

# Review of Children Diagnosed with Acute Myositis of Calves Admitted to a Regional Hospital in Hong Kong in the Period 2003-2012

CO SHAM, K TSE

## Abstract

**Objective:** To investigate the clinical features, management and outcome of all children admitted to a regional hospital in Hong Kong from 2003 to 2012 because of benign acute childhood myositis. **Method:** A retrospective study was conducted in a regional hospital. Hospital records of children admitted from year 2003 to 2012 with diagnostic coding of myositis, rhabdomyolysis and myalgia were reviewed. Those presented with acute onset of pain in the calves, preceded by a febrile episode, and with raised serum creatine kinase level were included. Data including gender, age, causative agent and outcome were analysed. Those with myositis of calves associated with influenza were compared with a comparative sample of influenza A and influenza B patients obtained randomly from the electronic medical record system. The age, sex and length of hospitalisation of this group of patients were compared with all patients with influenza admitted in the study period. **Results:** Seventy-one cases fulfilled our search criteria. Thirty-five cases were excluded for various reasons and the remaining cases were evaluated. The median age at presentation was 6-year-old and 75% of the affected patients were boys. The median length of hospitalisation was 3 days. Sixty percent of the cases were associated with influenza B virus. All patients well recovered with no mortality. The level of serum creatine kinase level at presentation did not correlate with length of stay in hospital. There was no statistically significant difference in length of hospital stay between the 24 cases of influenza associated acute myositis of calves and the 24 randomly selected cases of influenza without myositis for comparison. **Conclusions:** Patients with benign acute childhood myositis carried good prognosis. Unnecessary diagnostic investigations could be avoided with careful history and physical examination.

**Key words** Child; Influenza; Myositis

## Introduction

Benign acute childhood myositis is a syndrome that is classically characterised by pain over the calves in children after an attack of upper respiratory tract infection, usually caused by viruses.<sup>1,2</sup> The condition is most commonly

reported as associated with influenza infection.<sup>2,3</sup> There are also case series and case reports showing that the syndrome can also be associated with infection by human parainfluenza virus,<sup>4</sup> *Mycoplasma pneumoniae*<sup>5</sup> and dengue virus.<sup>6</sup> A German study group reported a large outbreak of influenza B associated benign acute childhood myositis in 2007/2008. In that case series, 76% of the physicians involved had not seen children with benign acute childhood myositis previously.<sup>3</sup>

In this study, we reviewed cases admitted to our hospital because of the syndrome, to look at the case characteristics and outcome. The aim of the study is to provide local data about the syndrome, to increase the awareness of doctors about the syndrome, so as to avoid unnecessary investigations on these children.

Department of Paediatrics and Adolescent Medicine, Tuen Mun Hospital, 23 Tsing Chung Koon Road, Tuen Mun, N.T., Hong Kong

CO SHAM (沈澤安) MBBS(HK), MRCPCH, PDipID(HK)  
K TSE (謝江) MBBS, FRCP(Edinburgh), FHKAM(Paediatrics)

Correspondence to: Dr CO SHAM

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## Method

This is a retrospective study conducted in Tuen Mun Hospital, a regional hospital in the Northwest part of Hong Kong. The electronic medical record system of the hospital was used in retrieving the medical record. Hospital records of Paediatric patients admitted to Tuen Mun Hospital from year 2003 to 2012 with diagnostic coding of myositis, rhabdomyolysis and myalgia were retrieved and reviewed. Those with diagnostic coding of dermatomyositis and polymyositis were not included in our study. The case would be included in the study if the patient was below 18 years of age at the time of presentation, admitted under the care of Department of Paediatrics and Adolescent Medicine, Tuen Mun Hospital, with acute onset of pain in the calf muscles, preceded (up to 14 days) by a febrile episode, and was admitted between 1st January 2003 and 31st December 2012. The muscle tone, deep tendon reflexes, and sensation should be normal. Patients should not have rash or overlying skin changes over the calves. Patients with abnormal level of consciousness, abnormal findings in examination of cranial nerves and neurological examination of upper limbs were excluded. The serum creatine kinase (CK) level of the patient, on admission, should be above the upper limit of normal. Patients that did not fit into the criteria mentioned were excluded from the study. Patients were also excluded if there were no associated febrile episodes, not only calf muscles were involved or if the patient could not clearly indicate where the pain was, e.g. patients with mental retardation or developmental delay. Patients who had seizure or vigorous exercise before admission, who were known immunocompromised, who had history of trauma prior to hospital admission, received intramuscular injection prior to or during hospitalisation were excluded from the study. The reasons of exclusion were noted down. The features of the patients including age, sex, creatine kinase level at presentation, length of hospital stay, any use of oseltamivir during hospitalisation and outcome were noted down. The associated viral agents, if any, were also recorded.

As there were case reports showing that influenza is associated with benign acute childhood myositis, the age, sex and length of hospital stay of all patients with age less than 18 and admitted with diagnostic coding of influenza A or influenza B from year 2003 to 2012 were retrieved, and used to compare with our study population, with disease associated with influenza. A comparative sample with same number of influenza A and influenza B patients was obtained randomly from the electronic medical record

system. These patients should be under the age of 18 on admission, admitted in the period from year 2003 to 2012 and was found to have influenza infection but no benign acute myositis of calves. This comparative sample would be analysed in details. The outcome and the length of hospital stay of the 2 groups were compared to see if one group had worse outcome than the other.

## Ethics Approval

Ethics approval was obtained from the Hospital Authority New Territories West Cluster Clinical and Research Ethics Committee (reference number NTWC/CREC/1141/13).

## Statistical Analysis

Statistical analysis was carried out using IBM SPSS Statistics version 21 and R statistical package. Median and range were presented for continuous data, whereas frequency and proportion were used for categorical data. Chi-square test or Fisher's exact test were used to determine any discrepancy on categorical data. One sample Wilcoxon signed ranked test, Mann-Whitney U test or Kruskal-Wallis test were used for comparing the differences between continuous data, where appropriate. Spearman's rho correlation was used to investigate the correlation among variables. A 5% level of significance was used in all of the significance tests.

## Result

From the electronic medical record system, 71 cases were retrieved from the system with the criteria mentioned. There were 35 cases excluded from the analysis. This was because in 19 of them the site of the muscle pain was not at the calf. The patient did not complain of pain in 4 cases. Four patients were excluded as they had rhabdomyolysis, in which the pain occurred over muscles of all four limbs. Two cases were excluded because the patient presented after convulsion. Two were excluded because the child complained of calf pain but without fever. Two patients received intramuscular injection before attending our hospital. One patient had vigorous exercise before hospital admission. One case was a patient with borderline intelligence, who could not tell exactly the site of muscle

pain. This left 36 cases for further analysis (Table 1). According to our data, 22.2% of these patients were admitted to the hospital in March of a year. Peaks were also noted in January, June and September of a year (Figure 1). Most of the cases occurred from January to March, which account for 44.4% of the cases. Figure 2 showed the distribution of cases by the year of presentation. There was not a particular year in which there was a surge of the illness over the study period of 10 years.

In Tuen Mun Hospital, children admitted because of febrile illness may have their nasopharyngeal aspirate taken and sent for viral studies. In some cases, paired serum would be sent for virus and Mycoplasma studies. Using the result of these virus studies, the aetiological agents of the disease may be identified. Among the 36 cases, virus study was performed in 30 cases (Table 1). Eighteen (60%) of these cases were caused by influenza B. Six (20%) of the cases were caused by influenza A. In one case, the myositis was caused by Mycoplasma. Aetiological agents could not be identified in the remaining 5 (16.7%) cases.

All patients included in the study had raised serum creatine kinase level detected during hospitalisation. The median value was 1,538U/L. The median of length of hospital stay was 3 days. Among the 17 patients with urine for myoglobin checked, none of them showed positive result. None of the patients included in the study received oseltamivir, and all of them recovered well from the disease and were discharged from the hospital without residual morbidity. There was no significant difference in the creatine kinase level at presentation ( $p=0.387$ ) and length of hospital stay ( $p=0.247$ ) between male and female. There was also no significant association noted between age of patient and disease aetiology ( $p=0.079$ ), age of patient and creatine kinase level at presentation ( $p=0.066$ ), and age of patient and length of hospital stay ( $p=0.246$ ). Using Mann-Whitney U test for pair-wise comparison, significant

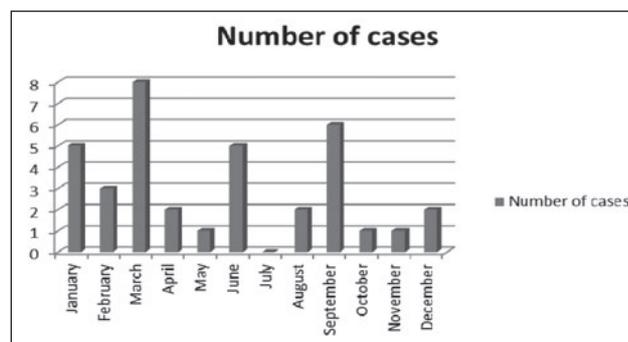
difference was detected in the level of serum creatine kinase level at presentation between patients with influenza B and influenza A ( $p=0.022$ ). However, there was no significant correlation between the serum creatine kinase level and duration of hospitalisation ( $p=0.461$ ). There was no significant difference in duration of hospitalisation among patients with different etiologies of the disease ( $p=0.202$ ).

The gender, median age and length of hospital stay of patients with influenza associated benign acute myositis of calves were compared with all patients admitted with diagnosis of influenza in the study period. Patients with influenza associated benign acute myositis of calves were older (median age 6 vs 3;  $p<0.001$ ) and had longer length of hospital stay (3 days vs 2 days;  $p=0.001$ ). More males was noted in both groups, but the difference was not significant ( $p=0.160$ ).

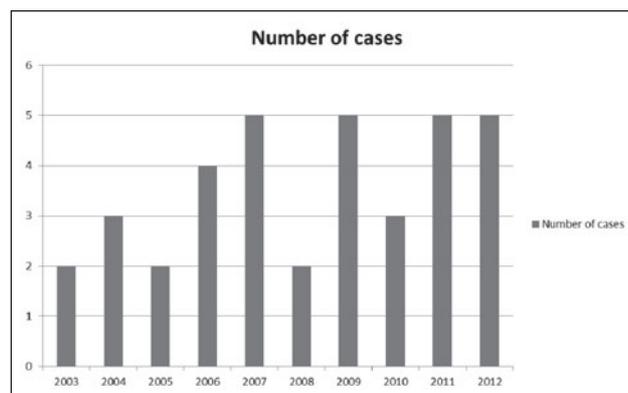
Patients with influenza associated benign acute myositis of calves were compared with the comparative sample. Eighteen patients with influenza B and six with influenza A but without acute myositis of calves, admitted in year 2003 to 2012, were obtained on random basis from the

**Table 1** Demographic data and aetiological agent of the 36 patients

| Item                | Result                              |
|---------------------|-------------------------------------|
| Median age          | 6 (Range 3-16)                      |
| Male : female       | 27 (75%) : 9 (25%)                  |
| Aetiological agents |                                     |
|                     | Influenza B 18                      |
|                     | Influenza A 6                       |
|                     | Mycoplasma 1                        |
|                     | No aetiological agents identified 5 |
|                     | Virology study not performed 7      |



**Figure 1** Case distribution according to time of presentation in a year.



**Figure 2** Case distribution by year of presentation.

electronic medical record system as comparative sample.

Concerning the baseline characteristics, the 2 groups were not statistically different in terms of age ( $p=0.827$ ), sex ( $p=0.505$ ), and timing (month) of presentation in a year ( $p=0.982$ ). On comparison of the 2 groups, there was no significant difference noted in the length of hospital stay ( $p=0.519$ ), and none in either group used oseltamivir. All patients from both the study and comparison groups recovered well from the disease with no mortality.

**Discussion**

Our study offered local data concerning the syndrome of benign acute childhood myositis. As in other case series reported in the literature and in different parts of the world, it was more commonly found in boys, and the median age at diagnosis was school age (Table 2).

Concerning the etiological agents, influenza is well known to be associated with the syndrome. A retrospective study done in Taiwan showed that influenza B is more

common than influenza A in causing the condition.<sup>2</sup> A German study group also reported that there was an outbreak of the syndrome in Germany in year 2007 and 2008, and the authors concluded that it was related to rise in incidence of influenza B infection in late 2007 and early 2008 in Germany.<sup>3</sup> According to the data from the Centre of Health Protection, Department of Health of Hong Kong,<sup>10</sup> seasonal influenza is more common in periods from January to March and from July to August in Hong Kong. However, from our data, while benign acute childhood myositis was more common from January to March, there were no reported cases admitted in July over the 10-year study period. In addition, in Hong Kong there was a pandemic of influenza A (H1N1)pdm09 in 2009,<sup>10</sup> and there was a surge of cases of influenza B infection in early 2012.<sup>11</sup> However, our data did not show that there was an increase in incidence of benign acute childhood myositis in these 2 years. This cannot be explained because the pathophysiological mechanism as to why influenza virus, particularly influenza B, is more associated with the syndrome is still not known,<sup>3</sup> Moreover, our sample size may be too small to draw a valid

**Table 2** Summary of data obtained from our study and from literature review

| Study                            | Year of study | Region of study | Number of subjects | % of male subjects | Median age (years) | Outcome            | Remarks   |
|----------------------------------|---------------|-----------------|--------------------|--------------------|--------------------|--------------------|---|
| Sham et al                       | 2003-2012     | Hong Kong       | 36                 | 75%                | 6                  | All well recovered | Current study   |
| Hu et al <sup>2</sup>            | 2000-2001     | Taiwan          | 46                 | 63%                | 6.5                | Not mentioned      | Among children with influenza B, 34% developed benign acute childhood myositis                        |
| Mall et al <sup>3</sup>          | 2007-2008     | Germany         | 219                | 74%                | 7                  | All well recovered | 173 cases were identified retrospectively and included in analysis                                    |
| Rajajee et al <sup>6</sup>       | 2001-2002     | India           | 40                 | 52%                | 5.3                | All well recovered | 55% of the cases associated with Dengue virus infection   |
| Mujgan Sonmez et al <sup>8</sup> | 2002          | Turkey          | 6                  | 83%                | 5.9                | All well recovered | One patient was reported to have decreased deep tendon reflexes                                       |
| Ferrarini et al <sup>9</sup>     | 2013          | Switzerland     | 49                 | 63%                | 6.3                | All well recovered | 3 patients did not have raised serum creatine kinase level  |
| Nucleolus et al <sup>14</sup>    | 2011          | Greece          | 7                  | 71%                | 7.2                | All well recovered |   |
| Agyeman et al <sup>16</sup>      | 2002-2003     | Switzerland     | 5                  | 80%                | 8.3                | All well recovered |   |
| Zafeiriou et al <sup>17</sup>    | 1996-1999     | Greece          | 32                 | 56.25%             | 6.3                | All well recovered | One patient complained of diffuse myalgia, 5 patients were reported to have decreased tendon reflexes |

conclusion on this issue. Dengue virus was reported to be associated with 50% of the cases reported in a case series done in Chennai, India, but none of our cases were found associated with this virus.<sup>6</sup>

From our data, the median length of hospital stay was 3 days. This was similar to that reported in the Swiss-Italian case series.<sup>9</sup> Patients with acute myositis of calves caused by influenza were found to have longer hospital stay than influenza patients without myositis, but there was no clinical significance (3 days vs 2 days). In addition, all our patients well recovered from the disease without any morbidity. All of them recovered without the use of oseltamivir. However, our case number is too small to conclude whether acute myositis of calves should be regarded as a complication of influenza, and that the patient should warrant anti-viral therapy.<sup>12</sup> Nevertheless, there was recent evidence showing that using neuraminidase inhibitors in the treatment of influenza infection may not be as useful as previously thought.<sup>13</sup>

Our current study also provided local data, to support reducing unnecessary investigations on children who suffered from benign acute childhood myositis in the future. Children who suffered from this disease are prone to extensive investigations. One of the reasons is that doctors are not familiar with the problem. In the German study, it was noted that 76% of doctors who managed these children had not seen children with benign acute childhood myositis previously.<sup>3</sup> A case series performed in Greece, which involved 32 children, also found that 78.1% of the children were given a diagnosis other than benign acute childhood myositis by their general practitioner or Paediatrician. Therefore it is hoped that with the provision of local data from this study, the benign nature of the disease can be reassured to doctors, patients and their relatives.

Another reason that these children are prone to extensive investigations is because of their clinical presentation. Children may present to their doctors because of refusal to bear weight.<sup>14</sup> Without a careful history and physical examination, this may be interpreted as bilateral lower limbs weakness. Differential diagnoses would then include Guillain-Barré syndrome, transverse myelitis, cerebellar ataxia, meningitis, osteomyelitis, juvenile idiopathic arthritis, dermatomyositis, fracture, thrombosis, metabolic myopathies and rhabdomyolysis.<sup>9</sup> Therefore these children may be subjected to repeated blood taking, lumbar puncture, sedation risk of neuroimaging, electromyography and nerve conduction tests.<sup>8,9,14</sup> Case series also reported that echocardiogram were performed in these children<sup>14</sup> to look for features of acute myocarditis. In our opinion, we agree

with the author groups from Switzerland<sup>9</sup> and Greece<sup>14</sup> that with careful history and physical examination, (i.e. acute onset of pain in the calf muscles in children, preceded by a febrile episode and normal physical examination except weakness as a result of muscle pain), a clinical diagnosis of benign acute childhood myositis could be made. The investigations aforementioned may not be necessary. Clinical observation with follow up is recommended until the functional status of the patient returned to normal. A bedside urine dipstick test may be done to exclude myoglobinuria. Blood test may be performed as raised serum creatine kinase level suggests the diagnosis of myositis. However as mentioned in our study, this parameter had no implication on the severity, duration or prognosis of the disease. Patients with rhabdomyolysis will usually have more generalised muscle pain instead of pain limited to calf muscles. Checking serum creatine kinase level, therefore, would not alter the management of these patients, if the clinical diagnosis can be made. Follow-up blood tests to ensure the return of creatine kinase level to normal may also be not necessary. A study performed for children with transiently raised creatine kinase level showed that in 130 children, only 1 patient was found to have metabolic myopathy.<sup>15</sup> Therefore the risk of missing a case of metabolic myopathy is not high. A number of red flags were suggested in Table 3, which if present, diagnosis other than benign acute myositis of calves may be considered.

There are several limitations about this study. This is a retrospective study. Selection bias was possible and list of patients could be incomplete. In addition, this is a single centre study with relatively small number of patients. A prospective study involving more hospitals not only increase the number of study subjects, but will also allow a better designed research protocol. The muscle power of the calves can be better graded and the time of blood taking for serum creatine kinase level can be better defined.

**Table 3** Suggested red flags that if present, diagnosis other than benign acute myositis of calves should be considered

|   |  |
|---|--|
| • Pain or tenderness over muscles other than calves | • History of trauma                    |
| • Abnormal conscious level                          | • Limb swelling                        |
| • Ascending muscle involvement                      | • Presence of joint pain               |
| • Bladder dysfunction                               | • Presence of bone pain                |
|   | • Symptoms lasted for more than 1 week |

## Conclusion

Our study provided local data concerning benign acute childhood myositis. As in case series reported in other parts of the world,<sup>2-4,6-9,14</sup> the syndrome was most commonly found in preschool and school age boys. It was commonly associated with viral infection particularly influenza B. These children would present with acute onset of pain over the calves with a preceding febrile illness, and the syndrome carried good prognosis. We hope that our study offered more information to local medical practitioners concerning the syndrome, and unnecessary diagnostic investigations can be avoided in these children. It remained uncertain why influenza B is more strongly associated with this condition than other viruses. There had been studies showing that influenza B has a greater potency of direct muscle cell invasion.<sup>2,9</sup> Further research is needed in order to answer this question.

## Competing Interest

None declared.

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