoV- HKU1)	1	4
H. influenza	1	4
Negative	2	8
SARS-CoV-2	1*	4

\*Could not be detected by PCR and antibody tests but suspected clinically findings. The length of hospitalization ranged from 1 to 12 days. The patient with suspected COVID-19 was given oseltamivinir, azithromycin and hydroxychloroquine.

None of our patients described trauma, muscular disease in the family, dark urine, arthritis or skin rash. Creatine kinase levels ranged from 216 to 8770 U/L. Fourteen of our patients had leukopenia and four had thrombocytopenia. Increase in eryhtrocyte sedimentation rate (ESR) in two patients, and high CRP in two patients were detected. One patient with high ESR and CRP was the COVID-19 considered case. Complaints completely resolved within 2–3 days. Levels of CK also returned to normal within 3–7 days. No myoglobulinuria was observed in any patient. Troponin levels measured and found normal in nine patients.

## **Case report of suspected COVID-19 patient**

Sixteen-year-old patient admitted to hospital due to fever, left side pain, myalgia and cough. Chest X-ray showed bilateral paracardiac infiltration. Thorax CT demonsrated 4-mm subpleural non-specific nodular density at the posterobasal segment of right lung, focal consolidated areas with ground glass image at the lingula segment of left lung and pleural effusion on the left side. These findings were atypical but compatible with COVID-19. Two SARS-COV-2 PCR and antibody tests were negative. As known, PCR test may be negative when lung involvement develops. Laboratory values were revealed D-dimer: 3767 ng/ml (N: 80-500 ng/ml), CK: 1135 IU, fibrinogen: 441 mg/dl, ferritin: 43.8 ng/ml. Ferritin and fibrin degradation products were found highly compatible with the COVID-19 infection and CRP was positive. Echocardiography revealed mitral valve prolapsus and mitral insufficiency, did not show any involvement of myocarditis. Patient hospitalized for 12 days. Control CK was 176 after a few days. Myalgia and chest X-ray resolved after antibiotic and antiviral treatment. Clinically he was diagnosed as suspected COVID-19.

#### Discussion

Acute benign myositis of childhood is a clinical condition of concern for families due to the rapid development of the signs but results with a very rapid recovery. It can be distinguished clinically from GBS and other muscular dystrophy and myopathies. Thus no further examination is required [2]. Compatible with the literature, the clinical onset and course of our patients was not different from the natural history of the disease that is just after the prodromal period of the upper respiratory tract infection generally 5–7 days.

The most common etiological agent detected is the influenza virus family. Capoferri et al. [1] reported 451

(325 boys, 126 girls) patients of whom the etiology was determined in 181 patients. More than half of them were infected with Influenza virus (n: 66-Influenza B, n: 27 Influenza A), the other most common etiologies were; Dengue virus (n: 41), EBV (n: 12), Parainfluenza (n: 9) and Mycoplasma (n: 7).

In the study conducted in India, the most common cause was influenza viruses, especially H1N1 and a small amount of Dengue viruses. Other etiologies investigated such as mycoplasma, cytomegalovirus, Epstein-Barr virus, leptospira, and scrub typhus were negative [3]. Tütüncü et al. [4] submitted 65 cases from Turkey, etiological evaluation of 15 cases were Influenza A, Influenza B, Lyme, Mycoplasma, RSV and adenovirus as descending order. Parvovirus was detected in another study [5]. The most common etiology in our study revealed Influenza H1N1 in accordance with the literature.

The frequency of viral infections varies seasonally. In a study conducted in Brazil, a higher frequency in the months of May, June, July, and September was found, when compared to the others, corresponding to the colder months of the year [6]. Most of the cases occurred in the month of July and August followed by January and February in India [3]; between August and November in Chili [7]. The highest rate of admission was in January with 13 patients in our study and most frequent cases were seen between January and April. Since the winter and spring are flu seasons in Turkey, it was expected that the number of cases would intensify in this period. Also in Tütüncü's study, the cases most frequently admitted in March and in December [4].

Acute benign myositis is often seen in the school age boys. In our study, the youngest age was 2.5 years and the average was 6.9 years. Our age group was similar to the mean age reported by Hlavacova and Ferrarini, which is 7.1 and 7.3, respectively [8, 9]. No difference was seen in terms of the male predominance.

In our study, we tried to find etiology in each patient. More than one etiology was detected in ten patients. No results were obtained for technical reasons in two patients, no pathogen could be shown in one patient. Patient suspected with COVID-19 could not be confirmed by PCR or antibody test.

Very similar to our suspected COVID-19 case with myositis has been reported in the literature. In that case, chest CT scan on day 5 showed bilateral lower lobe groundglass opacities, first and second SARS-CoV-2 nasopharyngeal swab remained negative but bronchoalveolar lavage (BAL) fluid was finally positive for SARS-CoV-2 [10]. Our patient also had ground glass opacity. Other laboratory findings (D-dimer, ESR, CRP) and his clinical signs were compatible with COVID-19. Because of the good clinical outcome of the patient BAL was not performed. Myositis and myalgia may be a part of COVID-19, it was reported that 11–35% of the patients infected with SARS-CoV-2 had muscle involvement [11–15]. Also less frequently Guillain-Barré syndrome; Miller Fisher syndrome; polyneuritis cranialis; and rare instances of viral myopathy with rhabdomyolysis in adults may be seen [16–20]. Rhabdomyolysis is not expected in childhood acute benign myositis.

Differential diagnosis of acute benign myositis are GBS, muscular diseases (dermatomyositis, muscular dystrophy), growth pains and dermatomyositis. Our patients had no reflex reduction or loss, no family history of muscle disease, no muscle weakness and persistent CK increase, no evidence of purulent infection, no skin findings such as purplish discoloration on the eyelids or gottron papules. For this reason, the diseases that could be considered in the differential diagnosis were excluded.

Refusal to walk due to calf pain which can be called as key feature of acute benign childhood myositis, boy dominance, school age, normal neurological examinations (DTR, sensory exam), elevated CK, normal urinalysis findings, spontaneous and rapid recovery with conservative treatment (within few days) made the diagnosis clear. The patients could climb to stairs or exam table but they did not want to walk or stand up on the foot because of the pain in the gastrocnemius muscle. Their CK levels (first on evaluation, second and last controls) given in Table 1 reveal the rapid recovery.

It is thought that viral or bacterial endemic or pandemic infections can lead to childhood acute myositis. There are not many publications associated with COVID-19-associated myositis in children. Our patient's PCR and antibody tests were negative, but his clinic was compatible with COVID-19. In addition, it has been reported in various articles that PCR and antibody responses can be misleading and up to 30% false negatives may be seen [21, 22].

## Conclusion

In cases of leg pain (especially involvement of the gastrochemius muscles different from myalgia), and inability to walk after seasonal (late winter-spring) infection, acute benign childhood myositis should be considered in schoolage children if there is no specific feature in the neurological examination. It is important to observe rapid improvement in clinical findings and CK level to avoid unnecessary examination. We have aimed to determine the etiology in our patients. In studies about etiology, we have seen that etiology can be detected in some, at a very low rate, and in some more than half. There may be etiological differences from region to region. We would like to state that acute benign childhood myositis can be seen during endemic and pandemic infections.

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Availability of data and material The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

#### Declarations

**Conflict of interest** The authors have no conflicts of interest to declare that are relevant to the content of this article.

**Ethics approval** The study was approved by the appropriate institutional and/or national research ethics committee (Trabzon Kanuni Research and Training Hospital) and certify that the study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

**Consent to participate** Informed consent was obtained from all individual participants included in the study. Informed consent was obtained from legal guardians.

**Consent for publication** Patients signed informed consent regarding publishing their data and photographs.

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