Fine Needle Aspiration Cytology of Pulmonary Epithelioid Hemangioendothelioma with Prominent Hyaline Degeneration

- A Case Report -

Kang Min Han · Dong Hoon Kim Na-Hye Myong
Department of Pathology, Dankook University Hospital, Dankook University College of Medicine, Cheonan, Korea

Received: April 1, 2010
Accepted: June 8, 2010

Corresponding Author
Na-Hye Myong, M.D.
Department of Pathology, Dankook University College of Medicine, 29 Anseo-dong, Dongnam-gu, Cheonan 330-714, Korea
Tel: +82-41-560-3891
Fax: +82-41-661-9127
E-mail: myongnh@dankook.ac.kr

Pulmonary epithelioid hemangioendothelioma (PEH) is a rare vascular tumor of low to intermediate malignant potential, and PEH can mimic other more common tumor entities pathologically as well as clinically. Compared to its well-recognized histological features, its cytological findings have been reported rarely to be plasmacytoid or epithelioid cells with abundant dense or finely granular cytoplasm, cytoplasmic vacuoles, round nuclei and prominent nucleoli. We report here on the fine needle aspiration cytologic findings of a 38-year-old woman with EH of the lung, that showed in addition to its classical cytomorphology, a somewhat peculiar cytologic finding such as big twig-like rosettoid structures with prominent hyalinized stroma. This tumor was histologically and immunohistochemically proven to be PEH by primary antibodies for CD31, CD34 and vimentin. We emphasize that the accuracy of making a cytologic diagnosis of this rare tumor can be increased by recognizing the peculiar cytologic finding that we report on here.

Key Words: Hemangioendothelioma, epithelioid; Lung; Biopsy, fine needle

CASE REPORT

Clinical history

A 38-year-old woman visited Dankook University Hospital due to chronic cough and a recent onset of pain in the left upper abdomen and flank. Chest radiography revealed about a 2.5 × 2.0 cm-sized round mass in the left lower lung zone and additional chest computed tomography (CT) showed multiple bilateral pulmonary nodules at both lower lobes along with plaque-like pleural thickening. Abdominal CT also revealed a small hemangioma-like lesion at the segment V in the liver. The possibility of pulmonary tuberculosis or a certain metastatic lesion was clinically suspected. Fluoroscopy-guided percutaneous needle aspiration was done on the main mass in left lower lung. Two weeks later, the patient underwent a wedge-resection of the lung mass. Postoperatively, she received one cycle each of chemotherapy and radiotherapy, with the maintenance of pain control. However, 8 months later she admitted again with the chief complaint of aggravated pain in the chest and a newly ap-
peared abdominal wall mass. The mass was histologically con-
confirmed by an excisional biopsy to be metastatic epithelioid hem-
angioendothelioma. Her clinical status was deteriorated despite
symptomatic treatment, and she died about 7 months after the
excision of the abdominal mass.

**FNA cytology findings**

FNA of the pulmonary lesion yielded a relatively abundant
fibrin-rich exudative aspirate. The Papanicolaou stain showed a
biphasic pattern throughout the area; a) loosely cohesive or dis-
cohesive cells and b) tightly cohesive cell clusters in the fibri-
nous inflammatory background (Fig. 1). The discohesive tumor
cells were epithelioid and the nuclei were eccentric. Some cells
exhibited bi- or multinucleation and intranuclear cytoplasmic
inclusions were occasionally found. The nucleoli were small,
but relatively prominent. The cytoplasm was dense and granu-
lar and intracytoplasmic vacuoles were occasionally observed
(Fig. 2). Aggregated tumor cell clusters revealed the big elon-
gated rosettoid arrangement with the central anuclear area and
the peripheral rosettoid cellular rimming (Fig. 2). On higher
magnification, mild nuclear pleomorphism was found, but there
were no mitotic figures. Based on the above cytologic findings,
adenoacarcinoma and epithelioid hemangioendothelioma were
considered as the main cytologic differential diagnoses.

**Histopathology**

Grossly, the pulmonary mass was a well-demarcated, yellow-
ish white, round, firm nodule that measured 1.8 × 1.7 × 1.6
cm. The cut surface was yellowish and solid with grayish white
myxoid peripheral rim.

On the low-power field of the light microscope, the tumor
was usually well-demarcated, but focally poorly demarcated due
to intraalveolar extension. The center of the tumor was predom-
inantly composed of an exuberant eosinophilic hyaline matrix
with necrotic cell shadows, but there were no calcified or ossi-
ified areas. Distinctively plump epithelioid cells were seen main-
ly at the peripheral rims, and these cells focally extended to the
alveolar spaces. The tumor cells were usually arranged in an
alveolar pattern along the scaffolds of interstitial connective tis-

sue septa (Fig. 3). Among the tumor cells, multifocal spotty
necrosis and chronic inflammatory cell infiltration were also
found. On close examination, the plump epithelioid cells fre-
quenty showed variable-sized intracytoplasmic vacuoles, along

**Fig. 1.** A fine needle aspirate of the lung shows the biphasic pat-
tern of a big cohesive cell cluster and some scattered discohesive
epithelioid cells (Papanicolaou stain).

**Fig. 2.** The epithelioid tumor cells are arranged in a big rosettoid
pattern (**"**), showing plump and occasionally vacuolated cyto-
plasms (arrows) and eccentric nuclei (Papanicolaou stain).

**Fig. 3.** The tumor cells are growing in nests along the alveolar spa-
ces and characterized by the plump epithelioid cells with occa-
sional intracytoplasmic vacuoles.
DISCUSSION

PEH is a rare vascular tumor of the lung of low to intermediate malignant potential, and this used to be described as “intravascular bronchioalveolar tumor (IVBAT)” because it was believed to have an epithelial origin with adjacent vascular invasion. In practice, it mimics epithelial cells or histiocytes histologically, but immunohistochemical and ultrastructural studies have demonstrated that it originates from endothelial cell rather than epithelial cells. Despite considerable similarities to epithelioid hemangioendothelioma of other sites, PEH has a distinctive clinical nature. In most cases, PEH occurs predominantly in females with the mean age of 39 years (range, 12 to 61 years), with over half of them under the age of 30 years. It is generally identified incidentally as multiple bilateral nodules on chest CT because it is usually asymptomatic, although clinical symptoms are occasionally presented with chest pain, cough, sputum and on rare occasion alveolar hemorrhage. The present case was first diagnosed due to her back pain and cough of a long duration. Due to its multiple bilateral nodularity, it may be initially regarded as metastatic carcinoma or chronic granulomatous disease, as in our case.

Following a thorough review of the literature, including a Korean cytologic report, we can summarize some distinctive cytological features of PEH as follows. The tumor cells are scattered singly or arranged in cords, nests or loosely cohesive clusters. The cells are epithelioid with dense granular cytoplasm. The nuclei are round to oval, eccentric (plasmacytoid) and often bi- or multinucleated. Each nucleus has a vesicular chromatin pattern and shows one or two small prominent nucleoli. Intranuclear inclusions may be sometimes observed. Cytoplasmic vacuolation is one of the most remarkable findings in PEH. Fragmented red blood cells are occasionally seen, which strongly supports that PEH is derived from a vascular origin.

In addition to the previously reported cytological features, we report here a somewhat peculiar cytologic finding, that is, the big twig-like rosettid epithelioid cell clusters with hyalinized stromal cores. This cytologic finding has not yet been reported in any of the cytologic literature.

Many neoplastic conditions can share the common cytomorphology in that they have epithelioid cells with cytoplasmic vacuolation and prominent nucleoli. First, primary adenocarcinoma should be initially included in the differential diagnosis because of its higher incidence. Adenocarcinoma has a female predominance and cytologic features of prominent intracytoplasmic vacuolation and often recognizable nucleoli. However, it lacks mesenchymal elements such as a hyalinized core. Second, the possibility of mesothelioma should be taken into account. While it is less frequent for the cytoplasm to be vacuolated, the vacuoles can be observed in mesothelioma cells. It can also show not only bi- or multinucleation but also a collagenous core. The only way to resolve this problem is to employ an immunohistochemical technique using mesothelial cell markers such as calretinin. Third, high-grade angiosarcoma should be considered due to endothelial differentiation. Epithelioid and discohesive features can be seen in some angiosarcomas. However, prominent cytoplasmic vacuolation is not commonly found in angiosarcoma. Additionally, other tumors should be excluded, including malignant melanoma, large cell lymphoma and anaplastic plasmacytoma. Thus, auxiliary immunohistochemical and ultrastructural studies are usually needed to arrive at a final diagnosis of PEH, in addition to the subtle morphological differential points.

In conclusion, the big rosettid pattern with a central hyalinized core can be a key cytologic feature of PEH with prominent hyaline degeneration. Therefore, when one encounters multiple bilateral nodules on chest imaging, having an awareness of the cytologic feature that we stressed here may help to achieve a more accurate cytologic diagnosis for PEH.
REFERENCES