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MR Imaging in a case of severe anorexia nervosa: the ‘flip-flop’ effect

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Abstract

We report an MR imaging phenomenon that can lead to misinterpretation. The unique appearance of the soft tissues and bone marrow in a 19-year-old severely malnourished woman with anorexia nervosa raised concerns about technical failure or systemic pathology. Due to extreme fat depletion, the T1-weighted images appeared to be fat-suppressed and the fat-suppressed fluid-sensitive images appeared to be non-fat-suppressed (“flip-flopped”). Failure to recognize the influence of a patient’s overall nutritional status on MR images may cause confusion and misdiagnosis.

Keywords

Marrow; MRI; Anorexia nervosa; Spectroscopy; Adolescent

Introduction

Anorexia nervosa is a prevalent psychiatric disorder associated with distorted body image, amenorrhea and refusal to maintain an appropriate body weight. It is well established that adolescents with anorexia nervosa are at high risk for skeletal abnormalities including low bone density for age and increased fracture risk [1]. The pathophysiological mechanisms

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Conflicts of interest None

underlying these skeletal deficits relate to mechanical, hormonal and cellular alterations. Abnormalities in osteoblast and osteoclast progenitors within the bone marrow contribute to the complex cascade of factors influencing bone health [2]. We report unusual MR imaging findings in a 19-year-old woman with anorexia nervosa who underwent evaluation for lower extremity swelling. The soft tissue and marrow appearances in this patient were so influenced by her severe malnutrition that the findings were initially mistaken for technical failure. Recognition of patient's nutritional status, especially with respect to fat metabolism, is essential to the accurate interpretation of musculoskeletal MR images.

Case report

This 19-year-old woman known to have a variant of anorexia nervosa, orthorexia nervosa, a disorder characterized by excessive preoccupation with avoiding foods perceived to be unhealthful, was admitted with worsening malnutrition. She also complained of bilateral ankle pain and swelling. Ankle radiographs revealed loss of soft - tissue fat planes and osteopenia. Bilateral lower leg MR imaging was requested to assess for occult fracture or infection.

Bilateral lower legs were initially imaged in a Siemens Trio 3-T scanner (Siemens Medical Solutions, Erlangen, Germany). The T1-weighted images (Fig. 1) appeared completely fat-suppressed, although fat suppression had not been selected, with a fairly homogeneous gray appearance to all tissues. The fluid-sensitive sequences, inversion recovery as well as T2 with chemical fat suppression (Fig. 1), showed bright subcutaneous tissues and bright bone marrow. Presuming equipment failure, the supervising radiologist moved the patient to a 1.5-T scanner (Twinspeed; General Electric, Milwaukee, WIS) and repeated the exam. The images at 1.5 T had the same appearance, and T1-weighted images without and with fat suppression were identical (Fig. 2). Examination of the patient and discussion with the referring clinical service led us to suspect severe depletion of soft tissue and marrow fat stores as an explanation for the imaging findings. This impression was confirmed with single-voxel MR spectroscopy that revealed a tiny lipid peak and huge water peak (Fig. 3) corresponding to an MR estimated fat fraction of less than 4% in both the marrow and subcutaneous soft tissues. Fat fractions of more than 85% fat are expected for females of this age [3, 4] (Fig. 3).

Further interrogation of the patient's clinical records revealed weight of 30.1 kg and height of 169.5 cm, equating to a body mass index (BMI)=10.5 kg/m², 49% of her median BMI. BMI <18 kg/m² is generally considered anorexic and the World Health Organization classifies BMI <16 kg/m² as severely underweight. This patient's complete white count showed leukopenia (white blood cell count 3.06 K cells/ L and absolute neutrophil count 1,750 cells/ L) and macrocytic anemia (hemoglobin=10.7 g/dL, hematocrit 30.7% and mean corpuscular volume=98.4 fL).

Following a 30-day hospitalization, the patient was discharged but continued to steadily lose weight. Within 1 month, she was readmitted for refeeding treatment for worsening malnutrition. A 2-month medical admission was planned in hopes that the patient would reach a sufficient body weight to allow transfer to a psychiatric facility for further treatment.

Discussion

Patients with anorexia nervosa have obvious depletion of soft-tissue fat stores. The bone marrow fat content, however, appears to be more variable depending upon the severity of the disease [5]. Marrow histology in moderately malnourished patients demonstrates an increased proportion of adipocytes [6], somewhat counterintuitive given the overall body fat depletion. Recently, MR and MR spectroscopy have been utilized to evaluate marrow fat in these patients. Our group previously reported an increase in distal femoral and proximal tibial marrow fat in 20 adolescents with anorexia nervosa compared with 20 age-matched normal-weighted control subjects [2]. The mean BMI of the subjects with anorexia nervosa was 16.9 kg/m², with a range 14.4–20.5 kg/m². Adolescents with anorexia nervosa exhibited higher T1 signal intensity and less red marrow in the distal femoral and proximal tibial metaphyses. Both qualitative and quantitative (MR relaxometry) findings supported a premature conversion of hematopoietic to fatty marrow in adolescents with anorexia nervosa. The observed increases in marrow fat were in direct contrast to a paucity of body fat. It is thought that the hormonal abnormalities associated with malnutrition, including hypoenestrogenemia and hypoleptinemia, may mediate adipocyte over osteoblast differentiation in the mesenchymal stem cell pool, leading to an imbalance between adipogenesis and osteogenesis, resulting in increased marrow fat [7].

Bone marrow biopsies in patients with extreme starvation, in contrast, reveal decreased adipocytes and an accumulation of extracellular hyaluronic acid, sometimes described as a gelatinous transformation, due to reduced hematopoietic and fatty marrow as well as increased free water [8]. This marrow hyperhydration and reduced fat fraction may be a physiological response to the decreased hematopoietic requirements of the individual with a severely reduced body mass [1]. Our patient was profoundly malnourished, with a BMI less than 50% of median for age. Her severely depleted fat stores, less than 4% within marrow and soft tissues, led to striking, and potentially confusing, MR imaging findings. The T1-weighted images appeared to be fat-suppressed with low signal marrow and soft tissues, while the inversion recovery images could have been misinterpreted as poorly fat-suppressed due to high signal intensity within marrow and subcutaneous soft tissues. This “flip-flop” phenomenon resulted from the predominance of water and near absence of normal fat, as confirmed spectroscopically (Fig. 3). Dixon technique for fat and water differentiation was not performed, as it is not part of our standard extremity imaging protocol, but it would likely have also confirmed the absence of fat and demonstrated the “flip-flop.”

In addition to malnutrition, the differential diagnosis for diffusely absent marrow and subcutaneous fat includes congenital generalized lipodystrophy, or Berardinelli-Siepe syndrome, and diabetic lipodystrophy. These conditions are generally associated with increased muscle and hepatic fat fractions due to insulin resistance. Marrow replacement disorders are easily differentiated from anorexia nervosa by the presence of subcutaneous fat. Lastly, hematopoietic marrow due to severe anemia still contains sufficient fat to be detected by MR. While this patient did not undergo bone marrow biopsy, her extremely low BMI would suggest gelatinous transformation of her marrow. The subcutaneous tissue signal intensity appears artifactually high in water content due to the paucity of fat.

MR signal intensities of tissues should be viewed as relative to their histologic composition. Awareness of the potential MR imaging “flip-flop” appearance in patients with severe malnutrition due to any cause is critical to accurate interpretation and diagnosis. This case also raises speculation as to whether there is a critical weight and percentage of subcutaneous body fat needed, below which generation of marrow fat is precluded. Although speculative, this hypothesis would explain why some case series of these patients have revealed increased marrow fat in moderately ill young women, while gelatinous degeneration has been noted in the most severe cases.

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Fig. 1.

3-T MR images of the lower legs. **a** Coronal T1-W image without fat suppression shows homogenous gray marrow that is somewhat lower in signal intensity than the soft tissues, which are also homogeneously gray, without normal high signal intensity fat. **b** The coronal inversion recovery image demonstrates high signal intensity marrow and subcutaneous tissues indicating relatively increased water and decreased fat content. **c** Similarly, the axial T2-W fat-suppressed images shows high signal intensity marrow and subcutaneous tissues. This is the “flip-flop” with T1-W images falsely appearing fatsuppressed and the fluid-sensitive images mimicking T1-W non-fat-suppressed images due to severe fat depletion

Fig. 2.
1.5-T axial MR images of the lower legs. **a** As seen at 3 T, the T1-W image without fat suppression shows homogenous gray marrow and soft tissues without normal high signal

intensity fat. **b** The fat-suppressed T1-W image is identical to the non-fat-suppressed image due to the complete absence of fat stores in this severely malnourished patient

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Fig. 3. MR spectroscopic “flip-flop.” **a** Single-voxel proton spectroscopy (TR/TE/NEX = 1,500/30/32) in this severely anorexic patient shows that the smallest peak is the lipid methylene protons (*arrow*) while the water resonance around 4.6 ppm dominates the spectrum. **b** Normal 18-year-old adolescent for comparison. In contrast to our patient, the smallest resonance seen normally is water (*arrow*) and the largest peak arises from the lipid methylene protons around 1.3 ppm