

## Case Reports

### HIBERNOMA: A NEW CASE IN THE SUBMANDIBULAR REGION

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The hibernoma is an uncommon, benign soft tissue tumor arising from vestigial remnants of so-called brown fat. It most commonly occurs in the interscapular regions, but there are also a number of cases originating in sites normally devoid of brown fat. Most of these tumors are subcutaneous; nevertheless, deep-seated hibernomas have been reported in intrathoracic sites. A hibernoma in the head and neck region is very rare, and few cases in this location have been reported.<sup>1-4</sup> We report a case of hibernoma in the submandibular space with immunohistochemical and ultrastructural study.

#### Case Report

A 55-year-old male was admitted with a six-month history of a slow-growing, painless mass in the submandibular area. There was no significant past medical or surgical history and a thorough examination of the head and neck revealed no other abnormalities. All laboratory studies were normal. With the clinical diagnosis of primitive submandibular gland tumor, the patient was scheduled for surgery. The surgical specimen consisted of a yellow-brown, well demarcated and encapsulated tumor measuring 3.5 x 2.5 cm, joined to the submandibular gland (Figure 1). Microscopically, the neoplasm displayed a distinct lobular pattern and four types of cells could be recognized: most cells contained numerous small round lipid vacuoles that did not indent the regular and spherical nucleus (cells with moruloid or mulberry appearance). The second type of cells were larger and showed an eccentrically displaced nucleus, indistinguishable from a normal mature fat cell (Figure 2). The third type of cells contained lipid vacuoles which indented the central nucleus, then became indistinguishable from a multivacuolated lipoblast

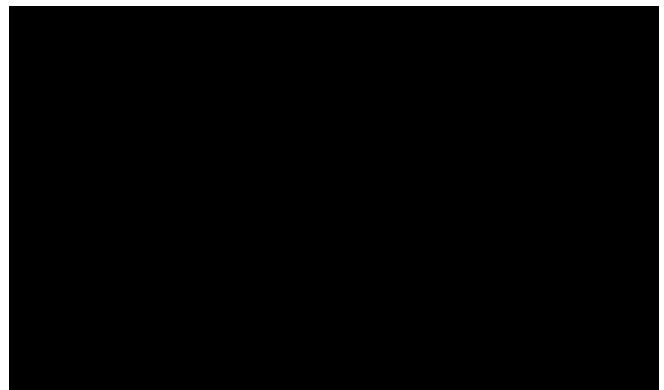


FIGURE 1. Cut section of the resected specimen showing a well demarcated tumor adjacent to the submandibular gland.

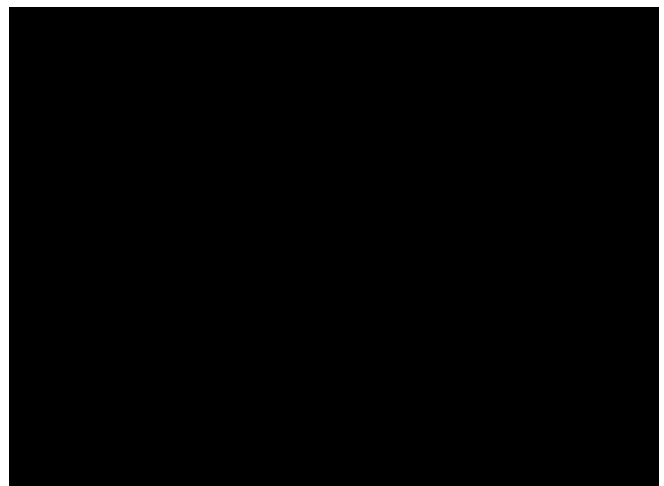


FIGURE 2. Hibernoma consisting mainly of multivacuolated cells with small round nuclei and adult adipocytes. (Hematoxylin and eosin 10x).

(Figure 3A), and the fourth type consisted of isolated polygonal cells with eosinophilic granular cytoplasm and small, regular spherical nucleus (Figure 3B). Mitoses and pleomorphism were absent. A rich vascular network was found. The histological features were considered to be those of a hibernoma. Ultrastructurally, the cells were

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FIGURE 3A. Some tumor cells contain vacuoles indenting the nucleus.



FIGURE 3B. Scattered granular eosinophilic cells are also identified. (Hematoxylin and eosin 50x).

polygonal with multiple well-defined droplets of lipid of variable size and large round to oval mitochondria which occupied much of the cytoplasm remaining between the fat droplets (Figure 4A). These mitochondria were tightly packed, with highly organized and parallel straight transverse cristae (Figure 4B). The mitochondrial matrix was of medium to high density and showed large and abundant dense granules. The endoplasmic reticulum was very scarce and the Golgi apparatus inconspicuous. The nuclei were round and contained uniformly distributed chromatin condensed under nuclear membrane. In some cells, multiple intracytoplasmic lipid droplets caused scalloping of the centrally situated nucleus. Hibernoma cells were surrounded by a well-defined basal lamina. Immunohistochemically, tumor cells showed diffuse vimentin reactivity. Staining for S-100 protein was focally positive. Hibernoma cells did not react with antibodies directed against cytokeratin, CD68, epithelial membrane antigen (EMA) and carcinoembryonic antigen (CEA). The postoperative course was unremarkable and the patient remains free of disease eight years after the diagnosis.

### Discussion

Hibernoma is an uncommon neoplasm derived from brown fat. This specialized form of adipose tissue was first described in animals. The term hibernoma arose due to their multivacuolated cells resembling the cells seen in the brown fat of hibernating animals. Brown fat is present in over 50 species of animals; it is prominent in hibernating animals, but is also found in nonhibernating animals such as rats, rabbits, monkeys, as well as man. Brown adipose tissue was first recognizable in the lateral cervical tissue of

fetuses of 21 weeks' gestational age and was also evidenced in the mediastinum and around the kidneys of fetuses older than 24 weeks' gestational age.<sup>5</sup> It is distributed mainly in the interscapular area, neck, mediastinum and retroperitoneum. Usually, the amount of brown adipose tissue decreases after birth, but small quantities persist in adults. Hibernomas have been reported to affect all age groups.

In the Enzinger and Weiss series of 32 cases, the median age was 26 years (range 18 to 52). Both sexes are equally affected.<sup>6</sup> The tumor most commonly occurs in the scapular region and other locations with vestigial remnants of brown fat. However, hibernomas in sites normally devoid of brown fat have been reported. We present a case of a hibernoma occurring in the submandibular space. A review of the literature has disclosed only two cases of hibernoma in this location.<sup>1,3</sup> Clinical findings of the three cases (including ours) are shown in Table 1. Interestingly, the ages of the three patients with hibernoma in the submental submandibular space were 40, 45 and 55, while in the Enzinger and Weiss series of 32 hibernomas at different sites, the mean age was 26 years. The tumor size was in the lower limit or was noticeably minor compared with hibernomas in other locations (range from 5 cm to 10 cm in diameter).<sup>6</sup> The ultrastructural features of this hibernoma are very similar to those described by Levine<sup>7</sup> and others.<sup>5,8</sup> The overall features have a close resemblance to those of brown fat. The mitochondria in the white adipose tissue are small and infrequent, whereas those in brown adipose tissue are large, numerous and lie adjacent to the fat vacuoles. The implication is that brown adipose tissue is arranged structurally for the rapid oxidation of fat. It has been noted that there is an increase in local skin temperature over the hibernoma. The skin



FIGURE 4A. Three polygonal cells totally invested by a basal lamina. These cells have numerous large and fairly uniform mitochondria and some lipid droplets, but other cytoplasmic organelles are rare (4500x).

over a lipoma, in contrast, is cooler than the corresponding area of the other side of the body, which is a feature of some diagnostic value.<sup>9</sup> This is a demonstration of the fundamental distinction between the heat-insulating white adipose tissue and the heat-generating brown adipose tissue.<sup>9</sup> Although the likelihood of confusion with other tumors is minimal, a variety of diagnoses may be entertained, including lipoma, adult rhabdomyoma, chondroid lipoma, liposarcoma, granular cell tumor and metastatic renal cell carcinoma. In cases with numerous univacuolar cells, the differential diagnosis from lipoma may be difficult but the ultrastructural features are different for both types of tumors. The vascular supply is considerably more prominent in hibernoma than lipoma. Adult rhabdomyoma is made up of similar eosinophilic cells but its cells are larger and contain glycogen and cross-striations can be seen. Chondroid lipoma contains round or polygonal eosinophilic cells, many with lipid vacuoles closely simulating lipoblast and it shows features of both lipoma and hibernoma, but the stroma presents chondroid material which does not exist in the hibernoma.<sup>10</sup> Liposarcomas do not contain a large profusion of hibernoma cells and display mitoses and nuclear pleomorphism. Granular cell tumors are distinguished by complete absence of lipid cytoplasmic vacuoles. Moreover, the granular cell's positivity has not been described for vimentin and the staining for S-100 protein was diffusely positive. The metastatic renal cell carcinoma is also different immunohistologically, showing reactivity for keratin. Immunohistochemically,



FIGURE 4B. The mitochondria are filled with distinct straight parallel transverse cristae and show large and abundant dense granules. Mitochondria and lipid droplets often are closely apposed (20,000x).

TABLE 1. *Hibernomas in submandibular region: A literature review.*

Number	Author and year	Sex	Age	Size	Treatment	Follow-up
1	Arsa JM (1992)	Female	40	2 cm	Local excision	No recurrence
2	Hall RE et al. (1988)	Male	50	5x5 cm	Local excision	No recurrence
3	Present report	Male	55	3.5x2.5 cm	Local excision	No recurrence

the hibernoma cells are strongly reactive for vimentin and show no reactivity for keratin. EMA and CEA are also absent, in accordance with the mesenchymal nature of tumor cells. Negative staining for CD68 indicates absence or scarcity of lysosomes in hibernoma. The hibernoma is a benign tumor and after surgical treatment, no recurrence has been reported.

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