Sporadic acute benign calf myositis: systematic literature review

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Abstract

Acute benign calf myositis is a rare infection-associated syndrome presenting with calves’ pain. It occurs in epidemics or sporadically. In order to better characterize the sporadic form and increase the awareness of this condition, we reviewed the literature reporting apparently sporadic cases. The National Library of Medicine was searched using the terms ‘myalgia cruris’ OR ‘benign childhood myositis’ OR ‘acute calf myositis’ OR ‘viral myositis’. We identified 72 reports, including 447 patients, 322 males and 126 females. Sporadic acute benign calf myositis affected subjects ≤18 years of age (N=446; 99%), followed a prodromal flu-like illness (N=405; 91%), presented with pain and tenderness affecting uniquely the calves for ≤1½ weeks (N=441; 99%) and was never complicated by acute kidney injury. The creatine kinase level was elevated in 441 (99%) out of 444 cases. Microbiological studies identified an infectious trigger in 177 cases, mostly Influenzavirus (type B more frequently than type A), Dengue, Epstein-Barr or Parainfluenza virus and Mycoplasma pneumoniae.

Sporadic acute benign calf myositis is a self-limited condition that can usually be diagnosed on a clinical basis. Differently from the epidemic form, many cases are due to microorganisms other than Influenzavirus B or A.

Keywords: Acute benign myalgia cruris • Acute toe walking • Benign childhood myositis • Bottom shuffling • Frankenstein walk • Review
1. Introduction

First described 60 years ago by the Swedish pediatrician Åke Lundberg as myalgia cruris, acute benign calf myositis is a peculiar infection-associated syndrome of muscle pain [1]. It presents with pain and tenderness affecting the calves, habitually recovers within a week and can occur in epidemics or sporadically. Epidemic cases are usually associated with Influenzavirus of type B [2]. Sporadic cases, however, might be associated with a large number of microorganisms. Furthermore, during an outbreak there is a great alertness that promotes earlier diagnosis. There is likely a lower awareness regarding the sporadic form, compromising an early and correct diagnosis and giving potentially rise to unneeded ancillary investigations. In order to characterize the sporadic form of acute calf myositis and increase the knowledge of this condition, we systematically reviewed the literature reporting sporadic cases of acute calf myositis.

2. Methods

2.1. Literature search strategy

Between September 2016 and June 2017, we performed a computer-based search with no date or age limits of the terms ‘myalgia cruris’ OR ‘benign childhood myositis’ OR ‘acute calf myositis’ OR ‘viral myositis’ in the National Library of Medicine database. Personal files and the bibliography of each identified report were also screened. We applied the principles underlying the U.K. Economic and Social Research Council guidance on the conduct of
narrative synthesis and the ‘Preferred reporting items for systematic reviews and meta-analyses’ statement.

2.2. Selection criteria

Reports published in Dutch, English, French, German, Italian, Portuguese or Spanish were included. When more than one article reported on the same patient, only the more comprehensive one was retained. For the final analysis, we included apparently previously healthy subjects of both sexes and all ages presenting with acute onset pain and tenderness principally affecting the calves, normal sensor examination, preserved ankle and knee reflexes, and spontaneous remission [2]. An elevated total creatine kinase level was not a prerequisite for diagnosis. The following cases were excluded: patients with acute benign calf myositis developing in the context of an outbreak of ≥10 cases and occurring during one season in a defined geographical area [1, 2], cases developing in individuals managed with potentially myotoxic drugs and cases possibly triggered by intense exercise or a sudden increase in exercise in an untrained person ≤3 days before leg pain onset. In order to ascertain the eligibility, authors of reports were sometimes requested for additional information.

The prodrome was considered typical if characterized by a flu-like illness (fever, malaise, nasal discharge or cough) lasting ≤2 weeks and atypical if characterized by a flu-like prodrome lasting >2 weeks, by non-flu-like symptoms and signs (e.g. diarrhea) or in cases without prodrome. The presentation was considered typical in cases with bilateral calf symptoms lasting ≤1½ weeks and atypical in cases with symptoms lasting >1½ weeks, in cases with unilateral
calf symptoms or in cases with calf pain associated with widespread muscle aches.

### 2.3 Data extraction

From each report, data on gender and age; general past history; prodrome; duration of calf pain; general and neurologic examination with emphasis on calf pains and gait abnormalities; highest enzyme levels; tests to identify an underlying infection; management; electromyography or muscle biopsy; and complications such as leukopenia (<4.5x10^9/L), thrombocytopenia (<150x10^9/L), acute kidney injury, cardiac or cerebral involvement and recurrences were excerpted [2] using a structured schedule established in advance. The literature search and the data extraction were carried out by two investigators independently. Disagreements were resolved by discussion until consensus.

### 2.4 Analysis

To pool the data of different studies, weighted central values were calculated using equations that assign weight in proportion to the size of the sample. In publications without statistical dispersion data such as standard deviation, range or interquartile range, the weighted dispersion was taken from the remaining reports. Continuous data are presented as median and interquartile range, dichotomous data as relative frequency and percentage. The Cohen’s index was used to assess the agreement between investigators on the application of the inclusion and exclusion criteria, the Fisher’s exact test to compare dichotomous variables and the Mann-Whitney-Wilcoxon test to compare continuous variables. Statistical significance was assigned at P<0.05.
3. Results

3.1. Search Results

The literature search process is summarized in figure 1. The chance-adjusted agreement between the two investigators on the application of the inclusion and exclusion criteria was 0.91. For the final analysis, we retained 70-72 scientific reports [3-72 3-74] published between 1973 and 2017: 26-28 from Europe, 19 from Asia, 15 from North America, 6 from South America and 4 from Oceania. They were published in English (N=54-55), Spanish (N=10), French (N=2), German (N=2), Dutch (N=1), Italian (N=1) and Portuguese (N=1). The communications included a total of 447-451 previously healthy subjects affected with apparently sporadic acute calf myositis.

3.2. Findings

3.2.1. Prodrome – presentation

Age, gender, clinical features, laboratory findings and disease course of the 447-451 patients appear in table 1. Calf myositis was preceded by a flu-like illness in >90% and presented with bilateral calf pain in 95% of cases. Muscle aches lasted ≤1½ weeks in 99% of cases. The typical prodrome, detected in 405 (91%) of cases was characterized by a flu-like illness (fever, malaise, nasal discharge or cough) lasting ≤2 weeks. A flu-like prodrome lasting >2 weeks (N=2), a diarrheal prodrome (N=4) or no prodrome (N=36) were observed in the remaining 42 (9%) cases. 419 (94%) patients showed a typical presentation and course, characterized by bilateral calf symptoms lasting ≤1½ weeks. In further 28 (6%)...
patients, presentation was atypical. It was characterized by
isolated unilateral calf pain (N=4), calf pain accompanied by
thigh pain (N=12; bilateral in 10 and unilateral in 2), severe
bilateral calf pain associated with mild widespread muscle aches
(N=8) or muscle symptoms lasting >1½ weeks (N=4). Three-hundred-
eighty-six (86%) patients characteristically presented with a flu-
like prodrome and bilateral calf pain lasting ≤1½ weeks.
Complexively, prodrome (N=37), presentation (N=23) or both
prodrome and presentation (N=5) were atypical in 65 (15%) and
typical in the remaining 382 (85%) cases. Age (7.0 [5.4-9.1]
versus 7.2 [4.9-9.8] years) and gender (278 283 ♂ and 102 103 ♀
versus 42 ♂ and 23 ♀) were not statistically different in cases
with typical prodrome and presentation characteristic features as
compared with the remaining 65 (14%) cases. Sporadic acute calf
myositis was preceded by a typical flu-like illness in 405 (91%)
cases. A flu-like prodrome lasting >2 weeks (N=2), a diarrheal
prodrome (N=4) or no prodrome (N=36) were observed in the
remaining 42 (9%) cases. Presentation and course were typical in
419 (94%) and atypical in 28 (6%) cases: isolated unilateral calf
pain (N=4), calf pain accompanied by thigh pain (N=12; bilateral
in 10 and unilateral in 2), severe bilateral calf pain associated
with mild widespread muscle aches (N=8) and muscle symptoms
lasting >1½ weeks (N=4).
Calf aches were reported to be associated with gait
abnormalities in at least 356 358 cases (table 2). A skin rash was
observed in 16 (4%) cases (including a petechial rash in 7 cases
affected with dengue and the characteristic slapped cheek and lacy rash in 2 cases of erythema infectiosum due to Parvovirus B19).

The total creatine kinase level, determined in 444 cases, was found to be elevated in 441 (99%) cases. The total creatine kinase ratio, calculated by dividing the measured level by the corresponding upper limit of normal, was ≥100 in 6 (<2%) cases. Elevated aminotransferases were also reported in 57 patients (the elevation of aspartate aminotransferase was more pronounced than that of alanine aminotransferase in these cases). The total creatine kinase to cardiac MB isoenzyme ratio, a myocardial injury marker, was measured in 33 (7%) cases and found to be always normal.

3.2.1. Microbiological studies

Microbiological studies were performed in 264 (58 59%) cases. A possible infectious trigger was identified in 177 181 (69%), as given in table 3. Influenzavirus (type B more frequently than type A), Dengue virus, Epstein-Barr virus, Parainfluenza virus and Mycoplasma pneumoniae were the most commonly identified microorganisms. Cases associated with Influenza or Parainfluenza virus and cases associated with other microorganisms did not differ with respect to clinical features, creatine kinase test and time to recovery.

3.2.2. Special investigations

Electromyography, performed in 21 (5%) cases, disclosed a characteristic myopathic pattern in 11 cases (52%) but was normal in the remaining 10 cases (48%). A needle biopsy of the soleus muscle, performed in 8 (2%) cases, revealed mild infiltration of
polymorphonuclear or mononuclear white blood cells, muscle necrosis and muscle fiber regeneration. Search for bacterial or viral genome was never performed.

3.2.3. **Management - complications - recurrences**

The patients were managed symptomatically and supportively. Macrolides were prescribed in the 7 cases associated with a mycoplasma infection. Antiviral agents such as oseltamivir were never prescribed.

The total blood cell count (table 1) disclosed mild leukopenia or thrombocytopenia in approximately two-thirds (62%) and one fourth (22%) of cases, respectively. Acute kidney injury and cardiac or cerebral involvement were never reported. Recurrences were observed in 13 cases (3%): one recurrence in 11 and two in 2 cases.

4. **Discussion**

This review of the literature reveals that sporadic acute benign calf myositis, like epidemic benign calf myositis [2], characteristically follows a prodromal flu-like illness and affects preschool- and school-aged children with a male-to-female ratio of approximately 2:1. It presents with pain, tenderness, and occasionally swelling affecting the calves, gait abnormalities, normal sensor examination, preserved tendon reflexes and elevated total creatine kinase level, is never complicated by myositis-associated acute kidney injury, mostly recovers within 4 days and recurs in <5% of cases. Furthermore, sporadic acute benign calf
myositis is often associated with mild leukopenia, 
thrombocytopenia or both (a common finding in a large number of 
viral infections) and is not associated with nervous system and 
cardiac involvement. Unlike epidemic cases, which are almost 
always due to Influenzavirus of type B or A [2], approximately 
half of the reported sporadic cases are temporally associated with 
进一步 microorganisms such as Epstein-Barr virus, 
Parainfluenzavirus, Mycoplasma pneumoniae and especially Dengue 
virus [75]. Finally, calf myositis is sometimes preceded by a skin 
rash or an infectious diarrheal disease.

Muscle biopsy studies, performed in a minority of sporadic cases 
presenting with a flu-like prodrome and bilateral calf pain, point 
out that acute benign calf myositis is an inflammatory muscle 
disease. Investigations in epidemic influenzavirus B-associated 
cases support the notion that in this condition muscle damage 
results from a direct viral invasion [2]. More studies are needed 
for further elucidating the mechanisms underlying this condition.

In the vast majority of cases, sporadic acute benign calf 
myositis is a stereotyped clinical condition (acute onset of 
bilateral calves’ pain following an acute flu-like illness, normal 
sensor examination with preserved ankle and knee reflexes), whose 
diagnosis can be presumed with an excellent degree of confidence 
based on history, physical examination and creatine kinase 
determination alone and subsequently confirmed based on the 
clinical course (spontaneous remission within 1½ weeks). Further 
evaluation [2, 57] might be recommended exclusively in subjects 
living in tropical and subtropical areas (or with history of
recent travel to the mentioned areas), with muscle symptoms not preceded by a flu-like illness, with unilateral calf pain or calf swelling, with calf pain associated with widespread muscle aches, with abnormal neurological examination or with muscle symptoms lasting >1½ weeks. The differential diagnosis includes arthritis, cerebellar ataxia, dermatomyositis, fractures, Guillain-Barré syndrome, osteomyelitis, thrombosis, transverse myelitis and vasculitides such as periarteritis nodosa or isolated calf muscle vasculitis [2, 76].

Finally, inherited diseases impairing the muscular energy production should be considered following two or more attacks [2].

The total creatine kinase level is substantially elevated in inflammatory muscle diseases including calf myositis. The activity of the creatine kinase cardiac MB isoenzyme, a marker of cardiac injury, was determined in a minority of patients affected by sporadic acute calf myositis and found to be normal. Since this test is occasionally pathologically altered in inflammatory myositis or after marathon running even in the absence of a myocardial damage, a sensitive troponin test is advised if to exclude a myocardial compromise. Electromyography, although integral in the evaluation of a suspected chronic myopathy, can notoriously be normal in a number of myopathies. No distinctive myopathic abnormalities were disclosed in many patients with sporadic acute calf myositis, confirming the assumption that a normal electromyography does not exclude the presence of a myopathy [76]. Finally, we suppose that, in some patients,
Electromyography was performed relatively late in the course of this brief-lasting disease.

The course of both sporadic and epidemic [2] acute benign calf myositis is never complicated by acute kidney injury. Hence, we recommend testing for kidney function only in cases with generalized muscle pain, red to brown urine and creatinine kinase values ≥100 times normal. This assumption is supported by observations in adults pointing out that a kidney injury occurs almost exclusively if the creatinine kinase is ≥40,000 UI/L on admission [77].

Sporadic acute calf myositis usually (75%) recovers within 4 days. This is why we advise for characteristic cases no more than adequate hydration, administration of analgesics if needed and sometimes bed rest.

The results of this review must be viewed with an understanding of the inherent limitations of the analysis process, which is based on the scanty available literature. Two limitations of this work should be specifically stated. First, available data do not allow documenting the prevalence of sporadic acute benign calf myositis. Second, since microbiologically uncharacterized cases are less likely to be published than cases caused by Dengue virus, our data might overestimate the frequency of this microorganism as a cause of acute calf myositis. Third, the reported recurrence rate is likely rather inaccurate because it depends on the length of follow up.
Many cases of sporadic acute benign calf myositis are due to microorganisms other than Influenzavirus B or A. Like epidemic benign calf myositis [2], sporadic acute benign calf myositis is a self-limited condition that can generally be easily diagnosed on a clinical basis. In characteristic cases, ancillary investigations such as electromyography and muscle biopsy are unwarranted. The information generated from this review will help physicians to become more familiar with this benign condition.
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**Competing interest**

The authors declare no conflicts of interest.

**Ethical approval**

Not applicable / not required (Review of the literature).

**Authors’ contribution**

- Study concept and design: Gioele Capoferri, Gregorio P. Milani, Gian Paolo Ramelli, Mario G. Bianchetti, Sebastiano A. G. Lava.
- Acquisition, analysis, and interpretation of data: Gioele Capoferri, Mario G. Bianchetti.
- Statistical analysis: Gregorio P. Milani, Sebastiano A. G. Lava.
- Drafting of the manuscript: Gioele Capoferri, Gian Paolo Ramelli, Alessandra Ferrarini.
- Critical revision of the manuscript: Gioele Capoferri, Mario G. Bianchetti, Gregorio P. Milani, Sebastiano A. G. Lava.

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Sporadic acute benign calf myositis. Flowchart of the literature search process. * We unsuccessfully contacted the authors of the study to ascertain eligibility.