

동면종의 압착도말 세포소견

-1예 보고-

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Imprint Cytology of Hibernoma -A Case Report-

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Hibernoma is a rare, benign adipose tumor composed of brown fat cells with eosinophilic granular or multivacuolated cytoplasm. The cytologic features of hibernoma have been rarely reported and may mimic other polygonal cell neoplasms. We report the imprint cytologic features of a case of hibernoma in the left thigh of a 68-year-old woman. Microscopic examination showed large, round, or polygonal brown fat cells. The cells were arranged in fragments or clusters. The nuclei were uniformly round with finely granular chromatin. The cytoplasm was multivacuolated or univacuolated. The abundant eosinophilic granular cytoplasm was also present. No nuclear atypia were present. Immunohistochemical staining showed that cells were positive for S-100 protein.

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Key Words : Hibernoma, Cytology

INTRODUCTION

Hibernoma is a rare benign adipocytic tumor first described by Gery in 1914.¹ It affects predominantly young adults, with a mean age of 38 years. There is a slight male predominance. The most common site is the thigh, followed by the trunk, upper extremity, head, and neck.² Hibernoma is a benign tumor that does not recur with complete local excision. Histologically, most hibernomas contain large numbers of multivacuolated brown fat cells with abundant granular or vacuolated cytoplasm. Cytologic studies of hibernoma have been described,³⁻⁷ but cytology may

produce an erroneous diagnosis of malignancy preoperatively, usually liposarcoma.⁴ Recognizing the cytomorphology of hibernomas is important. To our knowledge, the cytologic findings of the hibernoma have not been reported in the Korean literature. We describe here the touch imprint cytologic features of a case of hibernoma that arose in the left thigh of a 68-year-old woman.

CASE

A 68-year-old woman presented with a 7-year histo-

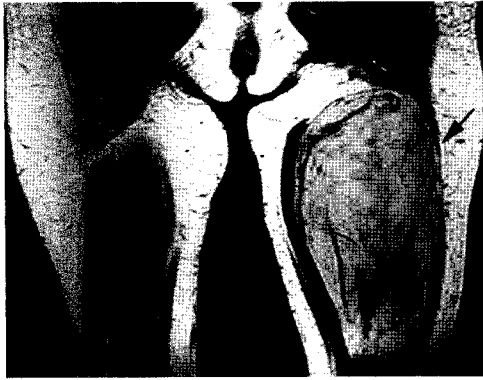


Fig. 1. Magnetic resonance imaging. Coronal T1-weighted image shows a well defined mass with intermediate signal intensity (arrow) in the left thigh.

ry of a mass in her left thigh. The mass was slowly growing. Physical examination showed a soft movable mass in the left posterior thigh. Plain radiographs revealed no bony lesion. Magnetic resonance images demonstrated a well defined soft tissue mass of intermediate signal intensity in the intermuscular space of the posterior compartment of the left thigh (Fig. 1). Positron emission tomography/computed tomography (PET/CT) showed a well circumscribed, hypermetabolic soft tissue mass in the left thigh (Fig. 2). Mass excision was performed and touch imprint cytologic smears were obtained from the mass.

Cytologic Findings

The alcohol-fixed smears were stained with hematoxylin-eosin and Papanicolaou stains. Microscopic examination showed large, round, or polygonal brown fat cells in fragments or clusters (Fig. 3A), with granular eosinophilic materials in the background (Fig. 3B) and large, multivacuolated cells (Fig. 3C). These cells had uniform, small, round nuclei, with finely granular chromatin. The nuclei were centrally or eccentrically located. The nuclear/cytoplasmic ratio was low. Cells with granular eosinophilic cytoplasm and with or without lipid vacuoles were also present (Fig. 3D), as were univacuolated fat cells (Fig. 3E). The cell borders were distinct, and mitotic figures were not found. No nuclear atypia was observed. On immunohistochemical stain-



Fig. 2. Positron emission tomography / computed tomography (PET/CT). PET/CT shows a well circumscribed, hypermetabolic soft tissue mass (arrow) in the left thigh.

ing, the brown fat cells were positive for S-100 protein (Fig. 3F).

Gross and Histologic Findings

The tumor measured 23.0 × 14.0 × 5.5 cm. The tumor was well circumscribed. The cut surface was yellow, red to tan, and soft (Fig. 4). Histologically, the tumor showed large, polygonal, brown fat cells in a lobular pattern demarcated by fibrous septa. The cells had uniform, small, round nuclei with abundant pale, eosinophilic granular or multivacuolated cytoplasm. Mature adipocytes were also admixed (Fig. 5). In focal area of the tumor, an admixture of spindle cells, ropy collagen, and mature adipocytes was present. Immunohistochemistry showed that brown fat cells were positive for S-100 protein and CD34 positive spindle cells were present. Nineteen months after surgery, the patient has remained alive and well, with no evidence of recurrence.

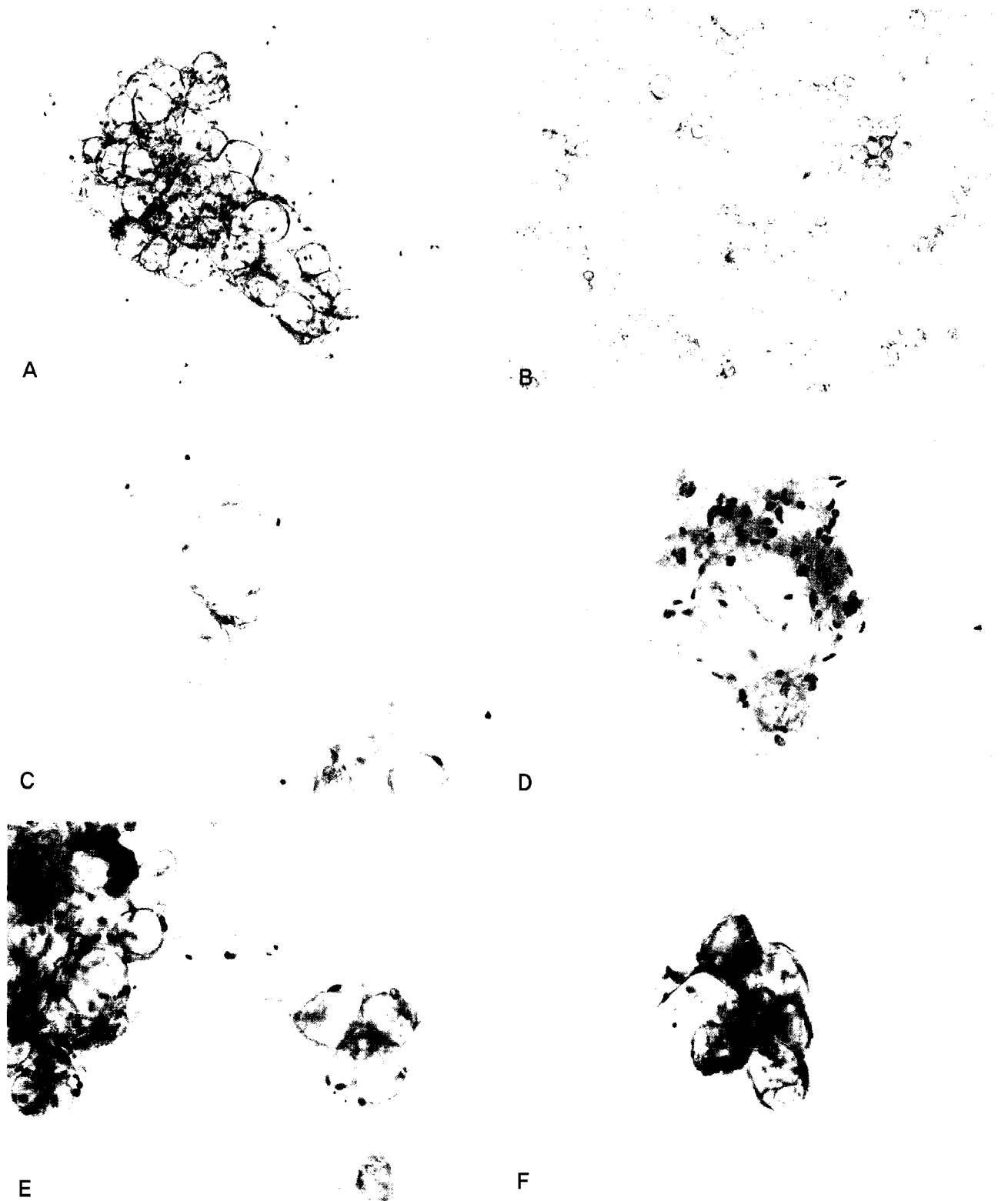


Fig. 3. Cytologic findings. (A) Tumor shows large, round, polygonal cells in a cellular fragment (Papanicolaou stain). (B) The background shows granular eosinophilic materials (H&E). (C) The tumor cells have multivacuolated cytoplasm. The nuclei of these cells are small and round and slightly eccentrically located in the cytoplasm (H&E). (D) Some tumor cells are round or polygonal and have eosinophilic granular cytoplasm (H&E). (E) Univacuolated fat cells are present (Papanicolaou stain). (F) These tumor cells are positive for S-100 protein (Immuohistochemical stain).

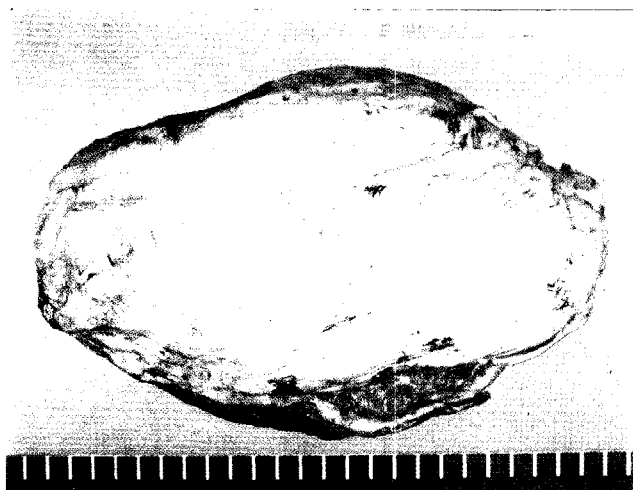


Fig. 4. Gross finding. Tumor shows a well circumscribed, yellow-tan soft cut surface.

DISCUSSION

Hibernoma is a rare benign tumor composed of multivacuolated brown fat cells.⁸ It usually affects muscle and subcutaneous tissue. Hibernomas are typically slow-growing and usually painless. Grossly, hibernomas are well circumscribed, lobular, and vary in color from yellow to red-tan.² Hibernomas mimic morphologically the brown fat of hibernating animals.⁹ The cytologic findings of hibernoma show round to oval cells with multivacuolated or granular cytoplasm.³⁻⁷ The nuclei are usually small and round with finely dispersed chromatin. Cytologic atypia may occur, but mitoses are rare. The cytologic features of the present case are similar to those of previously reported cases.

A summary of eight cases of hibernoma reported in the Korean literature is given in Table 1.¹⁰⁻¹⁷ The ages ranged from 16 to 60 years (mean age 38 years). The male-to-female ratio was 1:1. The tumor locations were scapular area in three patients, psoas muscle in two patients, scalp in one patient, chest wall in one patient, and axilla in one patient. Tumor size ranged from 0.8 cm to 11 cm (mean tumor size 5.6 cm). In a study of Furlong et al.⁹, the mean age was 38.0 years (age range, 2-75 years). The mean tumor size was 9.3 cm (size range, 1-24 cm). In the present case, the patient's age

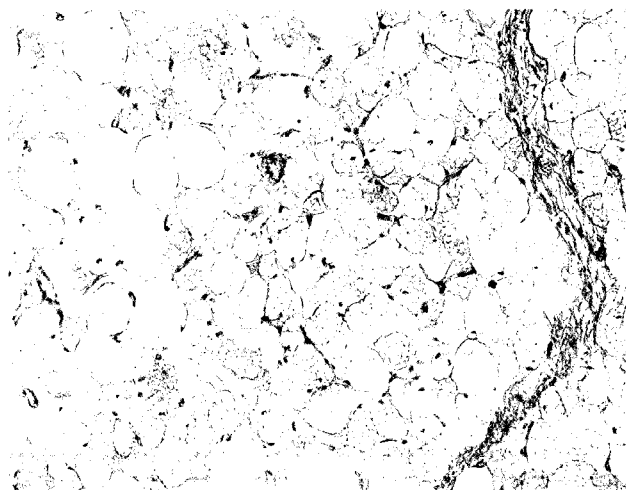


Fig. 5. Histologic finding. The tumor is composed of large polygonal cells with multivacuolated or eosinophilic granular cytoplasm and matured adipocytes (H&E).

Table 1. Published cases of hibernomas in the Korean literature

Authors	Age (y)/sex	Site	Size (cm)
Kim et al. ¹⁰	16/M	Right scapular area	0.8 × 0.5 × 0.5
Ahn et al. ¹¹	30/M	Right scapular area	2.0
Kim et al. ¹²	42/F	Scalp	3.5 × 2.5 × 1.0
Jeon et al. ¹³	60/F	Chest wall	7.0 × 5.0 × 4.0
Lee et al. ¹⁴	26/F	Right axilla	11.0 × 6.0 × 4.0
Kim et al. ¹⁵	33/M	Right scapular area	10.0 × 5.0
Ha et al. ¹⁶	50/M	Right psoas muscle	7.0 × 4.5 × 4.0
Kim et al. ¹⁷	50/F	Right psoas muscle	3.8 × 3.5
Present case	68/F	Right thigh	23.0 × 14.0 × 5.5

was 68 years, and tumor size was 23 cm in the largest dimension.

Hibernoma is derived from the remnant of fetal brown adipose tissue.¹⁸ Four morphologic variants of hibernoma can be identified: typical, myxoid, spindle cell, and lipoma-like.⁹ The present case showed predominantly variant and focally spindle cell variant features. Ultrastructurally, numerous large round mitochondria and lipid droplets are present in the cytoplasm.¹⁹ The karyotypes of hibernoma are complex and usually near or pseudodiploid. The only recurrent aberration is the involvement of 11q13-21.2. Homozygous deletions of the multiple endocrine neo-

plasia type I tumor suppressor gene, MEN1, have been reported.²⁰

Hibernomas should be differentiated on cytologic smears from the other polygonal cell tumors such as lipoma, chondroid lipoma, granular cell tumor, atypical lipomatous tumor/well differentiated liposarcoma, myxoid liposarcoma, adult rhabdomyoma, paraganglioma, and alveolar soft part sarcoma. When the univacuolar cells dominate, it is difficult to distinguish hibernoma from lipoma. The presence of multivacuolated or granular cells supports the diagnosis of hibernoma rather than lipoma. Lipomas with regressive changes show larger macrophages and lipophages, with more irregular and often more hyperchromatic nuclei, and variably sized fat droplets.⁴ Chondroid lipomas exhibit a mixture of benign adipose tissue with lipoblast-like cells, chondroblast-like cells, and a fibrochondroid matrix.²¹ The brown fat cells and S-100 protein positivity in hibernomas could be confused with a granular cell tumor,^{22,23} but the cytoplasm of granular cell tumors is not vacuolated. Multivacuolated hibernoma cells are often mistaken for liposarcomas containing multivacuolated lipoblasts.²⁰ The multivacuolated cells of hibernoma contain a larger number of vacuoles. The nuclei of hibernoma lack significant atypia and scalloping. Atypical lipomatous tumors/well differentiated liposarcomas show enlargement and atypia of at least some nuclei. Myxoid liposarcomas show a characteristic arborizing chicken-wire capillary vasculature.²⁴ Adult rhabdomyomas show abundant granular cytoplasm and peripheral nuclei.²⁵ Adult rhabdomyomas are positive for muscle markers such as desmin and myogenin, whereas hibernomas show positivity for S-100 protein. Paraganglioma may resemble hibernoma, but shows moderate nuclear pleomorphism and occasionally a gland-like or follicle-like pattern. In addition, paraganglioma is positive for chromogranin and synaptophysin. Alveolar soft sarcoma shows marked nuclear pleomorphism and prominent nucleoli, with an alveolar arrangement.

In conclusion, the cytologic smears of hibernoma

show large, round or polygonal cells with abundant granular or multivacuolated cytoplasm. A combination of the characteristic cytomorphology and immunohistochemistry is important for establishing the correct diagnosis of hibernoma.

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