

## 간에 발생한 혈관근육지방종의 압착도말 세포 소견

### -1에 보고-

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#### Imprint Cytology of Hepatic Angiomyolipoma -A Case Report-

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Angiomyolipoma of the liver is a rare benign tumor that's composed of variable mixtures of adipose tissue, smooth muscle and thick-walled blood vessels. We report here on the imprint cytologic features of a hepatic angiomyolipoma in a 47-year-old man. The smears showed spindle and epithelioid tumor cells in clusters, trabeculae and single cells. The spindle cells had elongated, cigar-shaped nuclei with finely granular chromatin and fibrillary cytoplasm. The epithelioid cells had round nuclei with a moderate amount of cytoplasm. Any adipose tissue was not found. Immunohistochemically, both the spindle and epithelioid cells revealed cytoplasmic positivity for smooth muscle actin and HMB-45.

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**Key Words :** Angiomyolipoma, Liver, Cytology, Imprint

## INTRODUCTION

Angiomyolipoma of the liver is a rare benign mesenchymal tumor. It is composed of three tissue components: mature fat cells, smooth muscle cells and thick-walled blood vessels. The proportions of the three tissue elements vary widely. Hepatic angiomyolipomas reveal morphological heterogeneity and they can mimic hepatocellular carcinoma or sarcoma. Therefore, making the correct diagnosis is important. The cytologic findings of hepatic angiomyolipoma have rarely

been reported on.<sup>1-7</sup> We report here on a case of hepatic angiomyolipoma in a 47-year-old-man, and the tumor was examined by touch imprint cytology.

## CASE

A 47-year-old man presented with a liver mass that was incidentally found during a health screening examination. Physical examination showed no specific findings. He had a past medical history of chronic hepatitis



Fig. 1. Computed tomography of the liver. Computed tomography shows a well demarcated tumor with peripheral contrast enhancement (arrow).

B twenty years ago. The radioimmunoassay for hepatitis B virus was positive for both hepatitis B surface antigen and hepatitis B e antigen in the serum. The serum level of alpha-fetoprotein was 3.61  $\mu\text{g}/\text{mL}$ . The computed tomographic scan revealed a well defined mass in the eighth segment of the liver (Fig. 1). The mass showed peripheral enhancement. The radiologic diagnosis was made as "suggestive of inflammatory pseudotumor". Segmentectomy with a mass resection was performed. The excised specimen was sent for intraoperative consultation. The smears imprinted from the hepatic mass were obtained and frozen sectioning then followed.

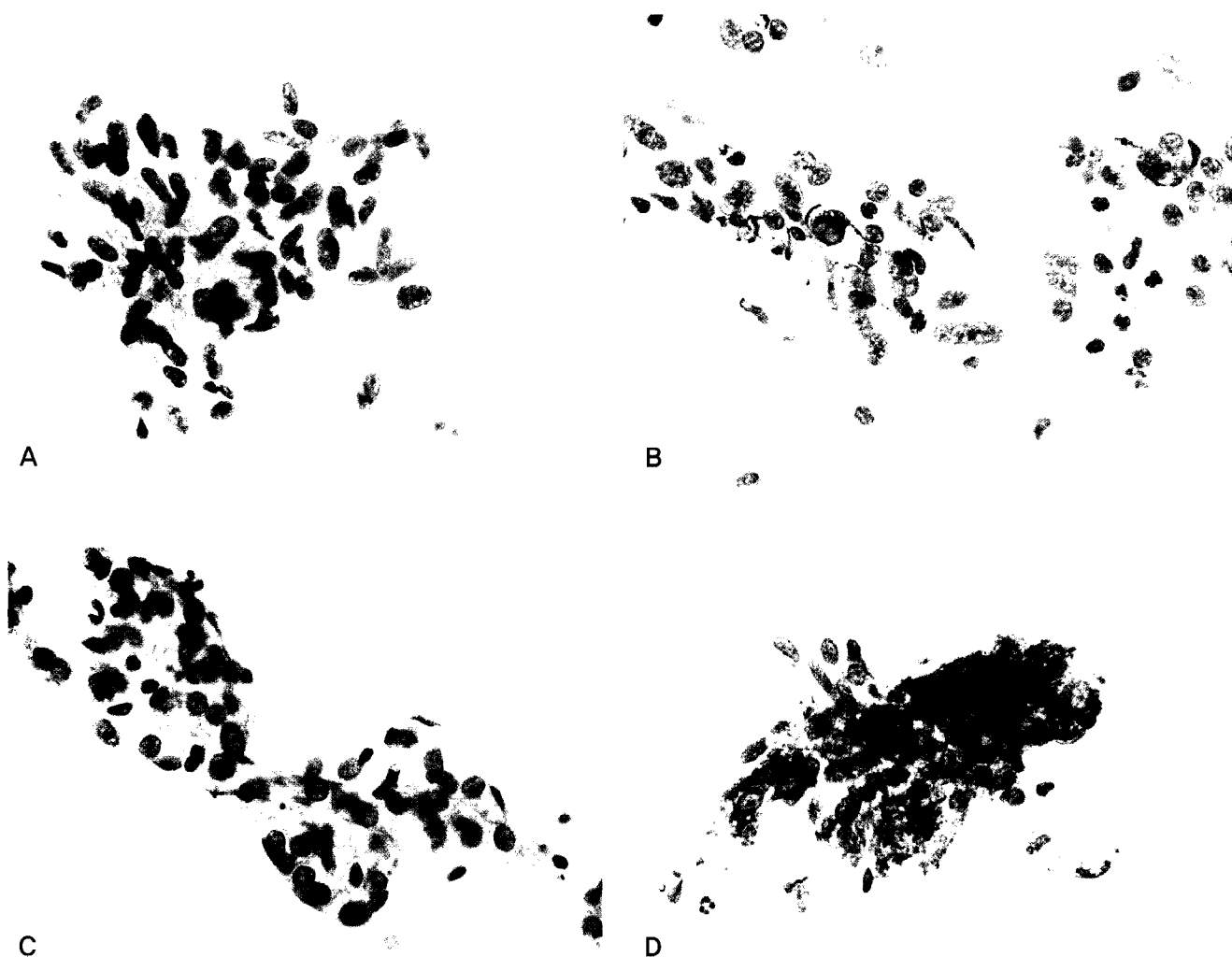
#### Cytologic Findings

The smears prepared from the touch imprints were fixed in 95% ethanol and they were stained with hematoxylin-eosin and Papanicolaou stains. The smears were highly cellular. Red blood cells were seen in the background. Spindle-shaped tumor cells were arranged in clusters, irregular bundles or single cells (Fig. 2A). The nuclei were elongated or cigar-shaped, with finely granular chromatin and small nucleoli. There was a mild nuclear pleomorphism. The cytoplasm was granular or fibrillary. The cytoplasmic border was indistinct.

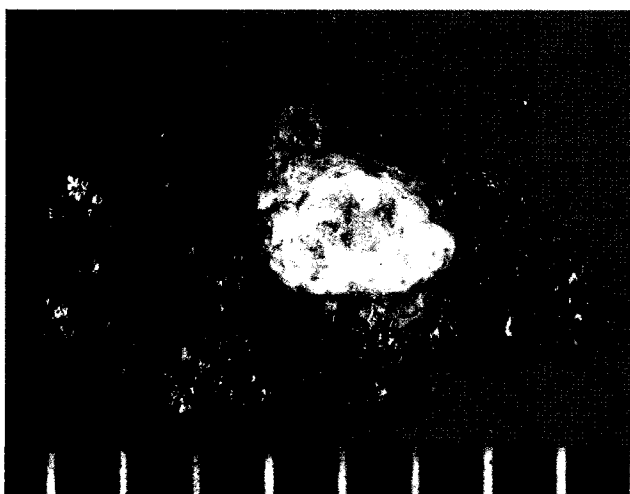
Naked nuclei were noted (Fig. 2B), and intranuclear cytoplasmic pseudoinclusions were occasionally found. Other fields revealed epithelioid tumor cells that had central, round or vesicular nuclei with fine chromatin and small nucleoli. These cells were arranged in solid nests or a trabecular pattern (Fig. 2C). There was no obvious cytologic atypia. Endothelial cells were occasionally found at the edges of the nests or trabeculae. Any mature fat cells were not observed. Immunohistochemical staining was performed on the smears. The tumor cells were positive for smooth muscle actin and HMB-45, and they were negative for hepatocyte common antigen and alpha-fetoprotein (Fig. 2D).

#### Gross and Histologic Findings

The segmentectomy specimen measured 9.0  $\times$  7.0  $\times$  4.0 cm in size. The tumor measured 4.0  $\times$  3.0  $\times$  3.0 cm in size (Fig. 3). The cut surface was yellow gray with a well-defined margin. Histologic examination showed spindle and epithelioid tumor cells arranged in sheets or a trabecular pattern (Fig. 4A, B). The spindle tumor cells had eosinophilic, fibrillary cytoplasm. The epithelioid cells had round vesicular nuclei with pale or clear cytoplasm. Thick-walled blood vessels were noted (Fig. 4C), but any mature fat cells were not found, and tumor necrosis was not present. Immunohistochemically, both the spindle and epithelioid tumor cells were positive for smooth muscle actin, HMB-45 and vimentin, and they were negative for hepatocyte common antigen, CD34, S-100 protein and cytokeratin (AE1/AE3) (Fig. 4B). The non-neoplastic liver showed chronic hepatitis with septal fibrosis. The patient has survived sixteen months after surgery, and there is no evidence of recurrence and metastasis.



**Fig. 2.** Cytologic findings, (A) Spindle tumor cells have elongated, cigar-shaped nuclei with eosinophilic fibrillary cytoplasm and indistinct cell border (H&E). (B) Spindle tumor cells show naked nuclei with fine chromatin and small nucleoli (H&E). (C) Epithelioid tumor cells are arranged in solid nests (Papanicolaou stain). (D) Tumor cells are positive for smooth muscle actin (Immuohistochemical stain).



**Fig. 3.** Gross finding. Tumor shows a well circumscribed gray-white solid cut surface.

## DISCUSSION

Angiomyolipoma is a rare benign mesenchymal tumor that's found in the liver. It occurs equally in males and females; the age range of these patients is from 10 to 72 years with a mean age of 50 years.<sup>8</sup> Angiomyolipomas can vary considerably in size from less than a centimeter to 36 cm. Most of the tumors are solitary, but a case of multiple lesions has been reported.<sup>7</sup> Grossly, it usually presents as a well circumscribed tumor, but it is not encapsulated. The color and consistency depend on the different proportions of fat and smooth muscle. Hepatic angiomyolipoma is histologi-

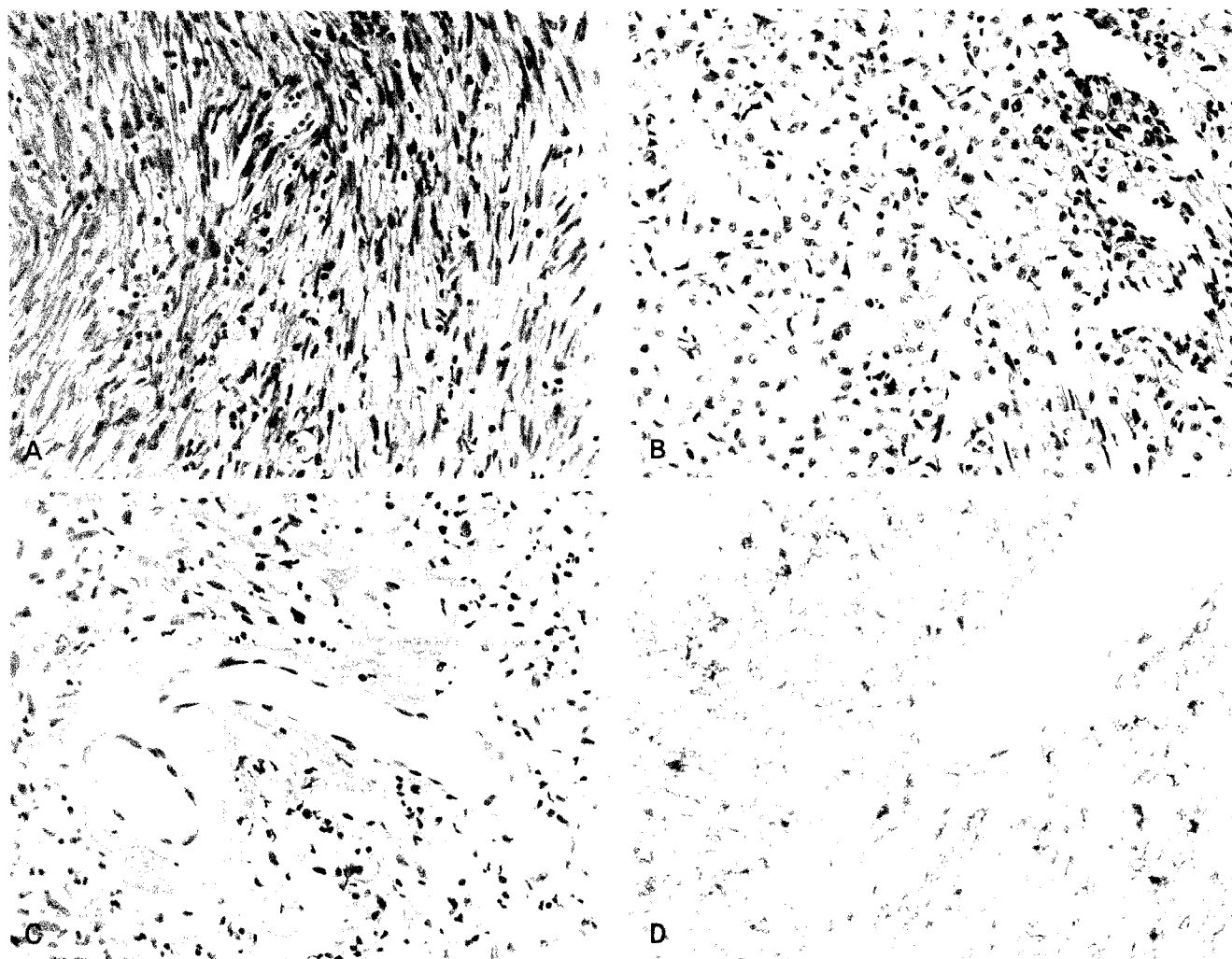


Fig. 4. Histologic findings. (A) Spindle tumor cells have elongated, cigar-shaped nuclei with eosinophilic cytoplasm (H&E). (B) Epithelioid tumor cells have round vesicular nuclei with pale or clear cytoplasm with trabecular arrangement (H&E). (C) Thick-walled blood vessels are present (H&E). (D) Epithelioid tumor cells show cytoplasmic positivity for HMB-45 (Immunohistochemical stain).

cally subclassified into the mixed, lipomatous, myomatous and angiomatous types.<sup>9</sup> The tumor of the present reported case was composed of a predominantly smooth muscle component and it is considered to be the myomatous type.

The cytological features of hepatic angiomyolipoma appear to be similar to the histologic features. Extramedullary hematopoiesis elements may be present. Mature adipocytes and thick-walled blood vessels can be rarely observed in epithelioid angiomyolipoma.<sup>5</sup> Diagnostic difficulty may arise when the fatty component is scant or focal, and it is not sampled.<sup>10</sup> In the present case, any mature fat cells were not identified.

Much of the adipose tissue generally dissolves during fixation and staining. The presence of nuclear pseudoinclusions should not be regarded as a specific criterion for the diagnosis of angiomyolipoma, but they may be considered as an additional nonspecific cytological feature in hepatic angiomyolipoma.<sup>4</sup> Intranuclear pseudoinclusions were occasionally found in the present case.

Angiomyolipoma simultaneously expresses smooth muscle and melanocytic markers. These findings suggest that this tumor has a capacity for muscular and melanocytic differentiation. In the present case, the tumor cells were positive for smooth muscle actin and

HMB-45. Although mature fat cells were not found in the present case, the cytologic features and the positivity for smooth muscle actin and HMB-45 support the diagnosis of angiomyolipoma. On cytogenetic study, neither LOH nor MSI appears to play an important role in the pathogenesis of hepatic angiomyolipoma.<sup>11</sup>

Hepatic angiomyolipoma should be differentiated from smooth muscle tumor, vascular tumor, hepatocellular carcinoma, malignant melanoma and metastatic carcinoma. Hepatic angiomyolipomas that are predominantly composed of spindle cells with cigar-shaped nuclei may be mistaken for smooth muscle tumors. Hepatic leiomyosarcomas show hyperchromatic, elongated, blunt-ended nuclei, and they often show coarse nuclear chromatin and occasionally a perinuclear halo. Immunohistochemical staining can be helpful for confirming the diagnosis because smooth muscle tumors are negative for the melanocytic markers such as HMB-45 and melan-A.<sup>12</sup> The cytologic features of hemangioma demonstrate the presence of blood in the aspirate, bland endothelial cells in clusters of various sizes, and longitudinal nuclear grooves in the endothelial cells.<sup>13</sup> Tumors with a large quantity of fat may be misdiagnosed as lipomatous or focal fatty change of hepatocytes. True hepatic lipoma is extremely rare. Epithelioid tumor cells with a trabecular pattern and nuclear pleomorphism may resemble hepatocellular carcinoma. Hepatocellular carcinomas show hyperchromatic atypical nuclei, a high nuclear cytoplasmic ratio and prominent nucleoli, and they sometimes produce bile. In order to avoid overdiagnosing angiomyolipoma as hepatocellular carcinoma, a careful search must be done to look for such components as blood vessels, smooth muscles and adipocytes.<sup>5</sup> Some angiomyolipomas may resemble malignant melanoma. Immunohistochemically, malignant melanoma is negative for smooth muscle actin. The presence of solid epithelioid areas in angiomyolipoma can mimic metastatic carcinoma and this can create a diagnostic pitfall. The metastatic carcinoma is positive for cytokeratin and it is negative for smooth muscle markers and melanocytic markers.

All tumors that show spindle cells, epithelioid cells or mature fat cells should be immunostained for smooth muscle markers and melanocytic markers to reach a correct diagnosis.

The biological behavior of the angiomyolipoma is benign, and surgical excision is curative,<sup>14</sup> yet malignant hepatic angiomyolipoma has been documented.<sup>15-17</sup> In our case, the patient has survived 16 months after surgery, with no evidence of recurrence and metastasis.

In conclusion, hepatic angiomyolipoma shows the morphologic spectrum ranging from spindle cells to epithelioid tumor cells. Hepatic angiomyolipoma can be diagnosed by cytologic examination if pathologists are aware of its variable cytomorphologic features. Immunohistochemical stains for smooth muscle markers and melanocytic markers are useful for making the correct diagnosis of this hepatic mass.

## REFERENCES

1. Nguyen GK, Catzavelos C. Solitary angiomyolipoma of the liver. Report of a case initially examined by fine needle aspiration biopsy. *Acta Cytol* 1990;34:201-4.
2. Ma TK, Tse MK, Tsui WM, Yuen KT. Fine needle aspiration diagnosis of angiomyolipoma of the liver using a cell block with immunohistochemical study. A case report. *Acta Cytol* 1994;38:257-60.
3. Blasco A, Vargas J, de Agustín P, López-Carreira M. Solitary angiomyolipoma of the liver. Report of a case with diagnosis by fine needle aspiration biopsy. *Acta Cytol* 1995;39:813-6.
4. Villari D, Grosso M, Vitarelli E, Tuccari G, Barresi G. Nuclear pseudoinclusions in fine-needle aspiration cytology of hepatic angiomyolipoma: case report. *Diagn Cytopathol* 2000;22:390-3.
5. Khalbuss WE, Fischer G, Bazooband A. Imprint cytology of epithelioid hepatic angiomyolipoma: mimicry of hepatocellular carcinoma. *Acta Cytol* 2007;51:670-2.
6. Lin KJ, Eng HL, Lu SN, Chiu KW, Kuo FY. Hepatic angiomyolipoma: report of two cases with emphasis on smear cytomorphology and the use of cell block with immunohistochemical stains. *Diagn Cytopathol* 2004;31:263-6.
7. Yim HL, Park KW, Lee KB. Multiple angiomyolipoma of the liver: report of a case with diagnosis by fine needle aspiration cytology. *Korean J Cytopathol* 1998;9: 79-84.

8. Ishak KG, Anthony PP, Niederau C, Nakanuma Y. In : Hamilton SR, Aaltonen LA. World Health Organization classification of tumours: pathology and genetics of digestive system. Lyon: IARC Press, 2000;193.
9. Tsui WM, Colombari R, Portmann BC, et al. Hepatic angiomyolipoma: a clinicopathologic study of 30 cases and delineation of unusual morphologic variants. *Am J Surg Pathol* 1999;23:34-48.
10. Wang SN, Tsai KB, Lee KT. Hepatic angiomyolipoma with trace amounts of fat: a case report and literature review. *J Clin Pathol* 2006;59:1196-9.
11. Xu AM, Zhang SH, Zheng JM, Zheng WQ, Wu MC. Pathological and molecular analysis of sporadic hepatic angiomyolipoma. *Hum Pathol* 2006;37:735-41.
12. Atkinson BF. Atlas of diagnostic cytopathology. 2nd ed. Philadelphia: Saunders, 2004; 554-5.
13. Guy CD, Yuan S, Ballo MS. Spindle-cell lesions of the liver: diagnosis by fine-needle aspiration biopsy. *Diagn Cytopathol* 2001;25:94-100.
14. Ishak KG, Goodman ZD, Stocker JT. Atlas of tumor pathology. Tumors of the liver and intrahepatic bile ducts, 3rd series Fascicle 31. Washington, D.C.: Armed Forces Institute of Pathology, 2001;99-108.
15. Dalle I, Sciot R, de Vos R, et al. Malignant angiomyolipoma of the liver: a hitherto unreported variant. *Histopathology* 2000;36:443-50.
16. Parfitt JR, Bella AJ, Izawa JI, Wehrli BM. Malignant neoplasm of perivascular epithelioid cells of the liver. *Arch Pathol Lab Med* 2006;130:1219-22.
17. Nguyen TT, Gorman B, Shields D, Goodman Z. Malignant hepatic angiomyolipoma: report of a case and review of literature. *Am J Surg Pathol* 2008;32:793-8.