

## Hepatoid Thymic Carcinoma – A Case Report –

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We report here on a rare case of hepatoid thymic carcinoma in a 34-year-old man. The patient complained of a high fever and headache, and a 6.6cm-sized anterior mediastinal mass was found on chest computed tomography (CT). There was no hepatic mass seen on abdominal CT. The resected mass consisted of epithelioid cells with abundant eosinophilic cytoplasm, pleomorphic vesicular nuclei and prominent nucleoli, and the mass was surrounded by thymic tissue. The tumor cells were immunopositive for cytokeratin 7,  $\alpha$ -1-antitrypsin, hepatocyte staining, and epithelial membrane antigen, but they were negative for CD5,  $\alpha$ -fetoprotein (AFP) and placental alkaline phosphatase, and this all led to a diagnosis of hepatoid thymic carcinoma rather than hepatoid yolk sac tumor. This entity should be included in the differential diagnosis of epithelioid thymic tumors.

**Key Words :** Thymus; Thymus neoplasms; Carcinoma, hepatocellular

Thymic epithelial tumors are divided into thymomas, thymic carcinomas and neuroendocrine tumors.<sup>1</sup> The WHO classification of thymic tumors subdivides the thymic carcinomas into squamous cell carcinoma, basaloid carcinoma, mucoepidermoid carcinoma, lymphoepithelioma-like carcinoma, sarcomatoid carcinoma, clear cell carcinoma, papillary adenocarcinoma, non-papillary adenocarcinoma, carcinoma with t(15;19) translocation, and undifferentiated carcinoma.<sup>1</sup> Non-papillary adenocarcinomas are a heterogeneous group of rare carcinomas that can be found in the thymus. Among them, the term hepatoid thymic carcinoma has been proposed.<sup>1,2</sup> We describe another case of hepatoid thymic carcinoma.

### CASE REPORT

A 34-year-old male patient was admitted to the hospital because of a persistent high fever and headache. Chest computed tomography (CT) revealed a 6 × 5.3 cm-sized right anterior mediastinal mass (Fig. 1). He did not have myasthenia gravis. His serum  $\alpha$ -fetoprotein (AFP), carcinoembryonic antigen (CEA), and

CA19-9 levels were within the normal limits. A biopsy was performed, and the lesion was diagnosed as malignant epithelioid tumor. We performed thoracotomy, and a 7 cm-sized firm mass was found abutting the trachea, and this mass originated from the thymus. The mass was resected, and the specimen was a well demarcated firm mass with a smooth outer surface. The cut surface was yellowish gray and lobulated with central necrosis; the mass measured 6.6 × 6.5 cm (Fig. 2). Microscopically, this was a well demarcated tumor that was surrounded by a fibrous capsule and normal thymic tissue (Fig. 3). The tumor resembled a hepatocellular carcinoma, and it was composed of solid or trabecular sheets of epithelioid cells with distinct cell borders, abundant eosinophilic cytoplasm, pleomorphic vesicular nuclei, prominent nucleoli, a thick irregular nuclear membrane and frequent mitoses (Fig. 4A, B). The tumor cells often showed clear cytoplasmic change (Fig. 4C). Among the tumor cells were some inflammatory cells. A total of seven representative sections from the tumor showed consistent cellular features. On immunohistochemical staining, the tumor cells showed positive reactions for CK7, CEA,  $\alpha$ -1-antitrypsin, hepatocyte staining and epithelial membrane antigen (EMA) (Fig. 5), but the tumor cells were negative for

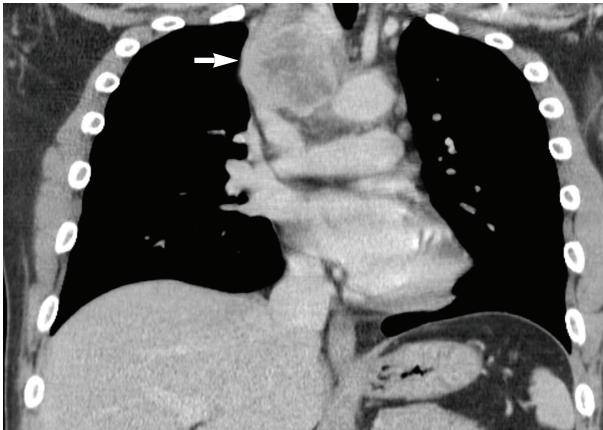


Fig. 1. Chest computed tomography shows about a 7 cm sized, well demarcated, slightly lobulated mass (arrow) at the right paratracheal area of the right anterior mediastinum.

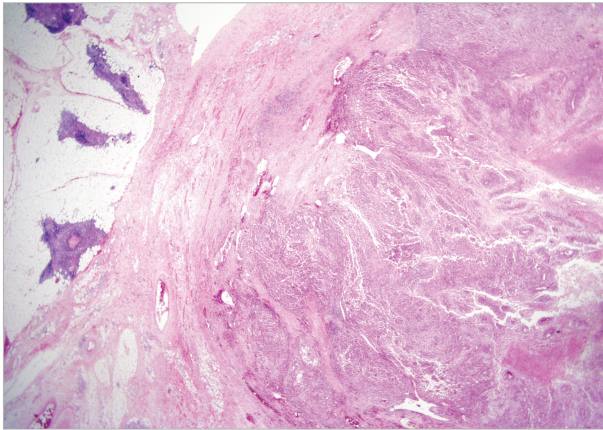


Fig. 3. The tumor is microscopically well delineated from the thymic tissue.

CK19, CD5,  $\beta$ -HCG, AFP and placental alkaline phosphatase. Particularly, the hepatocyte immunostaining was diffuse among the tumor cells.

One month after the operation, the patient developed a tender mass on the upper back, which turned out to be a metastatic lesion. On positron emission tomography (PET), hypermetabolic lesions were also found in the lung and left axilla. The patient underwent adjuvant chemotherapy without response, and he has been lost to follow up.

## DISCUSSION

In general, thymic carcinoma is a rare malignant neoplasm with a poor prognosis.<sup>3</sup> The case we are reporting on also showed aggressive behavior, but this present case deviates from common



Fig. 2. The cut surface of the specimen reveals a 6.6 cm sized well demarcated yellowish gray lobulating mass with central necrosis.

thymic carcinomas from several perspectives. First, the microscopic morphology of the tumor differed from those that commonly occur in the thymus. There are very few reports in the literature dealing with mediastinal tumors with these kinds of morphological characteristics.<sup>4-6</sup> Even the WHO classification gave only a small section to describe the morphology of this entity.<sup>1</sup> Second, the immunohistochemical staining results are unique. Thymic carcinomas are generally known to be CD5 positive.<sup>7</sup> However, this case showed negativity for CD5 immunostaining. Although a variable expression of CD5 in thymic carcinomas is already known,<sup>8</sup> there has been only one previously reported case of thymic carcinoma with negativity for CD5 and simultaneous positivity for hepatocyte immunostaining.<sup>2</sup>

Hepatoid carcinomas can be found in various organs, including the gastrointestinal tract, the lung, and the male and female genital tracts.<sup>9-18</sup> The main differential diagnoses include metastatic hepatocellular carcinoma and hepatoid yolk sac tumor. Metastatic hepatocellular carcinoma can be ruled out according to the evidence of no primary tumor in the liver, as in this case. The differential diagnosis from hepatoid yolk sac tumor can be problematic, but it can be aided by the histological and immunohistochemical characteristics of the tumor. Hepatoid yolk sac tumors of the mediastinum usually contain foci of conventional yolk sac tumor component with intra- and extracellular eosinophilic hyaline globules, and the tumor cells express AFP.<sup>5</sup> Unlike the hepatoid yolk sac tumors of the mediastinum, hepatoid thymic carcinoma shows a homogeneous hepatoid morphology and AFP negativity<sup>2</sup> with other immunohistochemical profiles, including the expressions of EMA and  $\alpha$ -1-antitrypsin and hepatocyte staining.

Compared with the previous case,<sup>2</sup> several clinical differences



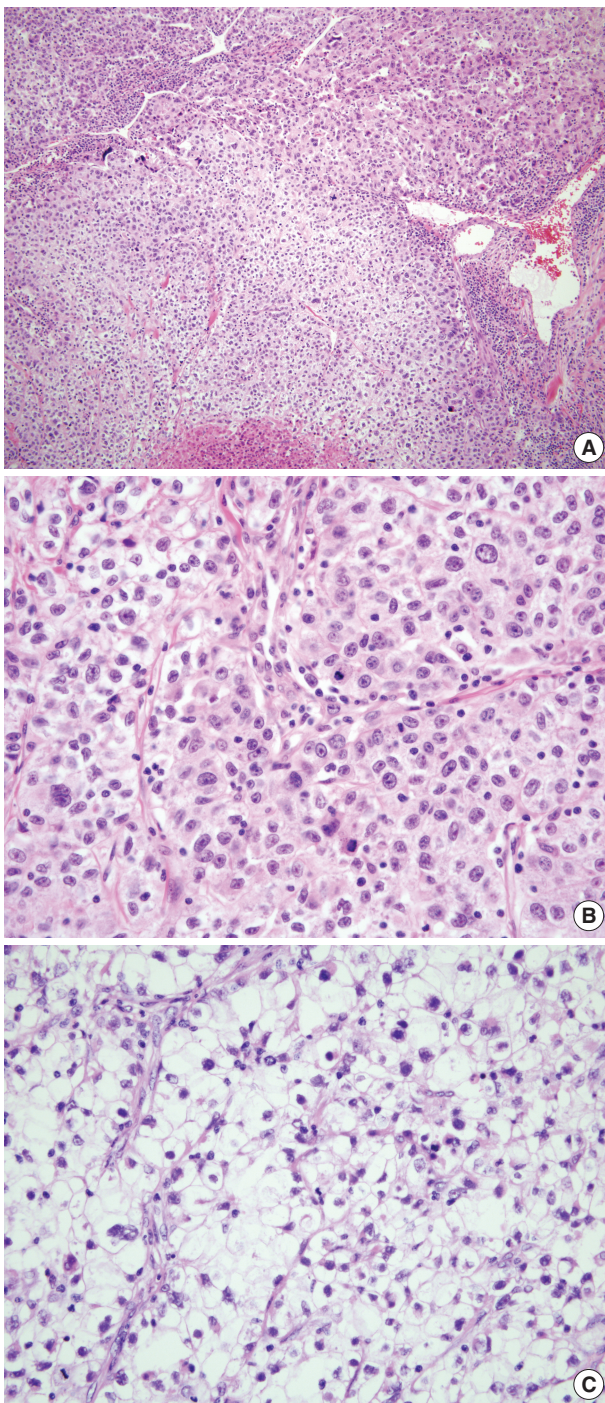


Fig. 4. The tumor histologically shows a nodular and trabecular pattern (A), epithelioid cells with distinct cell borders, abundant eosinophilic cytoplasm, pleomorphic vesicular nuclei and one or two prominent nucleoli (B), and focal clear cell change (C).

are present in our case, including the patient's younger age, the male gender, the smaller tumor size and more aggressive tumor growth. However, the histomorphologic and immunohistochemical similarities of the two cases strongly support the existence

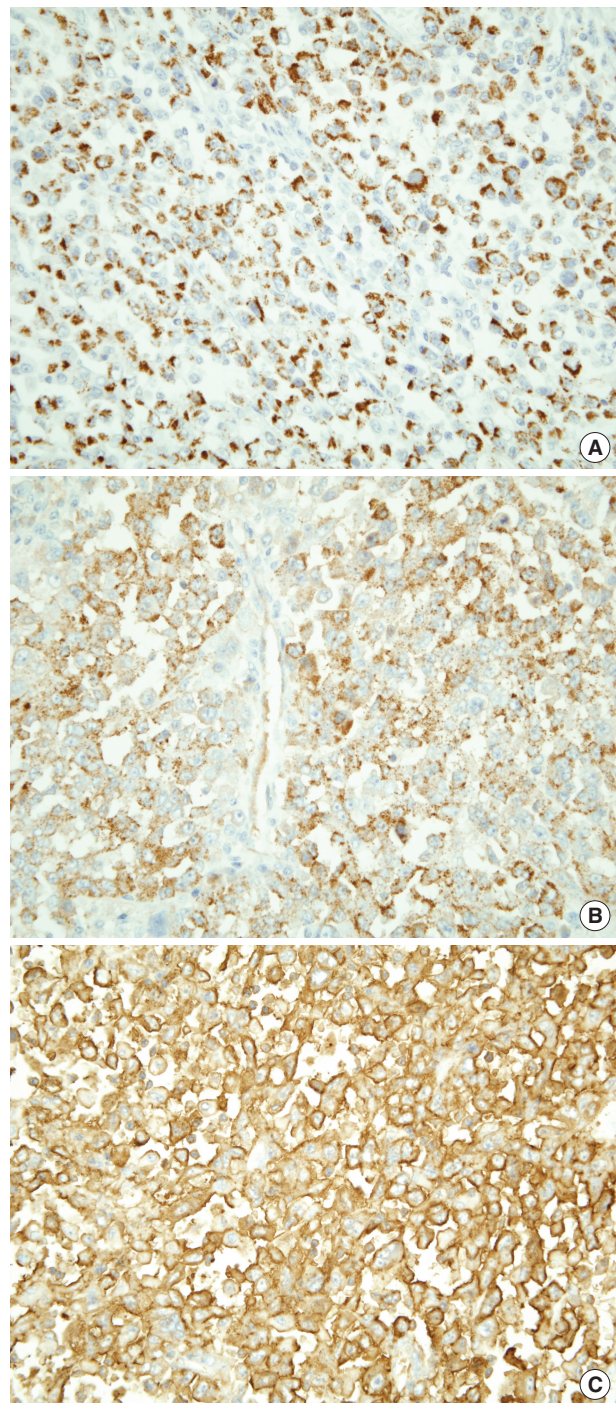


Fig. 5. Immunostaining positivity of the tumor cells for hepatocyte staining (A),  $\alpha$ -1-antitrypsin (B) and epithelial membrane antigen (C).

of hepatoid carcinoma of a thymic origin. As to the histogenesis of this peculiar tumor, the authors of the previous report favored an endodermal derivation rather than a germ cell origin.<sup>2</sup> More case studies are needed to firmly determine the pathobiological

and clinical characteristics of the hepatoid thymic carcinoma.

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