Hibernomas are rare benign adipose tumors composed of brown fat cells with granular, multivacuolated cytoplasm admixed with white adipose tissue. They account for 1.6% of benign lipomatous tumors and approximately 1.1% of all adipocytic tumors. They are more common in the third and fourth decades of life. The most common location is the thigh, followed by the shoulder, back, and head and neck. Four histological types have been reported; abundant vascularity is characteristic, and atypias are rare. The treatment of choice for hibernomas is complete surgical excision. Metastases or malignant transformation have not been reported.

This article presents a series of 17 patients with hibernomas diagnosed and treated at our institution from January 1986 to December 2009. Six men and 11 women (M:F, 1:2) had a mean age of 38 years (range, 10 months to 64 years). All patients underwent surgical treatment; 14 patients had marginal and 3 had wide excision. Adjuvants such as radiation therapy, chemotherapy, or embolization were not administered for any patient. The most common symptom was a painless palpable mass, followed by a tender or painful mass; in 2 patients, the tumor was an incidental finding. The duration of symptoms ranged from 1 month to 10 years (mean, 27 months). The most common location was the thigh, followed by the buttock, scapula, and neck. The most common histological variant was the typical variant followed by the lipoma-like variant. At a mean follow-up of 5 years (range, 1-9 years), local recurrences were not observed.

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Hibernomas, first reported in 1906 by Merkel,1 are rare benign adipocytic tumors composed of brown fat cells with granular, multivacuolated cytoplasm admixed in variable proportion with white adipose tissue.2,3 They account for 1.6% of benign lipomas in all adipocytic tumors,1,3 Their etiology is unknown. They were thought to resemble vestigial fat-storage organ cells analogous to those of hibernating animals, in which this tissue is believed to have a thermoregulatory function.2,4 Brown adipose tissue is rich in glycogen, cholesterol, and phospholipids5 and enables energy from oxidized lipids to dissipate as heat. This ability is dependent on the expression of uncoupling protein 1 (UCP1), a mitochondrial proton transporter that uncouples electron transport from ATP production.6 In humans, brown adipose tissue occurs normally in the fetus, being distributed in the neck, axillae, and subpleural regions, and gradually decrease.7 In adults, brown fat is confined to the more central parts of the body, which leads to a vest-like arrangement with the greatest yields of brown fat in perirenal, posterior cervical, and intercostals areas.8,9

This article presents a series of patients with hibernoma; reports their clinical, imaging, and histological features; and discusses their management and outcome.

MATERIALS AND METHODS

We retrospectively studied the medical files and histological slides of 17 patients with a diagnosis of hibernoma treated at our institution between January 1986 and December 2009. Six men and 11 women had a mean age of 38 years (range, 10 months to 64 years). Mean follow-up was 5 years (range, 1-9 years); all patients were included in the postoperative evaluation and gave written informed consent to be included in this study. The study was approved by the Institutional Review Board/Ethics Committee of our institution.

All patients underwent preoperative imaging studies (Figure) and biopsy; 13 patients underwent fine-needle aspiration, 2 incisional, and 2 excisional biopsy. All patients underwent surgical treatment; 14 patients underwent marginal and 3 underwent wide excision. Adjuvant treatments such as radiation therapy, chemotherapy, or embolization were not administered in any patient.

RESULTS

Ten patients presented with a 1-month to 10-year (mean, 27-month) history of a painless palpable mass, and 5 patients presented with a 1- to 10-month history of a tender or painful mass; in the remaining 2 patients, the tumor was an incidental finding. A female predominance was observed (M:F, 1:2). The most common tumor location was the thigh in 13 patients, followed by the buttock in 2 and the scapula and neck in 1 patient each.

At surgery, the tumors were encapsulated and intramuscular, with no bone erosion, and were easily separated from the surrounding soft tissues (Figures E-F). Mean tumor size was 11.8 cm (range, 3.5-23 cm). Hemorrhagic complications related to the biopsy or surgical treatment were not observed. The most common histological variant was the typical hibernoma (14 cases) (Figure G), followed by the lipoma-like variant (3 cases). At last follow-up, all patients were alive; local recurrence or distant metastases were not observed in any patient.

DISCUSSION

Benign adipocytic tumors are common in soft tissue and bone.2 These tumors have been categorized into 9 entities, including lipomas, lipomatosis, lipomatosis of nerve, lipoblastomas/lipoblastomatosis, angiolipomas, myolipomas of soft tissue, chondroid lipomas, spindle cell/pleomorphic lipomas, and hibernomas.3 We studied a series of patients with hibernomas to report the spectrum of morphological features and confirm their benign behavior. The small number of patients is a limitation. However, given the rarity of these tumors, independent institutional studies are useful to evaluate a disease process, management, and outcome.

Hibernomas, previously called adenomas of sebaceous gland, pseudolipomas, lipomas of immature adipose tissue, lipomas of embryonic fat, and fetal lipomas,1,2 most commonly occur in the third and fourth decades of life4,10,14; five percent occur in children and teenagers.3,15 A slight male predominance has been reported.10 The most common location is the thigh, followed by the shoulder, back, head and neck, mediastinum, and retroperitoneum. Residual brown fat, mostly seen around cervical and axillary lymph nodes, should not be classified as hibernoma.3 Multiple and bilateral hibernomas have also been reported.1,16 The majority present as firm, slow-growing, progressively enlarging, painless masses.10,12,13 Symptoms may occur from pressure effect on adjacent structures; occasionally, the tumors are rapid growing and infiltrating adjacent structures.14 Due to their vascular nature, some lesions are warm to the touch.2 In our study, hibernomas were more common in women. The most common presentation was a painless, slow-growing, palpable mass at the thigh, most commonly the medial compartment.

Radiographs in patients with hibernomas do not show calcifications or bony erosion.11,12 Sonography demonstrates a well-circumscribed uniformly hyperechogenic mass.2,18,19 Color Doppler flow imaging usually shows hypervascularization.23,20 On computed tomography (CT) scan, the lesions are usually lobulated, septated, and well circumscribed with fat density and variable contrast enhancement.17,18,21,22 Typical T1- and T2-weighted magnetic resonance imaging (MRI) shows a heterogeneous isointense or relative hypointense lesion compared to subcutaneous fat, and hyperintense compared to muscles, with contrast enhancement and linear septations.12,18,21,23 Diffuse heterogeneous en-
Enhancement is usually observed following contrast administration because of the hypervascularization of the tumor.22 On fat suppression sequences, there may be incomplete fat suppression because of the nature and amount of lipids.24 Hibernomas have been detected incidentally on technetium-99m tetrofosmin myocardial perfusion studies performed in patients with chest pain, appearing as mass-like areas of increased activity.18,25 Active uptake has also been reported on images obtained with 18-F fluorodeoxyglucose positron emission tomography (18F-FDG-PET).26

At angiography, hibernomas have rich vascularity and occasionally arteriovenous shunting.7,27 Magnetic resonance angiography may be useful for preoperative planning and identification of the efferent and afferent tumor vessels to facilitate surgical excision.28 In the present series, angiographic studies were not performed in any patient. In line with the literature, the typical imaging findings were observed.12,17,19,21-23 However, although a typical imaging appearance may suggest the diagnosis, we performed preoperative biopsy in all patients for accurate diagnosis; fine-needle aspiration biopsy was done in the majority of the patients, and excisional and incisional biopsy in 2 patients each. The hypervascularity and risk of significant hemorrhage may prompt fine-needle aspiration rather than other types of biopsy in cases of suspected hibernoma.29 Excisional biopsy should be performed for small, accessible, and superficial lesions, for which, by using clinical findings and imaging studies, the surgeon is certain of their benign behavior.

Histology shows the typical hibernoma cells consisting of large multivacuolated fat cells with finely vacuolated or granular cytoplasm, eccentric vesicular nuclei, and a small, single, round central nucleolus having evenly dispersed chromatin.10,30 Atypia is rare.14,31 Four histological variants have been described based on the quality of hibernoma cells, the nature of the stroma, and the presence of a spindle cell component.10

Figure: A 45-year-old man had a 3-year history of a painless, slow-growing posteromedial right thigh mass. Coronal proton-density MRI shows a well-circumscribed heterogeneous hyperintense mass with a maximum diameter of 23 cm at the right adductor major muscle (A). Axial T2-weighted fat suppression MRI shows a high-signal intensity heterogeneous mass with no suppression in fat-suppression sequences (B). Sagittal (C) and axial (D) T1-weighted fat suppression with contrast administration shows the heterogeneous hyperintense soft tissue mass. Complete marginal excision of the tumor was done. The tumor was encapsulated and intramuscular (E). The cut surface was yellowish, greasy, soft, and spongy, with areas of hemorrhage (F). Low- (10×; left) and high-power (20×; right) histological sections show multivacuolated brown fat cells with abundant, granular cytoplasm and a small, central nucleus. The brown fat cells vary from pale staining to variably eosinophilic (hematoxylin-eosin stain). These findings were consistent with the diagnosis of hibernoma (typical variant) (G).
The most common variant is the typical hibernoma (82% of cases) composed of a mixture of eosinophilic cells, hibernoma cells, and white fat cells.\(^{10,20}\) The myxoid variant (9% of cases) is composed of multivacuolated cells with focal eosinophilic cytoplasm separated by a myxoid stroma.\(^{10}\) This variant may be confused with myxoid liposarcoma.\(^{33}\) The lipoma-like variant (7% of cases) is composed of scattered adipocytes, spindle cells, and mast cells, and is composed of the typical multivacuolated cells observed in hibernoma, as well as adipocytes, spindle cells, mast cells, and collagen bundles.\(^{29}\) In the present series, the most common variant was the typical hibernoma; in 3 cases, histological findings were consistent with the lipoma-like variant. Myxoid and spindle cell variants were not found.

In view of the benign tumor behavior, marginal excision is considered curative for hibernomas.\(^{2,3,10,13,31,40}\) Intralesional or incomplete excision may result in continued growth and local recurrence.\(^{40}\) However, intralesional excision may be necessary for large tumors close to nerves or vessels. In these cases, embolization may be considered.\(^{29}\) All histological variants have the same good prognosis after complete excision.\(^{3,10}\) Malignant transformation or metastases of hibernomas have not been reported.\(^{10,31}\) Even rare atypical mitoses, an infiltrative pattern, and an intramuscular location should not be considered criteria for malignancy.\(^{10}\)

### References

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