ABSTRACT

Hibernoma is a rare benign neoplasm that shows differentiation towards brown fat. Most hibernomas occur in sites where brown fat persists beyond fetal life, however, they have been known to occur at many uncommon locations. We present a case of a 45 year old female with history of painless, slow growing mass in the pubic region for last seven years, initially diagnosed as hibernoma on fine needle aspiration cytology. The diagnosis was later confirmed on histopathologic examination. The preoperative diagnosis of hibernoma can be difficult because its clinical, radiological & cytological features may overlap with those of other benign & malignant lipomatous tumours.

Keywords: Hibernoma, Brown fat, Fine needle aspiration cytology diagnosis

INTRODUCTION

Hibernoma is a benign soft tissue tumour derived from brown fat and is of significantly rare occurrence as compared to lipoma that is a benign soft tissue tumour derived from white or adult fat. The cytological features of hibernoma on fine needle aspiration cytology (FNAC) are characteristic and can be useful in the preoperative investigation of lipomatous tumors. Despite of its characteristic appearance in cytology smears, reports on cytological diagnosis of hibernoma are few & far between. The cytological features of Hibernoma are highlighted and its differential diagnosis from other lipomatous tumors is discussed.

CASE REPORT

A 45 year old female was referred for FNAC from surgery OPD with a history of painless, slow growing mass in the pubic region since last seven years. The patient denied any other significant complaints or constitutional symptoms. She had a healthy surgical Pfannenstiel incision scar mark owing to abdominal hysterectomy done nine years back for dysfunctional uterine bleeding. On local examination, a 2x3 cm well defined, firm, non tender swelling, mobile in all directions, located in the superficial subcutaneous plane with no overlying skin changes was palpable. (Fig. 1(a)). Clinical suspicion was of a desmoid tumor or fibroma. Ultrasonography was suggestive of a soft tissue tumour with increased vascularity. FNAC was performed using a 23" gauge needle, which yielded oily aspirate. Smears were moderately cellular and showed cells of variable sizes and large cells having abundant multivacuolated cytoplasm and centrally placed nuclei in a fatty background (Fig. 1(b)). Some cells have granular eosinophilic cytoplasm. In multivacuolated cells, the nuclei were small and round and did not show indentation, differentiating...
these cells from lipoblasts (Fig. 2(a)). Taking into consideration the known comparable histologic features, a cytodiagnosis of "Benign Adipose tissue tumour" consistent with "Hibernoma" was made. Excision of the lesion was done. The histological sample consisted of a soft yellow, brownish encapsulated tumour mass measuring $3 \times 3$ cm and yellow brown cut surface. (Fig 2(b))

H&E stained sections showed a distinct lobular pattern. The tumour mass was composed of round cells that showed distinct cellular membrane and granular eosinophilic cytoplasm with centrally placed nuclei. Some cells showed distinctive multivacuolated cytoplasm and small round nuclei without indentation. These cells were admixed with large mature adipocytes with eccentric flattened nuclei. The cellular features appreciated in the cytology smears were comparable to those seen in histopathology sections. fig 3(a) and (b).

The cytological diagnosis of hibernoma was thus confirmed on histopathology.

**DISCUSSION**

Hibernoma is a rare benign adipose tissue tumour which shows differentiation towards brown fat. In 1906, Merkel described the first brown fat tumour as a pseudolipoma of the breast and the term hibernoma was coined in 1914 by Gery, due to morphological resemblance of the tumour to the brown fat of hibernating mammals.  

It is suggested that hibernomas represent altered programming of neoplastic fat cells towards brown fat differentiation. Clinically, hibernomas are usually painless soft tissue masses that arise in adults with peak incidence in the third decade and slight male preponderance. Tumour size can range from 1 to 24 cm diameter with an average of 9.3 cm. It often produces symptoms due to compression of adjacent structures. The most common site of hibernoma is subcutaneous tissue of the back, especially interscapular area. Other frequent locations include the neck, axilla, thigh, and intrathoracic area. They have been reported at uncommon sites including the scalp, buttock, popliteal fossa and scrotum, and intracranially, intraspinally and perireterically. Hibernomas that arise at unusual sites may dictate the clinical course. Literature also mentions case reports of hibernomas in paraglottic, cervical region and mediastinum. When hibernomas occur at an unusual location, it cannot be differentiated from other tumours that occur commonly at the site on the basis of clinical and radiological findings as the case described here. Routine radiography may demonstrate a faint soft-tissue mass or swelling. Ultrasonography shows a
hyperechoic mass, and hypervascularity with enlarged vessels may be noted on Doppler imaging.\(^7\) Cytology smears reveal clusters of uniform, round cells with well-defined borders as well as occasional single cells. The cell cytoplasm is filled with small, uniform fat globules that appear as empty vacuoles in cytology smears. Occasionally, the tumour cells display finely granular cytoplasm. The nuclei are centrally placed with smooth contours, evenly distributed chromatin, and small nucleoli. A delicate network of capillaries frequently surrounds the cells.\(^8\)

On gross examination, hibernoma is usually well defined, soft and mobile. Its colour varies from tan to red, brown, largely depending on the relative amount of intracellular lipid.

Microscopically, in tissue sections the tumour cells appear round or polygonal and are closely opposed to one another within the lobules. Three principal types of cells in varying proportions can be recognized: (a) a small cell with granular, eosinophilic cytoplasm and with or without, multiple small lipid droplets, distinct cellular membrane and centrally placed nucleus (b) a larger, multivacuolated fat cell with scanty granular, eosinophilic cytoplasm that shows the presence of multiple small oil-red O-positive lipid droplets and central nucleus. This cell is known as a mulberry cell and (c) a still larger, univacuolated fat cell with peripherally placed nucleus. Cells of the three principal types, with transitional forms, usually are dispersed randomly throughout the lobules. In most tumours, multivacuolated mulberry cells predominate.\(^9\)

Four morphologic variants of hibernoma have been identified: typical, myxoid, spindle cell, and lipoma-like. “Typical” hibernoma, that is the most common type, includes eosinophilic cell, pale vacuolated cell, and mixed cells based on the quality of the cytoplasm of hibernoma cells. The myxoid variant contains a loose basophilic matrix. Spindle cell hibernoma presents features of spindle cell lipoma and hibernoma; all occurring in the neck or scalp. The lipoma-like variant contains only scattered hibernoma cells.\(^10\) The case presented here belongs to 'the typical hibernoma' variety.

Cytological features of hibernoma are characteristic & are comparable to its histologic features; however studies describing cytological features of hibernoma are sparse other than case series by Maria et al.\(^11\) The authors have emphasised that differentiating hibernoma from other lipomatous tumours is difficult at times due to overlap between clinical, radiographic & cytological features. Immunohistochemically, 85% of these tumours are positive for S-100 protein.\(^3\) However, immunohistochemistry and special stains are not useful in differentiating hibernoma from other benign and malignant lipomatous tumours.

Preoperative differential diagnosis of hibernoma from various types of liposarcomas is important as it may affect patient management. While liposarcoma needs excisions with wide margins, hibernomas can be excised marginally.

The primary difference on cytology is between the brown fat-like cells of hibernoma and the lipoblasts of liposarcoma. The Hibernoma cell has abundant cytoplasm that contains multiple, small fat vacuoles & a uniform central nucleus with evenly distributed chromatin. An additional distinguishing feature of hibernoma is the presence of delicate capillaries surrounding individual hibernoma cells.\(^11\) We did not observe this feature in any of the cytology smears from the aspiration of abdominal wall swelling described here. Lipoblasts of well differentiated liposarcoma may be uni or multi vacuolated and vary in size & shape. They have a comparatively larger, hyperchromatic nuclei indented by cytoplasmic fat vacuoles. Myxoid liposarcoma in addition will have prominent myxoid background and rich capillary network. Nuclear atypia is prominent in Round cell liposarcoma.

Distinguishing hibernoma from lipoma with regressive changes is difficult, but not so significant clinically, both being benign tumours. Adult rhabdomyoma and granular cell tumours are readily distinguished from hibernoma by the complete absence of lipid vacuoles in the cytoplasm and lack of delicate vasculature.

Lipoblastoma, another benign lipomatous tumour is clearly distinguished clinically because of different ages of presentation and sites of occurrence. On cytology, it is more likely to be confused with liposarcoma.

The ultrastructural features of hibernoma include multivacuolated and univacuolated cells containing variable numbers of lipid vacuoles, abundant moderately pleomorphic mitochondria with transverse cristae, lysosomes, lipofuscin granules,
pinocytotic vesicles, well formed basal lamina, and prominent subplasmalemmal condensations.\textsuperscript{12}

Cytogenetic analyses of hibernomas have consistently revealed rearrangements of chromosome bands 11q13–21\textsuperscript{13}. Latest studies suggest that concomitant deletions of tumour suppressor genes MEN1 and AIP are essential for the pathogenesis of the brown fat tumour hibernoma.\textsuperscript{14} Hibernomas are also found to be characterized by Homozygous Deletions in the Multiple Endocrine Neoplasia Type I Region.\textsuperscript{15,16}

Local excision is the treatment of choice for hibernoma. Aggressive behaviour or local recurrences are not reported.\textsuperscript{2}

CONCLUSION

A reliable preoperative diagnosis of hibernoma can be made based on the combination of clinicoradiographic findings and characteristic cytologic features, provided the reporting cytopathologists is aware of the differential diagnoses.

ACKNOWLEDGEMENT

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Conflict of Interest: Nil

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