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Case Study

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Recurrent Benign Acute Childhood Myositis (BACM) and Incidental Generalised Joint Hypermobility (GJH); A Case Study and Discussion

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Abstract

Benign Acute Childhood Myositis (BACM) is rare clinical entity with an incidence of 2.69 cases per 100,000 that is caused by a range of viral, bacterial and rarely fungal pathogens. Recurrent BACM is even more rare with unknown incidence. Despite BACM being an unusual condition, it is widely reported in the literature, however a lack of knowledge results in missed, or delayed diagnosis. This case report discusses a rare presentation of recurrent BACM in an 11 year old female who presented to the authors' rural emergency department with her mother. She had an 3 day history of difficulty walking following an upper respiratory tract infection that began 5 days prior to onset of symptoms. Examination revealed bilateral tender calves, sacroiliac joints and reluctance to weightbear with an abnormal gait. An incidental finding of generalised joint hypermobility (GJH) was noted. CK level was 2324 U/L. The patient's mother disclosed a complex rheumatologic history on her side of the family and 2 identical episodes of BACM occurring within a 12 month timeframe. A discussion on current understanding of the pathophysiology of BACM and gaps in current literature is provided. BACM carries a small risk of rhabdomyolysis and renal failure and patients should be referred for assessment in the Emergency Department. No literature has explored the relationship between GJH and BACM and the relationship between recurrent BACM and other rheumatic diseases such as autoimmune juvenile myositis, or systemic myopathies is not known.

Keywords: Benign acute childhood myositis, Paediatric viral myositis, Autoimmune juvenile myositis, Rheumatic diseases, Paediatric viral myositis

Introduction

Paediatric viral myositis, also known as "Benign Childhood Acute Myositis (BACM)" is an uncommon clinical entity with an incidence of 2.69 cases per 100,000 children (<18 years) during epidemic seasons and 0.23 cases per 100,000 children during non-epidemic seasons according to Hyuczko [1,2].

Recurrent BACM is extremely rare with only a handful of cases reported in the literature. The true prevalence is unknown and whether there is any underlying immunologic, or other systemic predisposition remains to be discovered. BACM is often missed, or misdiagnosed [3] therefore the true incidence might be higher than currently reported values. Missing the diagnosis can result in unnecessary investigations [3].

The median age of presentation is 8 years [3] with conflicting reports of gender predominance [4, 5]. The disease is usually self-limiting and resolves within a week [1, 3, 6-8].

BACM was first described in a 1957 case series by Swedish doctor Ake Lundberg and initially known as "myalgia cruris epidemica" [9]. Since that time reports involving large outbreaks of BACM have been published [10].

BACM is characterised by muscle pain, usually involving the lower limbs more than upper limbs [6]. Severe calf pain and avoidance of weightbearing with subsequent abnormal gait, or refusal to walk are all characteristic of BACM [5, 6].

Differential diagnoses include: Guillain-Barré syndrome, idiopathic inflammatory myositis, juvenile inflammatory arthropathies, non-infective myopathies and non-accidental injury [5, 6,11].

Viral myositis is associated with a number of viral illnesses

including respiratory syncytial virus, herpes simplex virus 1, adenovirus, cytomegalovirus, rotavirus, dengue virus, coxsackievirus, Epstein-Barr virus, cytomegalovirus, human parainfluenza virus, echovirus, HIV, Sars-2-Covid-19 and others [6, 12, 13]. Paediatric cases are usually related to influenza viruses A and B [6]. Rarely BACM is associated with bacterial infections such as *Mycoplasma, Streptococcus pyogenes, Staphylococcus aureus, Legionella and Salmonella* spp and other bacteria [6, 12]. Adult infectious myositis has been associated with parasites and fungal infections [13, 14].

Pradhan [6] propose diagnostic crtieria for BACM in Table 1:

Pradhan (2018) Proposed Diagnostic Criteria for BACM [6]
Clinical criteria: 1. Onset in the first two decades of life 2. Viral prodrome, 3–4 days before the onset of symptoms 3. Weakness in proximal muscles with lower limb predominance 4. Cramps/myalgia alone, or accompanying weakness 5. Normal to decreased deep tendon reflexes 6. Resolution within 2 weeks after the onset of symptoms Laboratory criteria: 1. Raised muscle enzymes such as CPK, SGOT, and SGPT 2. Low or normal potassium levels 3. Myopathic or normal electromyography 4. Normal nerve conduction studies 5. Positive viral serology/PCR from nasal or throat swab

Pradhan [6] do not provide diagnostic cut off values, however state the higher the number of criteria met the greater the likelihood of BACM.

Case Study

An 11 year old Caucasian girl presented to the Emergency Department with her mother with a 5 day history of URTI-like symptoms and subsequent development of sore legs, lower back pain and refusal to walk. The patient was referred in by her GP as she had presented with similar symptoms twice in the past. On each occasion the patient had been found to have raised CK levels requiring hospitalisation for observation, intravenous fluids and monitoring of renal function. The episodes had spontaneously resolved over the course of 8-9 days.

On this occasion the symptoms were more severe and the mother was concerned some other disease process might be present as well.

The child had a significant medical history that included frequent severe UTIs with post-infectious urinary incontinence and encopresis. The patient had a similar episode of myositis following a parainfluenza infection in late 2022.

The patient's family history included maternal antiphospholipid syndrome, a maternal aunt with joint hypermobility spectrum disorder and a maternal uncle with an unknown autoimmune rheumatic disease (the mother advised the uncle could not disclose the name of the condition).

The infectious agent in BACM is not always identified.

Diagnosis is usually made based on history, clinical presentation and elevated CK levels which are often at levels at 25-30 times the upper limit of normal [15].

Muscle biopsies, MRI and electro-conduction studies are rarely performed and might be completely normal therefore their utility only has value, if an alternative diagnosis to BACM requires investigation.

On Examination

The patient presented as an emotionally-distressed 11-year-old girl who appeared to be in immense pain as she attempted walking from the waiting room to the bedside with assistance of her mother.

Observations were within normal parameters and the patient was afebrile. Despite difficulties walking she appeared systemically well. The patient had an unremarkable cardiac respiratory, abdominal and ENT examination. There was no lymphadenopathy of note.

The patient cried whilst walking with a sideways gait and limp and was extremely reluctant to wait bear due to severe pain. Bilateral calf tenderness was present with minimal palpation. The patient was tender over both sacroiliac joints. No effusions were noted of the ankle, or knees.

The patient was assessed for generalised joint hypermobility (GJH). A Beighton Score of 6/9 for elbow, knee, finger and thumb hypermobility was recorded. The patient had hyperextensible skin in several places including the dorsum of the hand, neck and backs of the arms. It was noted the patient had blue sclera.

No focal neurology was noted.

No rash was noted, but the patient's cheeks appeared flushed at

the time of assessment. This was attributed to pain and crying and subsequently resolved once she was settled.

Investigations

The patient's CK level was found to be 2324 U/L. This compared with 3357 U/L in early December 2022 when the patient presented with identical symptoms.

An MRI scan, electromyography and nerve conduction studies were not performed. This is not standard practice in the diagnosis of BACM, but might be useful where symptoms persist past 1 week and where systemic myopathies and other pathologies are suspected.

Viral PCR was negative for covid 19, adenovirus, influenza viruses and respiratory syncytial virus.

Treatment and Follow Up

The patient was reviewed by a paediatrician and admitted for observation, intravenous fluids and monitoring of renal function. The patient's symptoms and serology normalised over the next 72 hours and she was discharged with no further follow up.

The patient received advice that it was not necessary to represent to the hospital in the future, if similar symptoms returned. The mother expressed concern about this advice.

The authors recommended rheumatology follow up for assessment of Generalised Joint Hypermobility (GJH) in the context of recurrent BACM and other past medical history raising the suspicion for systemic rheumatic disease.

Discussion

The patient fulfilled 5/6 and 2/5 of the proposed Pradhan [6] diagnostic criteria for BACM.

Complications of BACM include rhabdomyolysis and renal failure, therefore urinalysis and renal function should be ordered and monitored closely. One retrospective study of 316 patients with influenza-related viral myositis reported 3% of paediatric patients developed severe rhabdomyolysis [4]. Another retrospective study reported that of 113 patients none developed renal failure [7]. These differences in reports could be related to different infectious agents, or patient characteristics that affect immunological response.

BACM is thought to result from direct viral invasion of muscle tissues [5]. Viral particles have been detected in muscle biopsies of patients with BACM [16, 17]. Why there is calf muscle tissue tropism in the majority of BACM cases is unknown. Immature muscles appear to be more susceptible [4]. Once invading viruses enter muscle cells, it has been proposed that an inability to effectively replicate results in muscle cell necrosis and associated elevation of CK levels [5]. The exact immunological mechanisms that underly BACM require further evaluation [4].

It is worth noting viruses are implicated in the pathogenesis of autoimmune rheumatic diseases [18, 19] including juvenile inflammatory myositis [20, 21]. Mechanisms are thought to include molecular mimicry, abnormal and inappropriate B cell and T cell responses [18] and dysregulation of the Type 1 IFN pathway [22]. Loss of tolerance of self-antigens following infections is recognised as a trigger in inflammatory myopathies [23, 24]. There is limited literature exploring the relationship between recurrent BACM and the subsequent development of juvenile inflammatory myositis, or other myopathies, however one study by Attainese [8] recommend screening for muscular and metabolic disorders cases of recurrent myositis and, or cases where CK levels are $\geq$5000 U/L.

Why some patients are predisposed to the development of recurrent BACM poses several questions relating to pathophysiological professes yet to be evaluated by current research. These include:

- Whether there exists a genetic predisposition to BACM
- Whether there is an underlying component of immunological dysregulation including impaired immunological response to infection resulting in BACM
- Whether patients with BACM will go on to develop other systemic rheumatic disease
- Whether there is a relationship between recurrent BACM and existence of systemic conditions such as GJH or heritable disorders of connective tissue (HCTDS)

The patient was noted to have GJH and features of connective tissue weakness on examination. With the patient's medical history this raises the likelihood of the presence of Joint Hypermobility Spectrum Disorder (HSD) in this patient. The presence of GJH combined with the patient's strong family history of rheumatic diseases raises the possibility of immunologic dysregulation contributing to development of recurrent BACM.

Increased infection risk is reported by many patients with GJH and HSD as well as the Ehlers Danlos Syndromes. There is an acknowledgement in current literature of immunologic dysfunction in these conditions including an increased prevalence of primary immunodeficiency [25-34]. The complete mechanisms that underly this relationship are still under investigation, but thin epithelium leading to increased permeability of pathogens, mast cell activation and genetic mutations resulting in primary immunodeficiency are known to play a role.

As BACM is extremely rare, with only a handful of case reports in the literature, there are many gaps in current literature requiring future exploration. A study to examine the relationship between BACM and the presence of GJH, HSD, Hypermobile-EDS might prove useful in understanding pathophysiology.

Key Recommendations

The true prevalence of recurrent viral BACM is not known due to a lack of data in this area. This requires further research.

Due to the risk of rhabdomyolysis and subsequent renal failure all patients should have renal function tested and if abnormal receive paediatric admission for intravenous fluids and close monitoring of renal function.

There is limited literature available on the association between recurrent BACM and the presence, or development of other systemic rheumatic diseases. This requires evaluation in future research.

The pathophysiologic mechanisms resulting in recurrent BACM require investigation.

Generalised joint hypermobility is known to be associated with mild immune dysregulation. No research has been identified on whether children with generalised joint hypermobility are at an increased risk of developing viral myositis. This is an area that should be explored in future research.

The authors agree with the previous study by [6] that screening for systemic muscular and metabolic disorders should be considered in cases of recurrent BACM, or where there is a CK level > 5000 U/L and additionally where children present with subtle features suggestive of other rheumatic diseases.

As 2.5% of patients with influenza-associated BACM develop renal failure, patients with BACM should undergo nasopharyngeal viral PCR testing and be assessed in the emergency department due to the small, but significant risk of rhabdomyolysis with renal failure [4].

There is a requirement to educate doctors working in emergency medicine and primary care to better recognise the features of BACM to assist with early diagnosis, treatment and avoidance of unnecessary investigations.

Conclusion

This case study highlights several aspects of BACM including the fact it is a frequently missed presentation. In this presentation incidental generalised joint hypermobility was noted in a paediatric patient with a complex rheumatologic family medical history.

Recurrent BACM is an extremely rare condition without a reported prevalence in current literature. Little is known about the condition and whether there is a relationship to other systemic muscular, or rheumatic diseases.

Further education regarding medical presentation to facilitate diagnosis is required. As rhabdomyolysis with renal failure is a small, but serious complication of BACM patients should be assessed in the emergency department and undergo urinalysis and renal function testing. Patients with high CK levels > 5000 U/L, or those with a history of recurrent episodes of BACM should have a paediatric admission with intravenous fluids and close monitoring of renal function.

Further research is required into this rare condition to further understand the pathophysiology and relationship between other rheumatic and muscular diseases.

Conflict of Interests

The authors have no conflict of interests to declare. No funding was received for the authoring, or publication of this paper.

Patient Consent

The mother of the patient provided consent for use of information and approval from the hospital CEO for authoring and publication of this paper has also been sought.

Contributors

The primary author contributed to the conception and design of the work, drafted the manuscript and conducted the literature review. The secondary author revised the paper for important intellectual content and critical evaluation. Both authors give final approval of the version to be published and agreed to be accountable for all aspects of the work.

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