# Axillary Hibernoma: An Unusual Benign Soft-Tissue Tumor

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**Citation**

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**Abstract**

Hibernoma is an uncoomon benign tumor that comes from the vestiges of the fetal brown fat. We report the case of a 29-year-old male with a 6-month history of a painless mass in his left axilla. Due to the low incidence and prevalence in the world, we decided to present one clinical case, focusing on the clinical finding and pathology along with a review and discussion of this rare pathology.

## INTRODUCTION

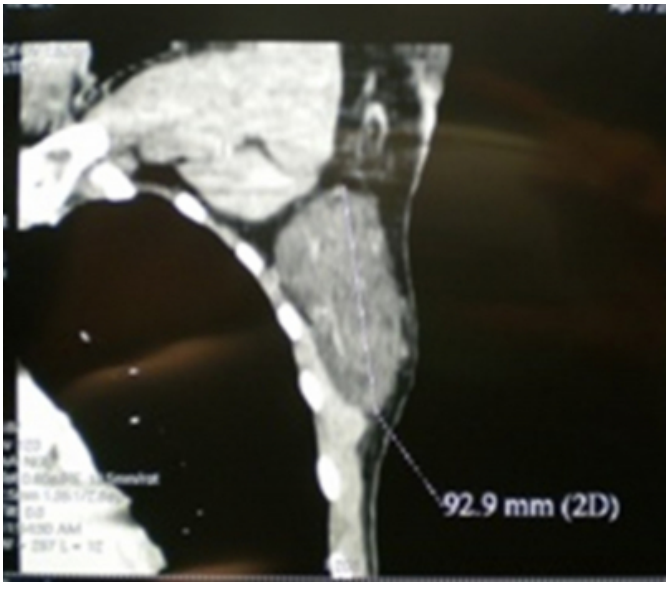
Hibernoma is a rare benign tumour consisting primarily of brown fatty tissue. It arises most often in adults from the remnants of fetal brown adipose tissue, even though not all hibernomas occur at the few sites in which brown fat is encountered in humans. It usually affects muscle and subcutaneous tissue and is asymptomatic and slow-growing. It is usually seen in locations where normal brown adipose tissue is found in foetuses and infants such as the periscapular or interscapular region, neck, axilla, inguinal region, mediastinum, periaortic and perirenal zones, and more rarely, the retroperitoneum, intrathoracic and special pleural locations[1]. We present a case of a hibernoma arising from the left axilla in a 29-year-old male treated by surgical resection. The diagnosis of hibernoma was only made after surgical excision, wich confirmed the presence of brown fat on histologic analysis. Clinical picture and therapeutics applied are explained.

## CASE REPORT

A 29-year-old male presented with a mass in his left axilla which had been steadily enlarging for more than 6 months. He was totally asymptomatic. His medical history was unremarkable. Physical examination demonstrated soft-tissue fullness within the left axilla, with a mixed consistency of fatty tissue combined with a firmer, interspersed soft-tissue component. No skin changes or dimpling were present, and the left upper extremity was neurovascularly intact. Laboratory findings did not reveal anaemia or inflammatory changes. Ultrasonography demonstrated echogenic soft tissue with increased vascularity. The lesion was described on CT scan (Fig. 1), as a well-defined mass arising from the left axilla with mass effect on the surrounding structures, but without evidence of invasion of adjacent skeletal muscle. The tumour measured 9x5cm.

**Figure 1**

Fig. 1. Abdomen CT scan showed an isodense, sharply demarcated mass arising in the left axilla and left lateral chest wall. Most of the mass demostrates a well-defined border, although there is obliteration of the fat plane between the mass and the subscapularis muscle.




Although the mass was thought to be a lipoma, elective resection was scheduled. Under general anaesthesia the left axilla was explored through a longitudinal incision. Subcutaneous dissection identified a circumscribed mass draped with multiple veins which were ligated and divided. Blunt dissection revealed extension of the mass high into the

axilla where it was loosely adherent to the axillary vein. The long thoracic and thoracodorsal nerves were identified. The tumour had a yellow-gray appearance. The surgical specimen measured 10x4cm (Fig.2). The incision was closed. The patient had an uneventful postoperative course and was discharged home four days after the surgery. On final pathology, the mass was classified as a hibernoma, a benign tumour of brown fat (Fig. 3). There are no signs of recurrence after 4 months.

**Figure 2**

Fig. 2. Intraoperative photography showed an encapsulated tumour consistent with a hibernoma. The surgical specimen measured 10x4cm.

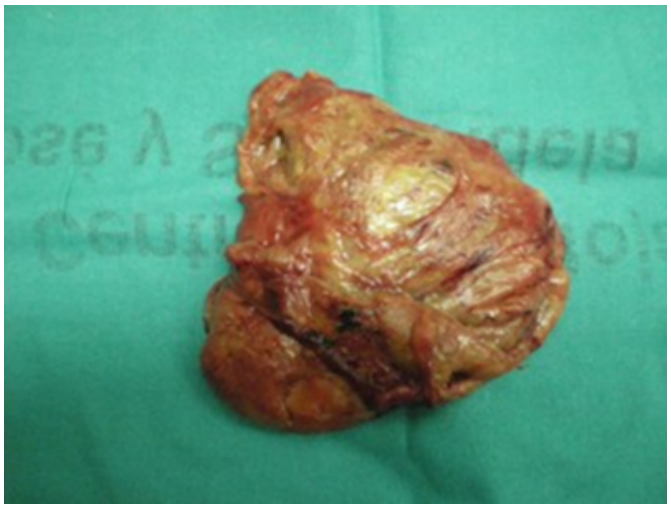
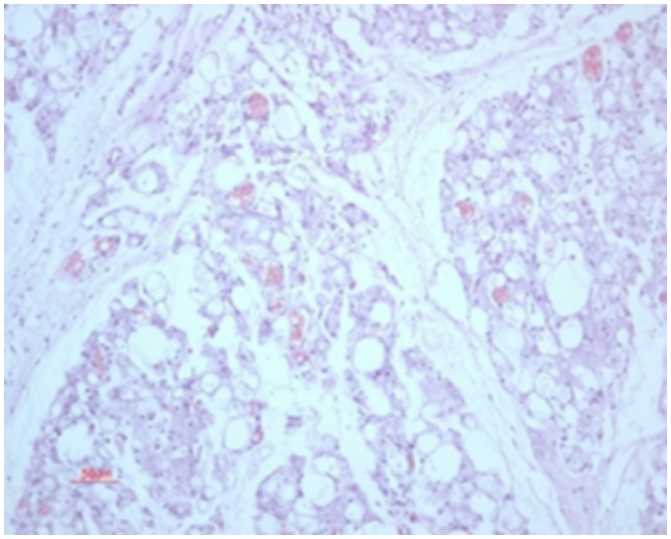


**Figure 3**

Fig. 3. Histology: High magnification photomicrograph of the lesion showing a typical hibernoma: multivacuolated cells with multiple lipid droplets, granular cytoplasm and eccentric vesicular nuclei with single prominent nucleoli (Hematoxylin-Eosin stain10x).



## DISCUSSION

Two types of fatty tissue exist: brown fat and white fat. The brown fat was described for the first time by Galés in 1670[2]. This tissue participates in the regulation of the metabolism and in the thermogenesis. It is more abundant in the animals that hibernate; however, it has been described in animals that do not hibernate as well as in man, mainly in newborns, infants and children. In the human, it diminishes after the eighth week of gestation, although small quantities persist in all the ages. In the adult, it constitutes 1% of the corporal mass. These remains are usually located in the interscapular, inguinal and axillary regions, nevertheless they can be located in any region of the body[3-5].

Hibernoma is an unusual tumour of brown adipose tissue. The term hibernoma is derived from the microscopic similarity of this tumor to the glandular brown tissue ocurring in the organs of hibernation of certain animal species. A first case of hibernoma was reported in 1906 by Merkel[6] who named it “pseudolipoma”. Gery[7] was eventualy credited with the term “hibernoma” in 1914, when he recognized the tumor´s similarity to brown fat in hibernating animals. Although Gery[8] disclaimed the term in 1951 once hibernation in animals was no longer linked to brown fat, the name continues to be utilized in the description of brown fat tumors. Hibernomas have been described only in a few case reports and small series. Until June of 2009, there are about 230 publications on this suject, in the MEDLINE data base and only a small number of them are in the axilla.

Furlong et al.[9], reviewed 170 cases of hibernoma and evaluated the morphologic features and the behavior of this tumor: It is more frequent in men than in in women with a ratio of 10 to 7. The tumor occurs most commonly in adults with a mean age of 38 years (age range: 2-75 yeras). Five percent occur in pediatric patients. It can be solitary or multiple[10]. The average duration of the tumor is of 30.6 months. This tumour usually arises in the lower extremities (33%), upper extremities (22%), trunk (23%), head and neck (13%), and abdomen and retroperitoneum (9%). Around 3.5% of the cases are located in the axilla[11]. These lesions have even been reported in the scrotum[12], mediastinum[13] and in intradural locations[14].

Brown adipose tissue, the function of which is to promote non-shivering thermogenesis, is present in the fetus and is gradually replaced by white adipose fat with advancing posnatal age. However, it persists in varying amounts throughout adult life and may be found in diverse places of

the human body. In some occasions this neoplasia is formed in places where habitually there is not brown fat in the adult. This is due to the fact that these tumors may arise from aberrant differentiation of mesenchyma cells or by ectopic growth or migration of adipose tissue[1].

## DIAGNOSIS

The diagnosis of this pathology is based on the clinical manifestations, image tests and aspiration cytology.

Clinically, hibernomas are usually painless and therefore often incidentally found during routine investigations, as in our patient. When symptoms are present, they often relate to compression of adjacent structures[4,15]. Significant weight loss is described and is attributed to excessive thermogenesis of the tumor tissue responsible for the catabolism of circulating lipids and carbohydrates into thermal energy[16]. In some cases, the patients can have fever and an increase of the inflammatory parameters (sedimentation rate, leucocytes, C-reactive protein)[1]. This lesion generally presents as a slow-growing, subcutaneous mass, which may be mobile and is usually asymptomatic. Localized warmth over the mass may be apparent due to its hypervascular nature. The majority lie in the subcutaneous tissue, although 10% are found intramuscularly[11]. These lesions tend to be 5 to 10cm in greatest dimensions but do occasionally exceed this size range[9]. The largest previously reported lesion, occurring in the retro-peritoneum space, measured 24cm[17]. The largest previously reported axillary hibernoma measured 18cm[18].

Imaging characteristics of the hibernoma tumor, using conventional radiography, ultrasonography and angiography, are well described in the literature: a) Routine radiography may demostrate a faint soft-tissue mass or swelling, but typically does not show areas of calcification or bony erosion. b) Ultrasonography shows a hyperechoic mass, and hypervascularity with enlarged vessels may be noted on Doppler imaging[19]. c) Angiography characteristically demostrates hypervascularity, although in some case neovascularity and arteriovenous shunts can be observed[20,21]. Increased arterial and venous flow can be seen both within and superficial to the mass using 3-D MR angiography[19].

Hibernoma has a wide spectrum of CT and MR imaging findings, which should be considered in differential diagnosis, especially with other lipomatous lesions. On CT examination, the lesions are slightly hyperdense, and on T1- and T2-weighted MR images, they are isointense or slightly hypointense compared to the subcutaneous fat. These lesions show contrast enhancement and internal linear septation[19,22], as in our case.

There has been some question whether MR imaging allows a specific preoperative diagnosis of hibernoma. Knowledge of its imaging characteristics, particulary on T1-weighted images, may suggest the correct diagnosis of this tumor. However, inasmuch as overlap exists in imaging features of hibernomas and a small number of the other lesions, a specific diagnosis may not always be possible. Many alternative diagnoses have been proposed, based on imaging findings, including benign processes such as angiolipoma, pleomorphic lipoma and lipoblastoma, as well as malignant processes including low-grade and myxoid liposarcoma. Alveolar soft part sarcoma is and additional tumor that may demonstrate increased T1-weighted signal intensities and is hypervascular. MR imaging does excel in its ability to characterize margins of lesions and to document involment of neurovascular structures, both of which are essential in preoperative planning[23,24,25].

These lesions usually demostrate intense fluorodeoxyglucose (FDG) accumulation on positron emision tomography (PET) scanning. This is rather explained by an increased number of mitochondria and a high rate of glucose metabolism present in brown fat cells, than by tumour activity[1]. Study of literature teaches that hibernomas are not the only benign tumours that can have markedly positive FDG accumulation on PET. Other benign tumours that result in hot lesions on PET scanning caused by increased glucose metabolism include benign thyroid follicular nodules, colonic adenomas, renal oncocytoma and benign plexiform neurofibroma[26,27]. Lipomas consistently show low FDG uptake and liposarcomas show low to intermediate FDG uptake. Unfotunately a considerable overlap in standardized uptake values was observed between benign and malignant soft-tissue lesions, so that the results of FDG uptake on PET do not accurately reflect the malignant potential of soft-tissue tumours[28].

Multiple studies have demonstrated the utility of cytology (fine-needle aspiration) or percutaneous biopsy (thick needle), attended or not attended by image tests, for the diagnosis of this pathology, with a specificity and sensitivity of 100 and 99%, respectively[29,30].

## PATHOLOGY

Hibernoma is often a solitary neoplasia, morphologically different to white fatty tissue, and of several sizes. The mean tumor size is 9.3cm (range: 1-24cm)[9]. Grossly, the tumors

are well circumscribed, partially encapsulated, lobulated, soft, mobile and hypervascular. The cut surface varies from yellow to brown and is occasionally mucoid with rare areas of hemorrhage.

Microscopically, the presence of multivacuolated fat cells with small, central nuclei is common to all lesions. The appearance and relative small numbers of these cells varies and, according to this, several histologic variants are recognized based on the tinctorial quality of hibernoma cells, the nature of the stroma and the presence of a spindle cell component. Four morphological variants have been identified: Typical, myxoid, spindle cellular and lipoma-like. Typical hibernoma (82%) is the most common variant and includes eosinophilic cell, pale cell, and mixed cell types. The myxoid variant (9%) contains a loose basophilic matrix. Spindle cell hibernoma (2%) presents features of spindle cell lipoma and hibernoma. The lipoma-like variant (7%), presents only scattered hibernoma cells. The importance of these variants is that they all should be recognized in the spectrum of hibernoma. All variants follow a benign course, but there is some difference in the clinicopathologic parameters. The median age for all variants is the third decade; however, it is highest for the typical variant (38 years) and lowest for the myxoid type (32 years). The anatomical localization also varies. The thigh is the most common site for typical hibernoma and the lipoma-like variant. The myxoid type is more frequent in the head and neck region, and the spindle cell variant is more frequent in the posterior neck and scalp[9,31,32].

Hibernoma cells are S-100 positive in all variants; however, positivity may range from focal to diffuse. S-100 positivity of hibernoma should no lead to confusion with granular cell tumor. Most hibernomas are negative for CD34, wich may outline clusters of granular cells in granular cell tumors[9].

Characteristic cytogenetic abnormalities described in hibernoma include structural rearrangements of 11q13 and 11q21, as reported in the few cases of hibernomas reported to date 11q13 rearrangements tumors such as typical lipoma and myxoid liposarcoma[33].

Differential diagnosis should be made with the following tumors: atypical lipoma, well differentiated liposarcoma ("lipoma-like"), rhabdomyoma, fibroma, neurofibroma, angiolipoma and granular cell tumor[31,32].

## TREATMENT

Surgical extirpation is the treatment of choice for hibernoma. These benign masses are usually removed surgically, because findings with angiography, CT and MR imaging are not characteristic of a benign lipoma and may suggest a more worrisome diagnosis. Although hibernomas do not show infiltrative growth, they tend to grow to large proportions. For this reason resection is advocated before they exert a mass-effect on adjacent structures[19].

At surgery, tumors may be encapsulated, adherence to skeletal muscle does occur and intramuscular tumors are also encountered. Complete excision is generally regarded as curative. Local recurrence has been noted after incomplete surgical resection. Due resection may be complicated by tumour hypervascularity.

The first large pathology series evaluating hibernoma published by Furlong[9] showed the benign nature of the tumor; none of the cases recurred during a mean follow-up period of 7.7 years. The authors described no cases of metastasis.

Despite their benign bahavior, some variants of hibernoma can be confused microscopically with the variant of round-cell liposarcoma with multivacuolar eosinophilic lipoblasts. An accurate diagnosis of these cases would require ultrastructural or possibly even cytogenetic analysis. Long-term follow-up seems advisable[34,35].

## CONCLUSION

Hibernoma is an uncommon benign tumor thought to arise from the vestiges of the fetal brown fat. Even though it is very uncommon, it should be included in the differential diagnosis of the axillary masses. Although the definitive diagnosis is obtained through the hystological study, image tests and aspiration cytology can guide the diagnosis. The prognosis is in function of the total extirpation of the tumor.

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