Hibernoma
A Case Series with Multimodality Imaging and Pathologic Correlation

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Abstract
Hibernoma is an uncommon, benign tumor of brown fat origin. The distribution of this tumor originally was described as following the location of persistent brown fat within the subcutaneous tissue of the thorax (especially the periscapular and interscapular regions), neck, axilla, shoulder, and retroperitoneum. Recently, hibernoma was described as being most common in the thigh.

Lipomatous lesions are the second most common soft tissue neoplasm. These tumors range from the simple lipoma to the liposarcoma. Other non-lipomatous tumors have regions with the imaging appearance of fat including hemangiomas and myositis ossificans. Hibernoma is interesting as it has imaging characteristics quite different from those we associate with fat. Positron emission tomography (PET) is a nuclear medicine modality that takes advantage of the fact that neoplastic cells, unlike normal cells, preferentially use glucose as a substrate for anaerobic metabolism when patients are imaged during fasting.1 By radioactively labeling a glucose derivative, such as 2-fluoro-2-deoxy-D-glucose (FDG), that accumulates once metabolized inside the neoplastic cells, these hypermetabolic cells may be localized and imaged. The hibernoma is a tumor wherein PET imaging has clinical relevance, since the brown fat contained within it is quite FDG avid.

Case 1
A 48-year-old female presented with a palpable, non-tender, slow growing mass in the right thigh. The patient had noticed the mass 18 months earlier, and it gradually increased in size. On physical examination, a mass was palpable on the lateral aspect of her distal thigh. This was firm, and non-tender to palpation. No overlying warmth or erythema was noted, and no lymphadenopathy was found. The patient had no neurological deficit but reported experiencing a pressure sensation in her lower right leg.

Figure 1 Frontal radiograph with vitamin E markers demarcating palpable mass shows a radiolucent mass within the expected lateral thigh musculature. There is an absence of mineralization and osseous pathology.
Radiographs demonstrated no radiographic evidence of periosteal reaction, osseous scalloping, or cortical breach. A faintly radiolucent ovoid lesion could be perceived. No internal mineralization could be identified (Fig. 1).

Ultrasound revealed a 10.5 x 3.8 x 6.3 cm (craniocaudal by anterior-posterior by transverse, respectively) encapsulated, smoothly-contoured mass within the vastus intermedius muscle. This mass closely abutted the femur. The mass was homogenously hyperechoic relative to the surrounding musculature and subcutaneous fat with echogenic through-transmission. There was intraslesional internal vascularity but no calcification and limited proximal muscular edema.

Figure 2 Transverse sonographic image of the right lateral thigh depicts a well circumscribed mass. Note the hyperechogenicity relative to the subcutaneous fat. Color illustration available at www.nyuhjdbulletin.org.

Figure 3 Longitudinal sonographic image of the right lateral thigh demonstrates intraslesional vascularity with color Doppler evaluation. Color illustration available at www.nyuhjdbulletin.org.

Figure 4 A, T1-weighted axial image right thigh intramuscular mass with slight hypointensity relative to subcutaneous fat, fairly homogenous with a prominent central vessel. B, Sagittal PD FS shows heterogeneity and incomplete fat saturation, minimal surrounding muscular edema, and well-circumscribed margins. C, Axial STIR demonstrates generalized decrease in signal with fat saturation but multiple internal curvilinear areas on the relatively hyperintense background. D, Coronal T1-weighted fat saturated postcontrast image shows minimal diffuse background enhancement, trace capsular enhancement, and subtle vascular enhancement. E, Light microscopy with haematoxylin and eosin staining demonstrates multiple multivacuolated brown fat cells. Note that the nuclei of brown fat cells are central rather than eccentric. Color illustration available at www.nyuhjdbulletin.org.
The MRI confirmed the presence of an intramuscular, lipomatous mass with comparable dimensions (11.8 cm CC x 3.4 cm AP x 5.4 cm TR). This was well-circumscribed. The mass was homogenously hyperintense to musculature but slightly hypointense relative to the subcutaneous fat on T1-weighted sequences (Fig. 4A). There was incomplete suppression of the intralesion signal in comparison to subcutaneous fat on PD FS (Fig. 4B), and this distinction from subcutaneous fat was more strikingly notable on STIR sequences. While the background signal intensity of the lesion became only slightly hyperintense, there were several internal hyperintense, curvilinear structures, which were contiguous with vessels (Fig. 4C). On postcontrast scans, there was subtle diffuse enhancement with avid enhancement of vessels (Fig. 4D).

On gross pathology, the rubbery yellow homogeneous mass while being well circumscribed did not possess a true capsule. There were a few thin fibrous septae. There was no concern for atypia or invasion. On microscopy multivacuolated brown tumor cells were identified between mature univacuolated adipocytes (Fig. 4E).

Case 2
A 32-year-old female with a history of neurofibromatosis presented with right knee pain of uncertain etiology. Initial radiographs and MRI (not shown) of the area did not identify a specific cause; however, a bone scan was suggested to further evaluate nonspecific marrow heterogeneity. A dedicated MRI of the buttock was recommended based on the nuclear medicine findings.

On the blood pool study, there was soft tissue hyperemia localized to the left buttock; an MRI was recommended to further evaluate this (Fig. 5).

On MRI, there was a large, well-circumscribed lipomatous mass deep to the glutus maximus muscle. This was extramuscular with no intrapelvic extension. The mass measured 9.6 cm CC x 9.7 cm TR x 3.4 cm AP. On T1 there was slight hypointensity relative to subcutaneous fat (Fig. 6A). On T2 fat saturated sequence, there was near complete suppression of signal and persistent flow voids (Fig. 6B). Postcontrast, there was subtle diffuse enhancement with avid enhancement of vessels (Fig. 6C). No grossly concerning septae, invasion, or nodular component was appreciated.

Case 3
A 66-year-old male presented with a 2 year history of large, painless left thigh mass that is firm but non-tender to palpation.

On ultrasound, there was a large circumscribed hyperechoic mass within the subcutaneous tissue (Fig. 7). Doppler confirms vascularity within the lesion (not shown). The mass measures 14.8 cm x 10.8 cm x 6.7 cm.

On MRI, there was an encapsulated mass in the subcutaneous tissue of the left medial thigh. Several presumed vascular structures were noted within it. There was no invasion of the adjacent musculature. On T1-weighted images, the mass was minimally hypointense to adjacent subcutaneous fat (Fig. 8A). On PD fat saturated images, there was a thin uniform capsule with incomplete fat saturation (Fig. 8B). Postcontrast, there was mild diffuse background enhancement, thin septal enhancement, and enhancement of the central vessels (Fig. 8C).

The lesion was resected under the presumed diagnosis of low-grade liposarcoma or atypical lipoma. On gross dissection the mass was homogeneous yellow adipose tissue with small fibrous septations. It had a thin capsule with no extracapsular

Figure 5 Blood pool image posterior projection, identifies a large area of moderately increased radiotracer uptake over the left posterior buttock.

(Figs. 2 and 3).

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Figure 6 A. T1-weighted axial scan with well-circumscribed, fairly homogenous, hypointense extramuscular mass. There are several serpiginous structures originating off of the anterior deep aspect of the lesion with flow voids. B. T2-weighted axial scan shows mass has incomplete fat suppression relative to subcutaneous fat, with several presumed vascular structures anteriorly. C. Axial T1-weighted fat saturated axial scan demonstrates subtle veil of background enhancement with avid curvilinear vascular enhancement.
extension. Microscopy revealed eosinophilic, multivacuolated brown fat cells interspersed with mature adipocytes. This was devoid of atypia, necrosis, or invasion (Fig. 9).

**Discussion**

Velsch was the first investigator to recognize the distinction between brown and white adipose tissue. In 1906, Merkel used the term “pseudolipoma” to describe benign brown fat tumors. In 1914, the actual term hibernoma was coined when Gery recognized a histologic resemblance between these tumors and the brown fat identified in hibernating animals. Due to the abundance of mitochondria and its high vascularity, brown fat is hypothesized as contributing to the non-shivering thermoregulation of hibernating animals and newborn humans. Brown fat gradually diminishes in volume from infancy and compromises less than 0.1% of total body weight by 70 years of age. Recent 18F-FDG PET studies indicate the persistence of brown fat in the neck, in the thorax, between the subscapularis and pectoralis muscles, around the brachial plexus, and in a paraspinal distribution.

On gross examination, hibernomas are soft to rubbery, encapsulated, yellow-brown macrolobulated masses. These typically range in size from 5 to 10 cm in diameter, although lesions reaching 20 cm have been documented. Their brownish hue may be attributed to the mitochondrial and vascular predominance. PET imaging is useful in the scenario of the commonly encountered lipomatous lesion because it may distinguish the simple lipomas that have only minimal metabolism from those lesions that may have a higher metabolic rate such as hibernomas and malignant liposarcomas.

Hibernoma is a rare, benign tumor, with less than 200 cases reported in the literature. They are usually seen in the third to fifth decades of life but can occur at any age. Although previously reported to be more common in females, more recent studies suggest a slight male predominance. Most cases present as an asymptomatic, slowly growing, painless mass, although the mass may occasionally cause symptoms due to compression of adjacent structures.

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Hibernomas manifest radiographically as radiolucent masses with an absence of calcification, osseous, or chondroid matrix and lacking associated aggressive osseous pathology, as illustrated by our first case. On ultrasound these are hyperechoic, circumscribed masses with hypervascularity on Doppler interrogation; both of the cases that were evaluated with ultrasound demonstrated these typical features.

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**Figure 7** Select sonographic image identifies a large mass in the left thigh with slight hyperechogenicity and fairly well-defined borders.

**Figure 8** A, T1-weighted coronal image of the thighs identifies a large encapsulated nearly isointense mass with faintly visible central vessels. B, PD fat saturated axial image shows incomplete, hazy fat saturation and a thin capsule delineating the mass from adjacent subcutaneous fat. C, Postgadolinium T1-weighted fat saturated axial scan shows diffuse subtle enhancement, no nodular enhancing components and thin rim of capsular enhancement.

**Figure 9** Interspersed between the mature white adipocyte cells are brown fat cells which have multivacuolated, eosinophilic appearance. Color illustration available at www.nyuhdbulletin.org.
characteristics. Due to this hypervascularity or arteriovenous shunting, core needle biopsy is a relative contraindication particularly in deep-seated lesions,\(^{19}\) where there may be difficulty tamponading a post-intervention hemorrhage. As in case 2, this hypervascularity may even be appreciated on bone scintigraphy as mild to moderate radiotracer uptake on blood pool and static images.\(^{14}\)

On CT, a fat attenuating mass is characteristic, although it is slightly hyperattenuating to subcutaneous fat. With intravenous contrast, there may be diffuse, mild background enhancement with more prominent enhancement of septae and vessels.\(^{14}\)

MRI features of hibernoma may vary according to their histological composition. These lesions are minimally heterogeneous and slightly hypointense to subcutaneous fat on T1-weighted images and fail to fully suppress on STIR or fat saturated T2-weighted images.\(^{17}\) The enhancement pattern is variable, as on CT.\(^{8}\) Not infrequently, there are associated prominent vascular structures.\(^{16,17}\) This type of vascularity is not seen in well-differentiated liposarcomas, and this is an important feature for differentiation.\(^{14}\) All of our lesions clearly demonstrate these typical MRI features.

Differential diagnosis based on the clinical and radiographic features would include other fairly homogeneous, noninvasive lipomatous lesions. Lipomas are more likely to parallel fat on all modalities. However, not all lipomas are homogeneous especially if traumatized or necrosed. Simple lipomas should suppress fully on fat saturation sequences and should not have more than thin capsular or mild septal enhancement.\(^{18}\) The septae in superficial lipomas are less than 2 mm in thickness, uniform, and may be nonenhancing; however, deeper lesions may have thicker, even nodular septae.\(^{14,19}\) Low-grade liposarcomas are more difficult to differentiate from lipomas. The septae in low-grade liposarcomas may be thicker, nodular, and more avidly enhancing than lipomas.\(^{14,19}\) The prominence of vascular structures are not seen in liposarcomas, and this is distinct to hibernomas.\(^{14}\) The avid metabolism on 18-FDG PET is unique to hibernomas and more metabolically-active liposarcomas.\(^{19}\)

Although hibernomas are always benign, their large size may cause compression of neighboring structures, such that surgical excision is usually recommended.\(^{20}\) There is no recurrence with complete surgical resection and metastases have not been reported.\(^{21}\)

Conclusion

These three cases of hibernoma clearly demonstrate the features as expected on each modality. Although it is not always possible to definitively diagnose a hibernoma, based on imaging alone, this histologic lipomatous variant should be considered in the differential diagnosis when radiologists encounter a lesion that does not exhibit the typical features of either a simple lipoma or a liposarcoma.

Disclosure Statement

None of the authors have a financial or proprietary interest in the subject matter or materials discussed, including, but not limited to, employment, consultancies, stock ownership, honoraria, and paid expert testimony.

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