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Acute myonecrosis at MRI: Etiologies in an oncologic cohort, and assessment of interobserver variability

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Abstract

Objective—To determine etiologies of myonecrosis in oncology patients and to assess interobserver variability in interpreting its MRI features.

Materials and Methods—Pathology records in our tertiary cancer hospital were searched for proven myonecrosis, and MRIs of affected regions in those patients were identified. MRI reports that suggested myonecrosis also were identified. Each MRI was reviewed independently by two of six readers to assess anatomic site, size, and signal intensities of muscle changes, and presence of the previously reported stipple sign (enhancing foci within a region defined by rim enhancement). The stipple sign was assessed again, weeks after a training session. Cohen kappa and percent agreement were calculated. Medical records were reviewed for contemporaneous causes of myonecrosis.

Results—MRI reports in 73 patients suggested the diagnosis of myonecrosis; pathologic proof was available in another two. Myonecrosis was frequently associated with radiotherapy (n=34 (45%) patients)); less frequent causes included intraoperative immobilization, trauma, therapeutic embolization, ablation therapy, exercise, and diabetes. Myonecrosis usually involved lower extremity, pelvis, and upper extremity; mean size was 13.0 cm. Stipple sign was observed in 55–95% of patients at first assessment (k=0.09–0.42; 60–80% agreement) and 55–100% at second (k=0.0–0.58; 72–90% agreement). Enhancement surrounded myonecrosis in 55–100% patients (k=0.03–0.32; 58–70% agreement).

Conclusion—Myonecrosis in oncology patients usually occurred after radiotherapy, and less commonly after intraoperative immobilization, trauma, therapeutic embolization, ablation therapy, exercise, or diabetes. Although interobserver variability for MRI features of myonecrosis exists (even after focused training), a combination of findings facilitates diagnosis and conservative management.

Keywords

myonecrosis; muscle necrosis; MRI; oncology; stipple sign; rhabdomyolysis

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Introduction

Acute muscle necrosis (myonecrosis) has commonly been described in the context of poor glycemic control in diabetic patients [1]. Diabetic myonecrosis manifests on MRI as a poorly defined, mass-like region of hyperintense signal on T2-weighted images and isointense to hypointense signal on T1-weighted images; associated perifascial, perimuscular, or subcutaneous edema may also be seen, usually in a lower extremity [1–3]. Thought to result from arterial damage, myonecrosis can occur due to various other vascular causes such as severe ischemia, sickle cell crisis, compartment syndrome, and crush injury [4].

Evaluation of acute myonecrosis with imaging has received relatively little attention in the radiology literature. One MRI finding, the stipple sign, has been reported to allow differentiation between acute necrosis and acute ischemia of muscle [5, 6]. The stipple sign refers to dot-like, streaky, or curvilinear enhancing foci within a region of muscle separated from normal muscle by an enhancing rim [5, 6] (Fig. 1b). Other findings, such as abnormal signal intensity within muscles on nonenhanced images, are nonspecific, occurring in a wide range of inflammatory, infectious, neoplastic, and vascular pathologies, including acute ischemia of muscle. Because of these overlapping findings, inappropriate tissue sampling or treatment might be undertaken if the MRI findings of myonecrosis are not recognized.

In our practice in a tertiary cancer center, we have noted acute myonecrosis at MRI occurring in patients in several clinical scenarios. The purpose of this study was to determine various etiologies of acute myonecrosis in oncology patients and to assess interobserver variability in scoring its MRI features.

Materials and Methods

The institutional review board at our tertiary referral cancer hospital waived the requirement for informed consent for this retrospective study, which was HIPAA compliant.

Study Population and MRI Examinations

Review of computerized pathology records identified all patients with pathologically proven myonecrosis diagnosed at our institution between January 2000 and September 2014. Also, all MRI radiology reports containing the keyword search terms “myonecrosis,” “muscle necrosis,” “necrotic muscle,” “dead muscle,” or “rhabdomyolysis” at our institution during the same time period were identified electronically.

Patients were eligible for inclusion in the study population if they had a proven malignancy and either (a) biopsy-proven myonecrosis and an MRI of the affected region or (b) the report of a dedicated MRI at least suggested the diagnosis of acute myonecrosis. The included levels of diagnostic certainty for the diagnosis in the radiology reports were based on our defined departmental lexicon for reporting certainty, which is nearly uniformly used by all our radiologists since its introduction in 2009: “possible,” “probable,” or “consistent with” (representing ~50%, ~75%, or >90% certainty, respectively, as noted by the reporting

radiologist). Reports stating that myonecrosis was "less likely" or "unlikely" were not included (representing ~25% and <10% certainty, respectively).

Two (8%) of 25 patients with myonecrosis noted in the pathology report had undergone MR imaging of the affected region at our institution. Seventy-three other patients had MRI reports that suggested the presence of acute myonecrosis with at least a 50% confidence level. Forty patients were male and 35 female (mean age, 52 years; range, 16–80 years). Primary tumors, in descending order of frequency, included bone and soft tissue (n=27), genitourinary (n=17), hematologic (n=9), gastrointestinal (n=8), breast (n=7), lung (n=5), hepatobiliary (n=5), and head and neck (n=4) cancers, and neuroblastoma (n=1). Eight (11%) of the 75 patients had more than one type of tumor. Eighty (95%) of the 84 total tumors were malignant.

Sixty-one MRI studies were performed at 1.5T and 14 at 3T (General Electric). T1-weighted sequences were performed in all patients. Fat-suppressed T2-weighted fast spin-echo sequences were performed in 65 studies, and short-tau inversion recovery sequences were available in 13. Seventy-four patients underwent fat-suppressed T1-weighted imaging after manual intravenous injection of gadolinium contrast material (0.1 mmol/kg); in one patient undergoing MRI of the neck, fat suppression was not used.

Image Review

MR images from each patient were independently reviewed by one of four teams. Each team consisted of one of two faculty musculoskeletal radiologists (with 10 and 16 years of experience, respectively), and one of four oncologic imaging fellows. The fellow-faculty pairing was done to balance the level of reader experience on each team. Faculty radiologist 1 served on two teams: with fellow 1 to assess cases 1–20 and with fellow 2 to assess cases 21–38. Faculty radiologist 2 served on two other teams: with fellow 3 to assess cases 39–56 and with fellow 4 to assess cases 57–75.

The anatomic region affected and the largest dimension of muscle involvement (measured in any plane) on fluid-sensitive or gadolinium-enhanced sequences were recorded. Signal intensity characteristics of the region of muscle abnormality were graded as less than, equal to, or greater than muscle on T1-weighted images, and less than muscle, equal to muscle, greater than muscle but less than fluid, or equal to fluid on fluid-sensitive images. The extent of enhancement within the entire region of myonecrosis was assessed visually (0%, >0–33%, >33–66%, >66–100% of region), as was its intensity (much less than, somewhat less than, or similar to signal of nearby vessels). The presence of fascial or intramuscular fluid collections, and subcutaneous or intramuscular hyperintense signal on fluid-sensitive sequences were recorded. Presence of the stipple sign was assessed once in the post-contrast images, and then again at least six weeks later by the same readers after a reader training session; cases used in the training session were not from the study population.

Serial MRI scans, when available, were reviewed to assess for changes in the region of myonecrosis. Follow-up MRI scans were not used to confirm or refute the diagnosis of myonecrosis.

Medical Record Review

The electronic medical record for each patient was reviewed for patient age, gender, and tumor type. Potential contemporaneous precipitating factors for myonecrosis were recorded. Morbidity and mortality due to myonecrosis were assessed.

Statistical Analysis

Cohen kappa statistic and percent agreement were calculated as measures of interobserver agreement. Kappa values range from +1 (perfect agreement), through 0 (no agreement), to -1 (perfect disagreement. Kappa value < 0 is considered less than chance agreement; 0.01–0.20, slight agreement; 0.21–0.40, fair agreement; 0.41–0.60, moderate agreement; 0.61–0.80, substantial agreement; and 0.81–0.99, almost perfect agreement [7]. If a reader scores every case as positive (or every case as negative) for some feature, the kappa statistic cannot be calculated for that feature.

Results

Imaging Findings and Interobserver Variability

Acute myonecrosis occurred most commonly in the lower extremity (28 (37%) of 75 patients) (Figs. 1 and 2), pelvis (28 (37%)), and upper extremity (13 (17%)); less common locations included chest (3 (4%)), abdomen (2 (3%)), and head & neck (1 (1%)). Sixty (80%) patients had a single site of myonecrosis within one anatomic region; fifteen (20%) had multiple sites (Fig. 3); and none had myonecrosis demonstrated in more than one region. The mean size of signal abnormality associated with myonecrosis was 13.0 cm (range, 1.4–35.6 cm).

MRI findings as categorized by each reader are summarized in Table, along with measures of interobserver variability. Myonecrosis was interpreted as isointense to muscle on T1-weighted sequences in the majority of cases. On fluid-sensitive sequences, myonecrosis was most frequently hyperintense to muscle; in no case were findings classified as isointense to muscle. Rarely, myonecrosis was classified as hyperintense to muscle on T1-weighted sequences, by only one reader in each group. Foci of enhancement were present within the region of myonecrosis in all cases (Fig. 4). Enhancement within the region of myonecrosis was less than that of normal muscle; the extent and intensity of enhancement around the region of myonecrosis were variable. Subfascial fluid collections were uncommon.

Interobserver percent agreement for signal intensity on T1-weighted and on fluid-sensitive sequences was high. Agreement for the stipple sign ranged from slight to moderate according to Cohen kappa values, with a high percent agreement (Table); focused training resulted in only a small increase in interobserver agreement. At least one of two study radiologists on each team recorded the stipple sign as present in 68 (91%) of 75 patients in the study. In the 7 cases in which neither study radiologist recorded the stipple sign as present, a third, experienced musculoskeletal radiologist then reviewed the images. Gadolinium-enhanced images were available in 6 of those 7 cases; in 4 of the 6, the third radiologist scored the stipple sign as present. Intense enhancement was present around a nonenhancing region of muscle in the two other cases with gadolinium-enhanced images,

without internal enhancing foci; both patients had clinical courses consistent with myonecrosis rather than abscess.

Follow-up MR imaging examinations were available in 32 patients (43%). Muscle changes decreased in size in 22 (69%) patients, fatty atrophy developed within involved muscles in 4 (13%), and non-fatty atrophy (i.e., a decrease in muscle size, without associated appearance of streaks of fat within that muscle) developed in 6 (19%); no patient was scored as having more than one of these outcomes. Stipple sign was not present at follow-up imaging. No patient developed MRI-demonstrable fibrosis in the region of prior myonecrosis.

Clinical Findings

Contemporaneous precipitating factors for myonecrosis were identified in 49 (65%) patients. External-beam radiotherapy to the region imaged (n=34 (45%) patients) was the most common such factor (Figs. 2, 3); mean dose was 34 Gy (range, 15–60 Gy). Six of these patients received additional boost treatments (mean dose, 15 Gy; range, 3–20 Gy). Mean duration of initial therapy was 15 days (range, 1–53 days); boost therapy extended treatment in six patients for a mean of 6 days (range, 2–15 days). The number of fractions delivered to the 34 patients varied: less than 5 fractions in 12 patients, 5–10 fractions in 11, 11–20 fractions in 1, and 21–30 fractions in 10. Boost doses were administered in less than 10 fractions in all six patients receiving boost therapy. Findings of myonecrosis on MRIs obtained after radiation therapy were considered associated with the therapy, given the known long lag period for radiation effects on vessels to occur.

Other precipitating factors included prolonged intraoperative immobilization (n=5 patients), local trauma (n=5), focal ablation or therapeutic embolization (n=3), intense exercise (n=1), and poorly controlled diabetes with diabetic neuropathy (n=1). The MRIs in the patients with the precipitants of immobilization, trauma, ablation/embolization, or exercise were obtained within days or weeks of the precipitating event.

Prolonged intraoperative immobilization (wherein the patient was unable to change position for several hours when anesthetized, unlike the usual turning that occurs during normal sleep) occurred in a patient who had been placed in the right lateral decubitus position for seven hours during a left posterolateral thoracotomy. The patient subsequently developed severe right lateral thigh pain, requiring narcotic analgesia; MRI of the thigh showed myonecrosis in the symptomatic region. A similar case involved a right posterolateral thoracotomy that lasted six hours, with subsequent development of myonecrosis in the anterior compartment of left thigh (Fig. 1). Two patients developed right gluteal myonecrosis after a seven-hour left radical nephrectomy and a six-hour left partial nephrectomy, respectively. Another patient developed myonecrosis of the right gluteus maximus muscle after an eight-hour surgical procedure to remove a sarcoma from the right groin.

Three patients with traumatic myonecrosis had chronic pressure on the affected region due to overall restricted mobility; each patient became acutely symptomatic, and MR imaging of the painful region was obtained. The MRI findings of acute myonecrosis in these cases were identical to those in the others, and are consistent with acute myonecrosis occurring in a region predisposed to myonecrosis due to chronic ischemia." In two other patients,

myonecrosis resulted from iatrogenic focal trauma: influenza vaccination injection in a patient with leukemia, and surgical trauma with vascular compromise from resection of a tumor of the hip.

One patient underwent radiofrequency ablation of a metastasis in the left inferior pubic ramus and subsequently developed adjacent myonecrosis with reactive hyperemia. In two patients, therapeutic embolization procedures were performed. The posterior division of the right internal iliac artery was embolized in a patient with sarcoma of the right iliac bone; myonecrosis subsequently developed in the ipsilateral gluteus maximus muscle. Branches of the profunda femoris artery were embolized to control an enlarging hematoma in the right thigh in a patient who was receiving anticoagulation therapy; myonecrosis subsequently occurred in the right rectus femoris and vastus medialis muscles.

Exercise-induced myonecrosis occurred in both inferior rectus abdominis muscles after the patient started a new exercise regimen involving multiple sit-ups (which involved those specific muscles) (Fig. 4); the patient had not received radiotherapy to this region.

Myonecrosis was considered idiopathic in 26 (35%) patients. No patient developed renal failure or other clinical signs of rhabdomyolysis.

Treatment for myonecrosis was required in three patients. Two underwent percutaneous drainage of associated infection, and one underwent decompression fasciotomy. No death was attributed to myonecrosis.

Discussion

Acute myonecrosis, representing infarction of skeletal muscle, presents clinically with pain and swelling of the affected region. Although myonecrosis is infrequently encountered in clinical practice, it is important to distinguish from other conditions because myonecrosis usually requires only conservative management [8]; inappropriate intervention can be avoided if myonecrosis is recognized as such. Poorly controlled diabetes is the most well-known cause of myonecrosis, typically involving muscle compartments of anterior thigh or posterior calf [2, 8–10]. MRI appearances reported in diabetic myonecrosis include diffuse muscle enlargement, partial loss of normal fatty intermuscular septa on T1-weighted images, fascial fluid collections, and subcutaneous edema [9]. Our study describes a range of other conditions associated with acute myonecrosis that were encountered in an oncology population.

Rhabdomyolysis, a related clinical syndrome, is characterized by extensive skeletal muscle injury, with associated release of toxins into the systemic circulation and frequently complicated by acute kidney injury [5]. Extreme exercise, crush injuries, and medications (such as statins) are among the recognized causes of rhabdomyolysis [11, 12]. Diagnosis of rhabdomyolysis is usually established by the presence of elevated serum creatine kinase levels in the appropriate clinical context [13, 14]. Although not required for evaluation, MRI findings may support the diagnosis and assist with delineation of the extent and severity of muscle injury [6].

Two distinct MR imaging patterns in rhabdomyolysis have been described based on muscle signal intensity and contrast enhancement characteristics [5, 6]. Type 1 changes, which represent potentially reversible muscle ischemia, manifest as homogeneous signal intensity that is isointense or hyperintense to muscle on T1-weighted images and hyperintense on T2-weighted and short-tau inversion recovery images, with enhancement after administration of gadolinium-based contrast material [6]. Type 2 changes, due to irreversible muscle necrosis, demonstrate predominantly heterogeneous signal intensity and rim enhancement, as well as the stipple sign [5, 6]. Due to its high soft tissue contrast, MRI is considered the best noninvasive method to identify necrotic muscle [4, 8, 15]. The diagnosis of acute myonecrosis in our study, as well as in our daily clinical practice, was based predominantly on the stipple sign described in type 2 rhabdomyolysis [5, 6]: enhancing foci within a region of muscle surrounded by rim enhancement. That region otherwise shows less enhancement than normal muscle. The underlying biologic assumption for the stipple sign is that dead muscle fibers do not enhance; the enhancing foci represent residual viable muscle fibers or inflammatory vessels [6]. The kappa values related to this and other signs of myonecrosis at MRI ranged from almost no agreement to substantial agreement, and the values for stipple sign increased only slightly after a focused training session. However, the diagnosis of myonecrosis was suggested by the initial radiologist reporting each of the 75 study MRI examinations, and also by at least one of the two study radiologists in 91% of those cases. This latter statistic served as a surrogate for consensus readings, which can be adversely influenced by the strength of the readers' personalities and the relative power structure of their relationship. Also, low kappa values are expected to occur when a finding is of either low or high prevalence [16]. The stipple sign and some other imaging features were very common findings in our study, resulting in low kappa values; however, the percents agreement were high. We believe that the results of our study remain useful and valid despite some unavoidable uncertainty related to lack of pathologic proof - a standard not likely to be obtained in any study of this entity.

Myonecrosis was interpreted as isointense to normal muscle on T1-weighted sequences in the majority of cases in our study, indicating that it would be difficult to recognize myonecrosis on this sequence alone. Rarely, myonecrosis was categorized as hyperintense to muscle on such sequences, which could be related to the presence of methemoglobin from hemorrhage, by only one of the readers in each group; intramuscular hemorrhage thus seems to be unusual or not extensive in acute myonecrosis.

Conversely, none of our cases were categorized by the readers as isointense to muscle on fluid-sensitive sequences. On these sequences, myonecrosis was most frequently hyperintense to normal muscle, which probably reflects the presence of edema. Such signal hyperintensity obviously is not specific for myonecrosis, as it also may occur, for example, in ischemic muscle; infectious or inflammatory myositis [4]; or after trauma.

Soft tissue and bone sarcomas were the most common tumor type in our patient study group, likely because subspecialized musculoskeletal radiologists interpret the follow-up MRIs of musculoskeletal sarcoma patients at our institution. This subgroup of radiologists may be more likely to recognize myonecrosis than would other radiologists. Such a bias would not likely affect the validity of our results, however.

Myonecrosis occurred after external-beam radiotherapy to the region in nearly half of our study patients (Figs. 2, 3). Radiation-induced myonecrosis has been described only rarely, as skeletal muscles are typically considered radioresistant at therapeutic doses [17–19]. A postulated pathogenesis for such myonecrosis, based on limited data, is ischemia resulting from vascular collagen proliferation that occurs within ten months of exposure [17]. Recent technological advances in radiation oncology, most notably the ability to distribute the radiation dose more precisely in three dimensions to conform to the tumor morphology, allow increasingly high doses to be delivered to target tissues in fewer treatment fractions while minimizing damage to adjacent normal tissue [20]. Of 34 patients in our study with radiotherapy-associated myonecrosis, 23 received their radiotherapy in ten or fewer fractions; all six patients who underwent additional boost treatment also received that therapy in ten or fewer fractions. Increased use of MRI after radiotherapy may account for the increased demonstration and recognition of this therapy-associated effect.

Myonecrosis due to immobilization during prolonged surgery usually has been reported in the context of neurosurgical spinal surgery, and in bariatric and urological procedures [21–23]. In our study, five cases of myonecrosis occurred after prolonged immobilization during thoracic, urologic and orthopedic operations (Fig. 1). This risk of such surgical morbidity can be minimized by ensuring appropriate intraoperative padding of the patient, minimizing operative times, and obtaining serial intraoperative serum creatine phosphokinase measurements in patients at risk; aggressive hydration can be administered if serum levels rise above a defined threshold [22].

Increasingly, minimally invasive therapies such as arterial embolization and focal ablation are employed in the treatment of various primary or metastatic neoplasms, including hepatic, musculoskeletal, renal and pulmonary tumors. For example, preoperative embolization may be performed to control intraoperative bleeding from hypervascular lesions such as metastases from renal or thyroid cancer. Focal ablative therapies, including cryoablation, radiofrequency ablation, and microwave ablation, lead to cellular necrosis and architectural tissue destruction by thermal effects on tumor cells [24–26]. Although often associated with lower morbidity compared to extensive open surgery, these therapies can cause complications related to thermal damage of surrounding tissues, including skin necrosis [27, 28]. Acute myonecrosis can also occur, and has been reported to affect the diaphragm after radiofrequency ablation of hepatocellular carcinoma at the dome [29]. Embolization has also been implicated in cases of acute myonecrosis, principally due to non-target embolization of arteries supplying skeletal muscle [30], or as a complication of embolization to control hemorrhage in severe pelvic fractures [31, 32]. Patients who have had prior radiotherapy are at increased risk of myonecrosis in this setting [30].

Trauma resulting from intense exercise (Fig. 4) or repeated intramuscular injections are relatively rarer causes of myonecrosis [33]. Necrotizing soft tissue infections, such as those associated with *Clostridia* species, can also lead to myonecrosis [34, 35]; no such case was found in our study.

Follow-up MR imaging in our study revealed a decrease in size of myonecrosis in 69% of cases. In 31%, atrophy occurred in regions of acute myonecrosis. Others have described

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follow-up MRI findings in regions of necrotic muscle, including interval decreases in signal intensity on both T1- and T2-weighted images, without contrast enhancement [5] — findings attributed to the development of intramuscular fibrosis and/or hemosiderin deposition from old hemorrhage. In our study, only three patients required treatment (drainage of associated infection, or decompression fasciotomy) for myonecrosis, and no deaths were directly attributed to myonecrosis. The time to diagnosis of myonecrosis in our study largely depended on when the MRI happened to be obtained. The indication for the MRI examinations in our study often was not related to the myonecrosis, such as evaluation for recurrent or metastatic tumor. Note that small regions of myonecrosis are expected to resorb over time, with no residua. Lack of abnormality at follow-up MRI would not indicate that the original MRI was false positive for myonecrosis.

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Another potential late sequela of acute myonecrosis is calcific myonecrosis, a rare condition characterized by latent formation of a dystrophic calcified mass [36]. The hypothesized pathogenesis implicates post-traumatic ischemia and cystic degeneration of muscle. On MRI, the lesion typically manifests as a well-circumscribed mass, located along the course of a muscle group, with central fluid [36]; the necrotic mass does not enhance [37, 38], and dense calcification may manifest as signal void at MRI. Blooming artifact from calcium may be visible on gradient-echo sequences, and subtle, feathery periosteal reaction may be evident on fluid-sensitive images [36]. Calcification was not assessed at CT or radiography in this study, as the clinical scenario and the MRI appearances were those of acute myonecrosis, not a centrally cystic mass.

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The majority of MRI examinations reviewed in this study demonstrated increased signal intensity in the affected muscle(s) on T2-weighted images. The differential diagnosis for such a finding is broad, and includes trauma, infectious myositis, autoimmune polymyositis, dermatomyositis, subacute denervation, compartment syndrome, early myositis ossificans, and metastasis [4]. Gadolinium-based contrast material, which was used in every case in our study, facilitated differentiation of myonecrosis from these other potential etiologies by demonstrating non-enhancing, dead muscle tissue (i.e., myonecrosis). An intramuscular abscess could show peripheral enhancement at MRI, but would show fluid signal centrally - a finding not present in myonecrosis. Also, an abscess would not show internal foci of enhancement as occurs in myonecrosis, and the clinical findings differ with abscess. Similarly, an intramuscular metastasis with extensive central necrosis might show mostly peripheral enhancement, but would appear cystic in regions of necrosis but not show internal foci of enhancement.

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The retrospective design of this study resulted in the unavoidable associated biases in patient selection, and nonuniform imaging technique. The key words chosen to find reports that at least suggested myonecrosis may have resulted in additional cases being missed if the reporting radiologist had used other words to describe the condition. Some patients with MRIs reported as "possible" or "probable" myonecrosis may in fact have had a condition other than myonecrosis. However, to our knowledge, the constellation of MRI findings used to suggest the diagnosis of myonecrosis has not been reported in other conditions. Due to lack of pathologic proof, we chose not to include cases that the original interpreting radiologist considered "less likely" or "unlikely." If the radiologist had low confidence in the

diagnosis, the probability of including cases of conditions other than myonecrosis would be high, and thus dilute the results of our study. Of note, each of the 73 cases without pathologic proof was identified as suggestive of myonecrosis by a faculty radiologist; that was a requirement for inclusion in the study. At least one of two study radiologists on each team recorded the stipple sign as present in 91% of all patients in the study." Thus, nearly all cases were deemed at least suggestive of myonecrosis by at least two radiologists. We do not believe that variations in MRI technique would have substantially altered the results.

Study readers were not blinded to the fact that the MRI studies had been reported as showing suspected myonecrosis; the purpose of the study was to assess interobserver variability, not the sensitivity or specificity of the various imaging findings. Four of the readers were oncologic imaging fellows without subspecialty training in general musculoskeletal radiology; although such lack of training might be regarded as a limitation, it also makes our findings more relevant and applicable to the large number of non-musculoskeletal radiologists who read MRIs that usually do happen to include muscle. Only two pathologically-proven cases of myonecrosis with dedicated MRI were available, precluding additional validation of the stipple sign as an imaging marker of muscle necrosis. However, the stipple sign has been previously reported with histopathologic correlation [5, 6], and no other plausible cause for it is known to the authors. Indeed, it is reassuring that only two patients in our study with MRI findings of myonecrosis underwent biopsy of the muscle, as the referring physicians accepted this imaging diagnosis as concordant with the clinical scenario in all other cases. Multivariate analysis of the various imaging features was not performed in our study. Although several clinical conditions known to be associated with myonecrosis were identified in our oncologic cohort, this study does not establish causation; however, the temporal associations with myonecrosis and the contemporaneous clinical scenarios were compelling. The number of cases associated with radiotherapy was too small to allow subgroup analysis based on radiotherapy dose rates or techniques. The possibility of potentiating effects of chemotherapy was not assessed in this study, given the numerous types and various temporal courses of such therapies received by the patients.

Summary

Acute myonecrosis in oncology patients most frequently occurred after radiotherapy, and less commonly after intraoperative or other immobilization; focal trauma; therapeutic embolization or ablation; intense exercise; or in patients with diabetes. Although interobserver variability for individual MRI features of acute myonecrosis exists (even after focused training), recognition of a combination of findings — enhancing foci within a region of otherwise nonenhancing muscle, surrounded by an enhancing rim — should facilitate making this diagnosis. Our findings emphasize the importance of awareness of the clinical context when considering a diagnosis of acute myonecrosis at MRI. Increased knowledge of the etiologies and MRI features of acute myonecrosis may prevent unnecessary tissue sampling and facilitate conservative management.

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A, **B,****Figure 1a**

Figure 1b**Fig. 1.**

16-year-old male with osteosarcoma. Patient underwent a thoracotomy in left lateral decubitus position, resulting in immobilization-induced myonecrosis.

A, Axial fat-suppressed T2-weighted MR image of left thigh demonstrates diffuse intramuscular edema and subfascial fluid in anterior compartment.

B, Axial post-contrast fat-suppressed T1-weighted image shows stipple sign (*arrow*) within a well defined, geographic region of vastus lateralis and intermedius muscles, surrounded by a thin rim of intense enhancement. Note the lack of generalized enhancement throughout large portions of the region of myonecrosis. A restraining strap on the thigh in place throughout the operation presumably compressed the subjacent muscle against the underlying femur, resulting in this band-like region of myonecrosis.

Fig. 2. 67-year-old male with metastatic thymic carcinoma. Patient presented with severe left hip pain, 6 months after radiotherapy to metastasis in left proximal femur. Axial post-contrast fat-suppressed T1-weighted MR image of proximal left thigh shows regions of stipple sign in rectus femoris (*arrow*) and sartorius (*arrowhead*) muscles, with prominent rim enhancement. Note that large portions of the region of myonecrosis show no enhancement. Metastasis is evident in femur.

A,

B,

Fig. 3.

56-year-old male with metastatic granular cell tumor of right upper extremity. Myonecrosis developed after adjuvant radiotherapy and chemotherapy.

A, Axial fat-suppressed T2-weighted MR image demonstrates heterogeneous high signal intensity within deltoid muscle (*arrow*) and medially within coracobrachialis muscle (*arrowhead*).

B, Axial post-contrast fat-suppressed T1-weighted image shows stipple sign (*arrowhead*) throughout both regions noted in **A**, with surrounding hyperenhancement. No enhancement is present within the majority of each region of myonecrosis.

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A, **B,** **Fig. 4.**

56-year-old female with endometrial cancer. Patient developed severe abdominal pain after commencing exercise, due to myonecrosis of rectus abdominis muscles.

A, Axial post-contrast fat-suppressed T1-weighted MR image of lower anterior abdominal wall demonstrates stipple sign (*arrowheads*) surrounded by rim enhancement (*arrows*) within diffusely enlarged rectus abdominis muscles bilaterally. Those muscles do not show generalized enhancement; their signal intensity is less than that of adjacent suppressed fat.

B, Axial fat-suppressed T2-weighted image shows diffusely, mildly increased T2 signal throughout rectus muscles (*arrows*). Note that myonecrosis could not be diagnosed based on **B** alone.

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TABLE

MRI Findings of Myonecrosis, by Reader

Parameter	Cases 1–20		Kappa (p value)	% Agreement	Cases 21–38		Kappa (p value)	% Agreement
	Faculty 1	Fellow 1			Faculty 1	Fellow 2		
T1 signal characteristics *								
Hypointense	0 (0)	8 (40)	N/A ^{\$}	55	0 (0)	0 (0)	N/A ^{\$}	80
Isointense	20 (100)	11 (55)			18 (100)	16 (89)		
Hyperintense	0 (0)	1 (5)			0 (0)	2 (11)		
Fluid-sensitive signal Characteristics *								
Hypointense	0 (0)	2 (10)	N/A ^{\$}	90	0 (0)	3 (17)	N/A ^{\$}	83
Isointense	0 (0)	0 (0)			0 (0)	0 (0)		
Hyperintense but < fluid	20 (100)	18 (90)			18 (100)	15 (83)		
Isointense to fluid	0 (0)	0 (0)			0 (0)	0 (0)		
Extent of enhancement								
0–33%	6 (30)	12 (60)	–0.05 (0.743)	35	2 (11)	4 (22)	0.12 (0.304)	44
33–66%	11 (55)	6 (30)			15 (83)	7 (39)		
66–100%	3 (15)	2 (10)			1 (6)	7 (39)		
Intensity of enhancement ^								
Much less	4 (20)	11 (55)	0.12 (0.416)	50	1 (6)	2 (11)	0.63 (0.000)	89
Moderately less	16 (80)	8 (40)			16 (88)	14 (78)		
Similar	0 (0)	1 (5)			1 (6)	2 (11)		
None	0 (0)	0 (0)			0 (0)	0 (0)		
Stipple sign (1 st reading)	11 (55)	15 (75)	0.38 (0.081)	80	15 (79)	14 (74)	0.42 (0.06)	74
Stipple sign (2 nd reading)	11 (55)	15 (75)	0.58 (0.004)	80	15 (83)	14 (78)	0.38 (0.091)	72
Peripheral enhancement								
Present	11 (55)	16 (80)	0.32 (0.004)	70	10 (55.6)	18 (100)	N/A ^{\$}	58
None	9 (45)	4 (20)			8 (44.4)	0 (0)		

Parameter	Cases 1–20		Kappa (p value)	% Agreement	Cases 21–38		Kappa (p value)	% Agreement
	Faculty 1	Fellow 1			Faculty 1	Fellow 2		
Subcutaneous hyperintensity&	14 (70)	14 (70)	–0.02 (0.891)	80	17 (85)	16 (80)	0.48 (0.028)	83
Intramuscular hyperintensity&	18 (90)	18 (90)	–0.11 (0.619)	80	18 (100)	18 (100)	N/A ^{\$}	100
Subfascial fluid collections	3 (15)	3 (15)	0.61 (0.007)	90	1 (6)	2 (10)	0.64 (0.002)	94

Parameter	Cases 39–56		Kappa (p value)	% Agreement	Cases 57–75		Kappa (p value)	% Agreement
	Faculty 2	Fellow 3			Faculty 2	Fellow 4		
T1 signal characteristics [*]								
Hypointense	2 (11)	1 (6)	0.29 (0.014)	78	1 (5)	3 (16)	0.36 (0.011)	79
Isointense	13 (72)	17 (94)			15 (79)	16 (84)		
Hyperintense	3 (17)	0 (0)			3 (16)	0 (0)		
Fluid-sensitive signal Characteristics [*]								
Hypointense	1 (6)	0 (0)	–0.03 (0.803)	89	0 (0)	0 (0)	N/A ^{\$}	100
Isointense	0 (0)	0 (0)			0 (0)	0 (0)		
Hyperintense but < fluid	17 (94)	17 (94)			19 (100)	19 (100)		
Isointense to fluid	0 (0)	1 (6)			0 (0)	0 (0)		
Extent of enhancement								
0–33%	7 (39)	9 (50)	0.15 (0.301)	39	8 (42)	4 (21)	0.23 (0.118)	47
33–66%	6 (33)	3 (17)			6 (32)	6 (32)		
66–100%	5 (28)	6 (33)			5 (26)	9 (47)		
Intensity of enhancement [^]								
Much less	3 (17)	3 (17)	0.51 (0.001)	78	1 (5)	4 (21)	0.03 (0.829)	58
Moderately less	12 (66)	14 (78)			14 (74)	14 (74)		
Similar	2 (11)	0 (0)			4 (21)	1 (5)		
None	1 (6)	1 (6)			0 (0)	0 (0)		
Stipple sign (1 st reading)	17 (85)	12 (60)	0.09 (0.348)	60	19 (95)	17 (85)	0.1 (0.305)	80

Parameter	Cases 39–56		Kappa (p value)	% Agreement	Cases 57–75		Kappa (p value)	% Agreement
	Faculty 2	Fellow 3			Faculty 2	Fellow 4		
Stipple sign (2 nd reading)	15 (83)	12 (67)	0.0 (1.000)	61	19 (100)	17 (90)	N/A ^{\$}	90
Peripheral enhancement								
Present	16 (89)	10 (56)	0.03 (0.867)	60	15 (79)	11 (58)	0.07 (0.719)	60
None	2 (11)	8 (44)			4 (21)	8 (42)		
Subcutaneous	14 (78)	14 (78)	1.0 (0.000)	100	16 (80)	17 (85)	0.77 (0.000)	95
hyperintensity ^{&}								
Intramuscular	18 (100)	18 (100)	N/A ^{\$}	100	19 (100)	19 (100)	N/A ^{\$}	100
hyperintensity ^{&}								
Subfascial fluid collections	6 (33)	3 (17)	0.0 (1.000)	61	6 (33)	5 (26)	0.36 (0.111)	74

Note—Numbers in parentheses are percentages, unless otherwise indicated

^{*} signal intensity relative to normal muscle

[^] signal intensity relative to vessel enhancement

^{\$} variable(s) are constants, precluding calculation of kappa

[&] evaluated on fluid-sensitive images