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FULL PAPER

Characteristic MR image finding of squatting exercise-induced rhabdomyolysis of the thigh muscles

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Objective: To describe the characteristic MRI appearance of squatting-induced rhabdomyolysis involving the thigh muscles.

Methods: This study consisted of 10 cases obtained at 3 institutions from 2005 to 2015. A retrospective review was performed to obtain clinical information and MR scans for rhabdomyolysis of the thigh muscles. MRI was analyzed according to the distribution and degree of muscle involvement; the degree was assessed and graded as normal, mild or prominent.

Results: The mean patient age was 20.2 years (range, 15–24 years), and 7 of the 10 patients were male. All patients had history of excessive squatting action, suffered clinically from bilateral thigh pain and were confirmed to have rhabdomyolysis through analysis of

serum creatine kinase (CK) levels. All of the patients (10/10) exhibited diffuse mild to prominent degree involvement of the anterior thigh muscles according to fluid-sensitive MR sequences. Among the anterior thigh muscles, the rectus femoris was spared in 8 patients (8/10) and mild degree involved in 2 patients (2/10). Thus, no cases exhibited prominent degree involvement of the rectus femoris muscle.

Conclusion: Preservation of the rectus femoris muscle on MRI in squatting-induced rhabdomyolysis may be useful for differentiating rhabdomyolysis from other aetiologies.

Advances in knowledge: Preservation of rectus femoris on MRI is distinguishable finding in squatting-induced rhabdomyolysis and reflects the functional anatomy of anterior thigh muscles.

INTRODUCTION

Rhabdomyolysis is a serious condition resulting from direct or indirect muscle injury, accompanied by clinical symptoms and specific laboratory findings.^{1–4} In rhabdomyolysis, damaged skeletal muscle tissue breaks down and releases its components into the bloodstream. This release is harmful to the kidneys and can lead to complications such as acute renal failure.^{5,6} In some cases, rhabdomyolysis can even cause death, and thus prompt diagnosis of rhabdomyolysis is important.^{7,8}

The diagnosis of rhabdomyolysis is made primarily on the basis of clinical symptoms, history and elevated creatine kinase (CK) levels in the blood. CK is released by damaged skeletal muscle, resulting in levels more than five times the upper normal limit value (60–400 IU l⁻¹).^{8,9} MRI is not considered to play a critical role in the diagnosis of rhabdomyolysis due to non-specific imaging findings of muscular injury or myopathy; however, it has a major role in evaluating

the extent and distribution of affected muscles.^{10–13} In addition, MRI could be helpful in assessing the possibility of reversible and irreversible changes in damaged muscles by identifying the presence of myonecrosis.^{14,15}

There are many causes of rhabdomyolysis, such as extreme muscle strain, medication, crush injury, metabolic disorder, muscle disease or infection.⁹ To our best knowledge, there are no published studies on the MRI features of exercise-induced rhabdomyolysis in the thigh. In this study, squatting exercise-induced rhabdomyolysis of the thigh muscles has characteristic MRI findings compared with rhabdomyolysis induced by other potential causes as well as other intramuscular oedema disease, which are already reported non-specific and overlapping image findings among them on MR.^{10–13}

Thus, the purpose of this study was to illustrate the typical MRI appearance of squatting exercise-induced rhabdomyolysis

involving the thigh and to discuss reason or physical mechanism of MRI features.

METHODS AND MATERIALS

Study population

This retrospective three-centre study was approved by the institutional review board and the need for informed consent prior to chart review was waived. We queried a database containing the radiology reports of MR performed between January 2005 and August 2015 using all of the following keywords in our picture archiving and communication system (INFINITT PACS or PiViewStar; Infinit HealthCare, Seoul, Republic of Korea) for each institution: “rhabdomyolysis” and “thigh”. Patients were excluded if they did not have history of excessive exercise or overuse the thigh muscle. A total of 10 cases of rhabdomyolysis involving the thigh muscles were obtained at 3 institutions.

All rhabdomyolysis in thigh muscles was diagnosed with clinical symptom, physical examination, typical exercise history, elevated CK level and serial follow-up laboratory study. Biopsy was not performed. To obtain the clinical history of patients with rhabdomyolysis of the thigh muscle, a review of electronic medical records, including outpatient charts and discharge summaries, was performed by one independent radiologist (EKY) who was not involved in image review. Patient age, sex, symptoms, history, time interval to imaging, presence of dark urine, serum CK levels and time to normalized serum CK level were assessed. Time interval was defined as the period from exercise to imaging. The number of days to the development of dark urine was calculated from the exercise day. The time interval of normalized serum CK level was calculated from the initial laboratory test.

Imaging technique

Patients diagnosed by laboratory findings and clinical history then underwent thigh MR to evaluate the distribution of rhabdomyolysis and presence of myonecrosis. In this study, MR performed at the three institutions was generated from 1.5-T or 3.0-T whole-body scanners with a standard cardiac dual coil. The axial view was used mainly because it provided a useful assessment of the distribution of the affected thigh muscles. Although various imaging protocols were used, the main protocol for thigh MR of rhabdomyolysis consisted of axial T_1 weighted imaging, fat-suppressed T_1 weighted gadolinium (Gd)-enhanced image and an axial fluid-sensitive sequence such as T_2 weighted or fat-suppressed T_2 weighted images. The following parameters were used most often for thigh MR: axial fast spin-echo T_1 weighted (repetition time/echo time, 567/20; echo-train length of 3; 7-mm section thickness, 3-mm interslice gap, 284×280 matrix and 20×20 -cm field of view), axial fast spin-echo T_2 weighted (repetition time/echo time, 2946/100; echo-train length of 16; 7-mm section thickness, 3-mm interslice gap, 284×280 matrix and 20×20 -cm field of view), axial fast spin-echo T_2 weighted with fat saturation (3115/100, echo-train length of 16, 7-mm section thickness, 3-mm interslice gap, 284×280 matrix and 20×20 -cm field of view) and axial fast spin-echo Gd-enhanced T_1 weighted with fat saturation (583/20, echo-train length of 3, 7-mm section thickness, 3-mm interslice gap, 284×280 matrix and 20×20 -cm field of view). Follow-up MRI protocol is the same as described above.

Image analysis

MRI interpretation of subjects with rhabdomyolysis of the thigh was performed independently by two board-certified radiologists with subspecialization in musculoskeletal radiology (KNR and JSP, with 25 and 10 years' experience, respectively).

The distribution of rhabdomyolysis was analyzed based on axial scans of T_1 weighted, fat-suppressed T_1 weighted Gd-enhanced image and fluid-sensitive sequences such as T_2 weighted or fat-suppressed T_2 weighted images. All patients underwent bilateral thigh MR from which the symmetry of MR findings in both thighs was assessed. Distribution of rhabdomyolysis was divided into three compartments consisting of anterior, posterior and medial groups, and each of the affected muscles in those compartments was recorded.

We arbitrarily categorized the degree of muscle involvement in rhabdomyolysis into three degrees as normal (grade 0), mild (grade 1) or prominent (grade 2) involvement according to fluid-sensitive sequences. Normal was characterized by the absence of muscle oedema and increased signal intensity. Mild involvement was defined as increased signal intensity on axial fluid-sensitive sequences but absence of scant fluid signal intensity in the intermuscular fascia. Prominent involvement was defined as increased signal intensity and the presence of scant fluid signal intensity in the intermuscular fascia. Gd-enhancement study was assessed by diffuse or partial enhancement and homogeneous or heterogeneous enhancement of affected muscles.

According to the definition of grade and distribution of rhabdomyolysis at MRI, the same two radiologists (KNR and JSP) performed a second reading. One of the two readers (KNR) was blinded to all clinical information and read all images twice with a 1-month interval, so we could evaluate intrareader reliability. Discrepancies were resolved by means of consensus.

Statistical analysis

Intra- and interobserver reliability in the qualitative evaluation of distribution and grade of rhabdomyolysis was determined with the Cohen k value. The following ratings for the interpretation of k were used: $k < 0.40$ indicated poor agreement; $k = 0.49$ – 0.59 indicated moderate agreement; $k = 0.60$ – 0.80 indicated good agreement; and $k > 0.80$ indicated excellent agreement. Statistical analyses were performed by using R for Windows® software v. 3.0.2 (R Development Core Team, Vienna, Austria).

RESULTS

Clinical data

The clinical results of patients with rhabdomyolysis in the thigh muscle are summarized in Table 1. The study group consisted of 10 patients comprising 7 males and 3 females. The average patient age was 20.2 years (range 15–24 years) at the time of MRI. The mean interval time to imaging was 4.1 days (range 2–7 days). All patients had a history of excessive squatting action (sitting down and standing up repeatedly more than 150–700 times) for exercise and suffered clinically from bilateral thigh pain. All subjects experienced dark urine within 3 days of the most recent episode of squatting, and rhabdomyolysis was confirmed based on serum CK levels. In Case 4, the patient's CK level was more than 5000,

reflecting the hospital laboratory upper limit of detection. Although we were unable to determine the exact initial CK value in this patient, we confirmed rhabdomyolysis based on clinical information and serial CK levels. Time to normalized CK level was 12.2 days (range 9–15 days). Symptoms tended to improve earlier than serum CK. Only one patient had follow-up MRI after 7 weeks because the patient wanted evaluation of the thigh muscle, but there was no specific symptom.

Image analysis

The results of imaging studies and features of patients with rhabdomyolysis are summarized in Table 2. All patients underwent bilateral thigh MR, and the axial images showed bilateral symmetry in nearly all of the patients. All cases of thigh MRI included fat-suppressed T_2 weighted images, and a Gd-enhancement study was performed in six cases. On fluid-sensitive sequences, all patients (10/10) showed diffusely mild-to prominent-degree involvement of the anterior thigh muscles. Among the anterior thigh muscles, the rectus femoris was completely spared in 8 patients (8/10), whereas the 2 remaining patients had mild-degree involvement of rhabdomyolysis (2/10). Thus, there were no cases with prominent degree involvement of the rectus femoris muscle (Figures 1–4).

Among the affected vastus muscles observed in the axial plane, 4 cases (4/10) showed diffuse, homogeneous involvement, whereas the remaining 6 cases (6/10) showed partially heterogeneous involvement. Considering the signal change and the extent of

involvement, the vastus intermedius was the most affected muscle compared with the vastus medialis and lateralis muscles. With respect to the affected vastus muscles, the anterior portion was more prominently affected than other portions regardless of the extent of heterogeneity in the involvement pattern.

4 patients (4/10) had mild-degree involvement in the posterior or medial thigh muscles. Two of these patients (two of four) showed involvement of the posterior compartment of thigh muscles such as the hamstring muscles, whereas the remaining two patients (two of four) exhibited involvement of the medial compartment such as the adductor muscles of the thigh. In addition, only 6 patients (6/10) underwent Gd-enhancement study in which all of them (6/6) showed diffusely homogeneous enhancement of the anterior thigh muscles except the rectus femoris muscle. None of the patients (zero of six) exhibited heterogeneous signal changes and enhancement, an indicator of myonecrosis.

Table 2 shows the results of the reproducibility of the evaluation of thigh muscles at MRI. There was excellent intra- and interobserver reproducibility in the qualitative evaluation of distribution and grade of rhabdomyolysis involvement of thigh muscles.

DISCUSSION

Rhabdomyolysis is a serious condition caused by muscle injury.^{1–4} A diagnosis of rhabdomyolysis is made on the basis of typical clinical symptoms consisting of dark urine and laboratory evaluation of serum CK levels.^{7,8} Rhabdomyolysis is the

Table 1. Demographic and clinical data of patients with rhabdomyolysis

Patient	Age (years)	Sex	History	Time to imaging (days)	Dark urine	Serum CK level (IU l ⁻¹)	Time to normalized serum CK level (days)
1	15	Female	Squatting 170	4	Present	157,000	14
2	16	Male	Squatting 150	5	Present	21,395	12
3	20	Female	Squatting 200	7	Present	85,868	13
4	15	Female	Squatting 200	3	Present	>5000 ^a	10
5	23	Male	Squatting 100	4	Present	1216	12
6	24	Male	Squatting 700	4	Present	21,700	15
7	22	Male	Squatting 300	3	Present	93,370	11
8	23	Male	Squatting 300	2	Present	45,980	14
9	20	Male	Squatting 200	2	Present	79,610	12
10	24	Male	Squatting 200	7	Present	688	9

CK, creatine kinase.

Unless otherwise specified, data are numbers of patients.

^aThe institution was only able to provide the upper limit of detection for creatine kinase.

Table 2. MRI data of patients with rhabdomyolysis

Patient	Distribution and signal intensity grade on fluid-sensitive MRI sequence											Gd-enhanced T1FS
	Anterior group				Posterior Group			Medial group				
	VL	VI	VM	RF	BF	ST	SM	SA	GC	AL	AM	
1	2	2	2	0	0	0	0	0	0	1	1	O
2	2	2	2	0	0	0	0	0	0	1	1	O
3	2	2	2	1	1	0	0	0	0	0	0	X
4	2	2	2	0	0	0	0	0	0	0	0	X
5	1	2	1	0	0	0	0	0	0	0	0	X
6	1	1	1	0	0	0	0	0	0	0	0	O
7	1	1	1	0	0	0	0	0	0	0	0	O
8	1	1	1	0	0	0	0	0	0	0	0	X
9	1	1	1	0	0	0	0	0	0	0	0	O
10	2	2	2	1	1	0	0	0	0	0	0	O
k ¹	0.8	0.9	0.8	1	1	1	1	1	1	1	1	–
k ²	0.9	1	1	1	1	1	1	1	1	1	1	–

AL, adductor longus; AM, adductor magnus; BF, biceps femoris; GC, gracilis; RF, rectus femoris; SA, sartorius; SM, semimembranosus; ST, semitendinosus; T1FS, fat-suppressed T₁ weighted; VI, vastus intermedius; VL, vastus lateralis; VM, vastus medialis.

Figures indicate grade of muscle involvement.

O Data is performed enhancement study.

X Data is not performed enhancement study.

k¹ is interobserver reliability.

k² is intraobserver reliability.

result of physical and non-physical factors such as extreme muscle strain, medication, crush injury or metabolic disorder,⁹ and the mainstay of treatment is to preserve kidney function. To this end, fluid, medication and, in some cases, dialysis may be required to augment and restore kidney function.^{7–9}

The presence of intramuscular oedema on MRI includes an extremely variable and broad differential diagnosis including trauma, inflammatory myopathies, infective myositis, compartment syndrome, vascular caused muscle infarction and rhabdomyolysis. MRI is not considered to have a critical role in the diagnosis of rhabdomyolysis due to the non-specific and overlapping image findings with other muscular injuries and myopathy.^{16–22} Likewise, rhabdomyolysis is usually diagnosed on the basis of typical clinical symptoms, history and a laboratory finding of elevated serum CK levels.^{1,9} Especially compartment syndrome can be characterized with similar clinical and radiological finding, such as pain, swelling, necrosis and muscular oedema. But rhabdomyolysis does not exhibit clinical sign such as pulseless, pallor, paraesthesia and paralysis. Markedly elevated serum CK level can be helpful in differentiating rhabdomyolysis from compartment syndrome. But rhabdomyolysis may also be complicated with compartment syndrome, therefore we performed serial follow-up physical examination and laboratory study to rule out compartment syndrome.

Generally, MRI findings of rhabdomyolysis consist of a high signal intensity in fluid-sensitive sequences such as T₂ weighted and fat-suppressed T₂ weighted images in affected muscles, which

reflect the increased interstitial water content of oedematous or necrotic muscles in the acute phase.^{10–12} Homogeneous signal changes and enhancement in involved muscles suggest reversible rhabdomyolysis without myonecrosis, whereas inhomogeneous signal changes and enhancement, such as “stipple sign” are indicative of areas of myonecrosis and irreversible changes.²⁰

In the present study, all cases of squatting exercise-induced rhabdomyolysis in the thigh showed a characteristic MR signal intensity pattern when compared with rhabdomyolysis induced by other potential causes as well as other intramuscular oedema disease. Specifically, we noted relative preservation of the rectus femoris muscles in all of the evaluated patients and considered the possibility that sparing of the rectus femoris could be used to differentiate squatting exercise-induced rhabdomyolysis from other aetiologies of rhabdomyolysis.

A plausible explanation and mechanism for the MRI finding of a spared rectus femoris in exercise-induced rhabdomyolysis is as follows. The quadriceps femoris, located in the anterior portion of the thigh, is the largest muscle group in the thigh and consists of four separate muscles named the rectus femoris, vastus medialis, intermedius and lateralis. Although the muscles of the quadriceps femoris share a common conjoined tendon that eventually inserts into the tibial tuberosity *via* the patella, they have different sites of origin. Specifically, the vastus medialis, intermedius and lateralis comprise three-quarters of the quadriceps, and while they appear to be only one muscle, they have different points of attachment on the medial, front and lateral

Figure 1. A 15-year-old female with bilateral thigh pain and dark urine 3 days after an episode of squatting exercise performed over 200 times. (a) Axial T_1 weighted image showing homogeneously intermediate to low signal intensity involving the right quadriceps femoris muscles. (b) Axial T_2 weighted image showing diffusely increased signal intensities involving the vastus lateralis, medius and intermedius muscles sparing of the rectus femoris. (c) Axial fat-suppressed T_2 weighted image demonstrating diffusely increased signal intensities involving the quadriceps femoris (grade 1) except the rectus femoris. (d) Axial fat-suppressed T_2 weighted image showing spared rectus femoris and symmetry with the right thigh. RF, rectus femoris; VI, vastus intermedius; VL, vastus lateralis; VM, vastus medialis.

sides of the femur, respectively. Conversely, the point of origin of the rectus femoris is the anterior inferior iliac spine of the ilium not the femur.²³ These anatomically different sites of origin contribute to different functions in the anterior thigh muscles.

All of the cases included in our study were attributed to excessive squatting action, which consists of repetitive rising and sitting motions. Such repeated squatting action requires knee extension and flexion, although knee flexion is in the same direction as gravity, knee extension requires a force in the opposite direction to gravity. Muscles undergo considerable stress when working against the direction of gravity, and it is this action that provides the main strain on the knee extensor muscles. Although all four quadriceps powerfully combine to work as the primarily extensor of the knee joint, the rectus femoris has additional functions and responsibilities owing to its attachment to the anterior inferior iliac spine of the ilium, namely, to assist as a hip flexor. As a result, the rectus femoris could be relatively less stressed from repeated squat position exercise than other vastus muscles. An additional implication of the results of this study, we hypothesize that the main function of rectus femoris is as a hip flexor rather than a knee extensor.

Among the affected vastus muscles, the vastus intermedius was the most affected muscle compared with vastus medialis and

Figure 2. A 20-year-old female with bilateral thigh pain and dark urine 2 days after an episode of squatting exercise performed over 200 times. (a) Axial T_1 weighted image showing homogeneously intermediate to low signal intensities involving left quadriceps femoris muscles. (b) Axial T_2 weighted image showing diffusely increased signal intensities involving the vastus lateralis, medius and intermedius muscles and mildly increased signal intensity at the rectus femoris muscle (grade 1). There is subfascial fluid collection and adjacent subcutaneous oedema. (c) Axial fat-suppressed T_2 weighted image demonstrating diffuse involvement of the vastus lateralis, medialis and intermedius muscles (grade 2) and mild involvement of the rectus femoris muscle (grade 1).

lateralis muscles. Within the affected vastus muscles, the anterior portion was the most affected compared with the other vastus muscles, meaning that the primary function of the vastus intermedius is to extend the knee compared with other vastus muscles. Considering its anatomical position at the anterior aspect of the knee, which is the most stressed area in squatting action, one can deduce that the vastus intermedius muscle could be more actively involved in dynamic knee extension compared with other vastus muscles.

In 2010, Huang et al²⁴ reported that rectus femoris was also relatively spared in diabetic myopathy of the thigh muscles because the smaller size muscle tends to be less affected and has a better collateral vascular supply. In the present study, the affected muscle such as the vastus muscle from squatting-induced rhabdomyolysis shows a pattern of even distribution or diffuse involvement of elevated signal compared with diabetic myopathy, although the rectus femoris is relatively spared.

Our study has several limitations. First, this was not a prospective study, which could have affected our results in the extent of muscle involvement in rhabdomyolysis. Specifically, the different time intervals from injury onset to MRI reflect possible different stages of rhabdomyolysis on analyzed MR images,

Figure 3. A 16-year-old male with bilateral thigh pain and dark urine after an episode of squatting exercise performed over 150 times. (a) Axial T_1 weighted image showing homogeneously intermediate to low signal intensities involving the right quadriceps femoris muscles. (b) Axial T_2 weighted image showing diffusely increased signal intensities involving the quadriceps femoris except the rectus femoris, with mildly increased signal intensity at the adductor muscle (arrow). (c) Axial fat-suppressed T_2 weighted image demonstrating diffuse involvement of the quadriceps femoris (grade 1) with a spared rectus femoris and mild involvement of the adductor muscle (grade 1, arrow).

resulting in imprecise categorization of the degree of muscle involvement based on signal intensities. Secondly, the study population was quite small, and only 10 subjects underwent MRI of rhabdomyolysis. Another limitation was the absence of a comparison group for other actions. Specifically, all of the patients were injured as a result of the squatting action such as repeated rising and sitting down, and thus there was limited comparison with other physical actions such as running, jumping or cycling. In addition, only 6 patients (6/10) underwent Gd-enhancement study because contrast media can be a burden on the kidneys and harmful to renal function.

Figure 4. A 15-year-old female with bilateral thigh pain and dark urine after performing squatting exercise over 170 times. (a–c) Images taken 4 days after exercise, and (d) image taken on follow-up 7 weeks later. (a) Axial T_1 weighted image showing homogeneously intermediate to low signal intensities involving the right quadriceps femoris muscles. (b) Axial T_2 weighted image showing diffusely increased signal intensities involving the quadriceps femoris (grade 1) except the rectus femoris. (c) Axial Gd-enhanced T_1 weighted image with fat suppression demonstrating diffusely homogeneous enhancement of the anterior thigh muscle with sparing of the rectus femoris and without evidence of myonecrosis. (d) Follow-up images showing the improved state of anterior thigh muscle swelling and return to normal signal intensity in Gd-enhanced T_1 weighted images.

CONCLUSIONS

This study showed that intact rectus femoris muscle in squatting exercise-induced rhabdomyolysis may be a specific MRI feature not found in rhabdomyolysis induced by other aetiologies or other intramuscular oedema disease. This MR finding is also thought to reflect the functional anatomy of the thigh muscles during repetitive physical movement.

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