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Evaluation of Benign Acute Childhood Myositis by Ultrasound Elastography

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Abstract

Objective: Herein, we aimed to determine the diagnostic contribution of ultrasound elastography (UE) technique to the assessment of muscle stiffness in pediatric patients with myositis.

Material and Methods: This study enrolled 16 patients who presented to our hospital's Pediatric Neurology Outpatient Clinic with the complaint of inability to walk and who had a clinical presentation of benign acute childhood myositis (BACM). The patients were referred to the Radiology Department to undergo muscle ultrasonography (USG), where they underwent UE of the gastrocnemius muscle (GCM).

Results: Children with myositis and healthy children are similar age (7.06 ± 1.52 year (5–11) vs. 7.00 ± 1.59 year (5–11) year) (P: 0.908) and body mass index (BMI) (20.04 ± 1.58 (18.6–24.2) vs. 22.08 ± 1.43 (19.9–24.4) (P: 0.946). The mean serum creatine kinase (CK) was measured as 1520.3 ± 1163.6 U/L (min: 456, max:4100) in children with myositis. In the children with myositis, the thickness of the medial and lateral GCM increased compared with that in control group (medial; 18.15 ± 3.02 mm vs 13.10 ± 2.26 mm, p<0.001, lateral; 13.51 ± 3.07 mm vs 9.34 ± 1.86 mm, p<0.001). The medial and lateral GCM ratio in group 1 was slight bigger than that in group 2 (medial; 1.10 ± 0.37 vs 1.00 ± 0.34, p: 0.274, lateral; 1.22 ± 0.44 vs 1.10 ± 0.29, p: 0.243). GCM strain values were mildly elevated in patients with myositis compared to controls.

Conclusion: In the children with myositis, the thickness of the medial and lateral GCM increased compared with that in control group. GCM strain ratio values were slightly higher in myositis patients compared to the control group. We think that the increase in muscle thickness values is mainly secondary to the edema seen in myositis. In addition, UE is a clinically applicable quantitative analysis for changes in myositis.

Keywords: child, elastography, myositis, ultrasonography

Introduction

Benign acute childhood myositis (BACM) is a benign self-limiting condition affecting school-age children that heals with supportive care without complications, which usually develops suddenly after an episode of upper respiratory tract infection (URTI) and manifests itself with bilateral calf pain and difficulty in walking (1, 2). Although many causes of URTI (respiratory syncytial virus, adenoviruses, herpes simplex virus, Epstein Barr virus, cytomegalovirus, mycoplasma, and rotavirus) may lead to myositis, the disorder most commonly occurs due to influenza viruses (2, 3). It was first described in 1957 by Lundberg among 74 pediatric cases (4). It is more common among boys. Its typical laboratory finding is elevated serum CK level (5, 6). It's important to make its differential diagnosis from Guillain-Barré syndrome and more severe disorders that cause myoglobinuria (6). In acute benign myositis muscle biopsy frequently yields nonspecific findings and thus it is unnecessary (7). Moreover, as myositis may be unevenly distributed in affected muscles among cases requiring a muscle biopsy, muscle imaging is especially useful for determining single or multiple muscle involvement and selecting the biopsy site (8).

The aim of the present study was to measure muscle stiffness with UE technique among children with BCAM and compares it with that of healthy children.

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Material and Methods

This study enrolled a total of 32 children, 16 of whom had been diagnosed with BCAM after being referred by various pediatric clinics to Pediatric Neurology Clinic for inability to walk, and 16 healthy volunteers. Because all participants in this study were younger than 18 years, informed written consent and verbal assent were obtained, respectively, from, parents and children before participation in the study.

Clinical Assessment: Acute benign myositis was diagnosed on the basis of the criteria including sudden-onset bilateral calf pain, inability to walk or walking disturbance, history of URTI prior to and/or during the attack, moderately elevated serum CK level, and the absence of a marked abnormality of the nervous system or in muscle examination. Patients whose clinical condition did not start to improve within 48 hours, those with a family or past history of muscular or rheumatic disease or any systemic disorder, and those with a history of long-term medication use or trauma were excluded.

The patients' demographic information, haemogram, full urine analysis, C-reactive protein (CRP), kidney function tests and serum muscle enzymes around the USG examination, including CK, alanine aminotransferase (ALT), and aspartate aminotransferase (AST) were recorded. Both patients and volunteers were instructed to sit still for 30 min before the USG examination.

Imaging Assessments: Axial B-mode USG and real-time elastography (RTE) images were obtained using a digital sonography scanner (Aplio 400, Toshiba Medical Systems Corporation, Otawara, Japan) supplied with SE software with a 12 MHz linear array transducer of the medial and lateral GCM. All measurements were performed by the same radiologist (10 years of experience for ultrasonography and 7 years of experience for strain elastography). Ultrasound gain, depth, focal points and transducer frequency settings were kept constant in all image scans. The thickness of GCM was measured by using an electronic caliper at real-time B-mode USG (Fig.1).

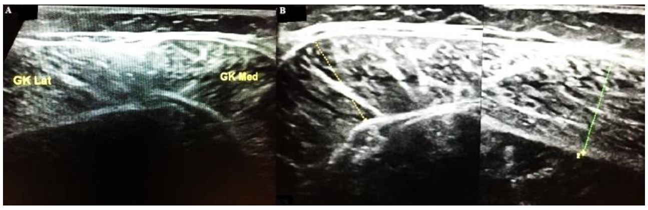

Figure 1: B-mode ultrasound image of lateral (A) and medial (B) gastrocnemius muscle shows the thickness by an electronic caliper.

Manually, RTE image was obtained by applying light repetitive compression in the form of rhythmic compression and relaxation cycles with the transducer. The RTE image appeared as a translucent, colour-coded, real-time image superimposed on the B-mode image. On the elastogram, while areas of low strain were displayed in red, areas of high strain were displayed in blue. More than 3 RTE images were obtained with repetitive compression.

A 4-mm- diameter circular regions of interest (ROI) were used for measuring SR. A 4-mm- diameter circular regions of interest (ROI) were used for measuring SR. For each patient, the ROI of the medial or lateral GCM (A) and the ROI of adjacent subcutaneous fatty tissue (B) were compared and the SR value (B / A) was automatically calculated by the sonography scanner. For each of the three images the mean values were obtained.

Statistical Analysis: Differences between bilateral medial and lateral GCM SR between children with myositis and healthy children was of primary interest. Data were analyzed using SPSS v. 22.0 software (SPSS Inc., Chicago, IL). Variables are expressed as mean ± standard deviation (SD). When parametric test assumptions are provided, Independent Samples T Test was used to compare independent group differences. If the parametric test assumptions were not met, Mann-Whitney U test was used to compare independent group differences. The P value less than 0.05 was considered statistically significant.

Results

A total of 32 children participated in this study: 16 children with myositis and 16 healthy children with typical development. Among 16 patients enrolled in the study, 12 (80%) were male and 4 (20%) were female. The age range was 5-11 years, with a mean age of 7.06 ± 1.52 years. Children with myositis and healthy children are similar age (7.06 ± 1.52 year (5–11) vs. 7.00 ± 1.59 year (5–11) year) (P=0.908) and body mass index (BMI) (20.04 ± 1.58 (18.6–24.2) vs. 22.08 ± 1.43 (19.9–24.4) (P: 0.946). All patients had pain and stiffness in the calf muscles but no muscle weakness. None of the patients had abnormal signs in neurological examination. In all cases signs and symptoms began to improve within 24-48 hours and completed by three day at the latest. The mean serum CK was measured as 1520.3 ± 1163.6 U/L (min: 456, max:4100) in children with myositis.

USG and elastographic images of medial and lateral GCM were taken in both groups and muscle stiffness was assessed with the RTE technique. In the children with myositis, the thickness of the medial and lateral GCM increased compared with that in control group (medial; 18.15 ± 3.02 mm vs 13.10 ± 2.26 mm, p<0.001, lateral; 13.51 ± 3.07 mm vs 9.34 ± 1.86 mm, p<0.001). There was no significant difference between children with myositis and healthy children with typical development for SR. The medial and lateral GCM ratio in group 1 was slight bigger than that in group 2 (medial; 1.10 ± 0.37 vs 1.00 ± 0.34, p:0.274, lateral; 1.22 ± 0.44 vs 1.10 ± 0.29, p:0.243).

While subcutaneous fat predominantly appears as a green/red mosaic, abnormal muscle is stiffer (blue) tissue in an elastogram in the muscles of patients with myositis (Figure 2). Also, there was no significant difference between right and left GCM for SR. Demographic characteristics, thickness of muscle, and SR of children with myositis compared to healthy children with typical development are in Table I.

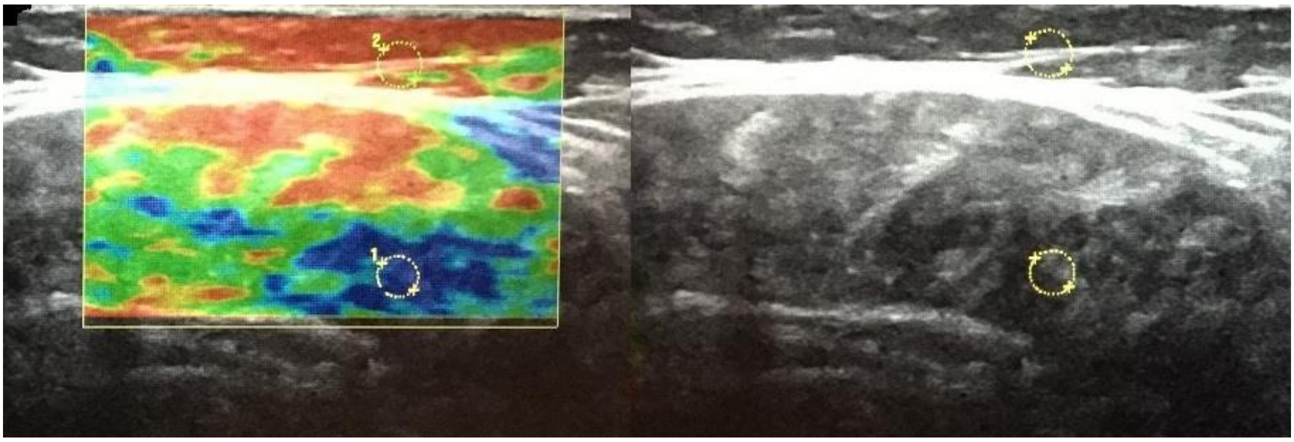

Figure 2: Ultrasound elastography image of gastrocnemius muscle from 9 year-old boy with myositis. Elastogram shows that subcutaneous fat appears green/red. Affected areas of the muscle are stiffer (blue) than normal muscle (green/red).

Table I: Demographic characteristics, thickness of muscle, and strain ratio of children with myositis compared to healthy children with typical development.

	BACM Patients (n=16) mean ± std. dev	Control (n=16) mean ± std. dev	p
Year	7.06 ± 1.52	7.00 ± 1.59	p>0.05
BMI	20.04 ± 1.58	22.08 ± 1.43	p>0.05
Lateral GKM thickness (mm)	13.51 ± 3.07	9.34 ± 1.86	**p<0.05**
Medial GKM thickness (mm)	18.15 ± 3.02	13.10 ± 2.26	**p<0.05**
Lateral GKM strain ratio	1.22 ± 0.44	1.10 ± 0.29	p>0.05
Medial GKM strain ratio	1.10 ± 0.37	1.00 ± 0.34	p>0.05

Discussion

Evaluation of gastrocnemius muscles by UE may be potentially useful for managing myositis by providing quantitative information on disease. In this study, the clinical applicability of elastography method in GC muscles was examined in 16 patients with myositis and 16 healthy controls. In the children with myositis, the thickness of the medial and lateral GCM increased compared with that in control group. We think that the increase in muscle thickness values is mainly secondary to the edema seen in myositis. There was no significant difference between children with myositis and healthy children with typical development for SR. However, GCM strain ratio values were mildly higher among patients with myositis than the controls. Based on these results, we believe that our statistical power was low due to a small sample size. Significant results in strain ratio may be obtained in future studies with larger sample size. UE is a clinically applicable quantitative analysis for changes in myositis.

In acute benign myositis, muscle biopsy commonly yields a nonspecific result and is unnecessary. Bove et al. took biopsy samples from 12 cases of acute benign myositis and showed signs of nonspecific minimal inflammatory infiltration and necrosis in 11 cases and a normal microscopic appearance in one case (7). As myositis may have a heterogeneous distribution, muscle imaging is especially helpful in determining single or multiple muscular involvement and selecting the biopsy site (8).

Thanks to its high spatial resolution, perfusion CT study with intravenous radiopaque contrast agent can assess both muscular and skeletal tissue. However, repeat screening protocols results in the exposure of patients to a substantial amount of radiation. Furthermore, the risk of adverse events with contrast material is higher in CT compared to contrast materials used for MRI and ultrasonography (9).

Advanced magnetic resonance imaging (MRI) techniques can assess a variety of muscular pathologies including acute or chronic muscle injuries, intramuscular collections, and soft tissue masses (10). MRI may also be useful to diagnose focal myositis (11, 12) and other inflammatory myopathies like BCAM that most commonly affects the gastrocnemius and soleus muscles (13, 14). In MRI, muscles with inflammatory edema appear hyper intense in T2 weighted images. Additionally, certain techniques such as fat suppression T2 weighted images or short tau inversion recovery (STIR) series can be used to eliminate fat signal.

Although T2 weighted signal hyper intensities commonly represent edema as a sign of early myositis, this sign may be misleading because it may also be observed in metabolic and traumatic myopathies, neuropathies, muscle dystrophies, myotonic dystrophy, rhabdomyolysis, diabetic muscle infarction, and even after physical exercise (15). However, MRI has some disadvantages such as being affected by motion artifacts, difficulties experienced by patients with claustrophobia or loud sound phobia, and a high cost (8).

Compared to computerized tomography (CT), ultrasonography has the advantages of being cheap and easy-to-perform. It has a high spatial resolution and offers an opportunity of real-time imaging without exposure to ionizing radiation (8). A study found no significant difference between muscle USG's sensitivity (83%) than that of electromyography (92%) or serum CK activity (69%) for myositis. That study found that USG had a positive predictive value of 95% and a negative predictive value of 89% (16). Different types of inflammatory myopathies present with typical, although not entirely specific, USG properties. In prolonged muscle disease, muscle mass is reduced due to muscle atrophy and echogenicity increases due to fat infiltration. Nevertheless, echogenicity may also decrease in less active myositis (8). As contrast-enhanced USG can diagnose edema and increased muscle perfusion in many patients with myositis, it can be used to increase diagnostic specificity when edema-like changes were detected in muscles by MRI (16).

UE is a quantitative USG study based on the principle that, depending on the elastic properties of a tissue, stress applied to that tissue causes a change in it. It is cheap, easy to apply, takes short time and has no adverse effect (17). SE is an operator-dependent technique where training and experience are crucial. In this technique, probe movements should be in the same direction and at a regular frequency (18, 19).

UE has been used frequently to evaluate tendons, plantar fascia pathologies and soft tissue masses (20-22). Measurement of passive muscle stiffness is perhaps the simplest measurement method but it should be performed in a standardize manner (23). In children, elastography study performed prior to and after standard exercise found a higher muscle elasticity (24). In contrast, another study in adults reported that muscle elasticity was found to decrease before and after muscle exercise (25). It is difficult to compare these contradictory results with each other due to the inadequate standardized application of strain elastography and the differentiated evaluation of elastograms (20, 26, 27).

This study has some limitations. First, a relatively low number of patients with myositis were studied, and the patients are relatively heterogeneous in regards to age and gender. Therefore the statistical significance is limited. Further studies should preferably be designed with a larger number of cases. Elastography is user-dependent, requires a learning curve to a certain extent, and is flawed by technical problems related to image reproduction due to pressure imbalance applied with free hand technique. To reduce the impact of this problem, SR measurements were performed by a single radiologist. UE is technically very challenging in terms of the proper application of the technique. Experience with technical problems and situations to solve these problems will be guided by the use of free hand compression elastography. Lastly, elastography measurements are not truly quantitative and are considered subjective in nature.

Conclusion

In this study we aimed to establish the diagnostic value of elastography technique in assessing muscle stiffness among patients with myositis. We believe that the increase of muscle strain ratio values is mainly caused by myositis. SE is a promising technique for assessing changes in muscle elasticity. Although studies or case reports have been recently published that assess the elastic properties of musculotendinous tissue, we did not come across any study that specifically examined the role of elastographic examinations in patients with BCAM (28, 29). Although there is a need for more comprehensive studies with larger sample size are needed in this field, we are of the opinion that elastography technique may be a helpful tool in addition to USG findings among patients with myositis. RTE is one of the available elastography techniques and may particularly evolve to become a useful ancillary technique for investigation of muscular disorders.

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Author's Contributions: GG, OG; Research concept and design, Patient examinations, Research the literature, preparation of the article **GG;** Revision of the article.

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