J Med Sci,
Vol 42, No. 1, March 2010: 52-57

Metastatic poorly differentiated adenocarcinoma of the sternum unsolved diagnostically by immunohistochemical staining: a case report

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ABSTRACT

A 42 year-old male admitted to Dr. Sardjito Hospital, Yogyakarta because of a painful sternal mass that was becoming larger since 6 months before hospitalized. He was diagnosed as malignant thymoma based on microscopic examination of specimen obtained from FNAB. Histological examination from biopsy specimen showed a tumor, composed of epithelial cells and arranged in nests, solid, partly tubular and glandular structures considered thymic carcinoma with differential diagnosis a poorly differentiated adenocarcinoma. PAS staining was positive and PAS diastase was negative, considered that the cytoplasm contained glycogen. The tumor cells showed expression of polykeratin (CAM5.2, TTF1, and CD10). Neurogenic and neuroendocrine markers (S100, CD56, CD57), mesothelial markers (calretinin, EMA), and mesenchymal markers (vimentin, CD68, desmin, SMA) are negative. The impression was metastatic adenocarcinoma. In case of metastatic one could consider a metastasis of a lung adenocarcinoma or thyroid carcinoma (TTF1 +, but CD10 expression did not fit) and renal cell carcinoma (CD10+, but TTF1 did not fit). The final considered diagnosis was poorly differentiated adenocarcinoma, metastasis from the lung, thyroid, or kidney.
The aim of this presented article is to report a difficult case of metastatic poorly differentiated adenocarcinoma of the sternum in which immunohistochemical staining could not solve the morphological diagnostic problems, to emphasize the importance of clinical information and good morphologic evaluation to determine the diagnosis.

Key words: metastatic - poorly differentiated adenocarcinoma - thymic carcinoma - sternum - immunohistochemical staining

INTRODUCTION

Sternal tumors encompass a kaleidoscopic panorama of bone and soft tissue tumors. Included among these are benign and malignant primary neoplasms, invading neoplasms from breast, lung, pleura, or mediastinum, and neoplasms by metastases.[1] Primary malignant tumors of the sternum are very rare and most of them are sarcomas, including several histological types.[2] Primary neoplasm of manubrium and sternum constitutes 15% of all primary chest wall bone tumors. Two-thirds of sternal tumors are metastatic. Most frequently, these are breast cancer invasion, lung or pleural malignancy invasion or rarely, solitary metastasis from kidney and thyroid.[1] In case of metastatic tumors with a limited biopsy, it may be difficult to determine the exact histopathological diagnosis and the site of origin. In this setting, immunohistochemical staining has an important role and becomes the standard of practice. However, immunohistochemical staining is not always able to solve the diagnostic problems. Otherwise in that case, pathologists have to reevaluate clinical information and morphologic examination to determine definitive diagnosis.

In this presented article, a difficult case of metastatic poorly differentiated adenocarcinoma of the sternum in which immunohistochemical staining

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could not solve the morphological diagnostic problems was reported to emphasize the importance of clinical information and good morphologic evaluation to determine the diagnosis.

CASE

A 42 year-old male admitted to Dr. Sardjito Hospital, Yogyakarta because of a painful anterior chest wall mass that was becoming larger since 6 months before hospitalized. He also had decreasing appetite and body weight. He had no complains of difficulty in breathing, urination, and defecation. He had history of nephrolithiasis. At the time of his visiting, there was no complain of bloody urine.

Clinical examination revealed a poorly demarcated mass, 10 cm in diameter, fixed, with hard and rubbery consistency on anterior chest wall. The chest X ray revealed a mass in sternum bone extending into right chest cavity. The chest CT scanning revealed a mass destructing sternum bone extending into right chest cavity with enlargement of parasternal lymph nodes. Its feature suggested a sarcoma with differential diagnosis of lymphoma. The abdominal CT scanning suspected a metastatic lesion in liver. USG impressed liver cirrhosis with a mass in the right side of the liver suspecting metastatic lesion, enlargement of the spleen, and nephrolithiasis. Complete blood count revealed leucopenia and anemia. Liver function test revealed increased ALT. Urine analysis revealed microhematuria. Electrolyte levels and kidney function test were within normal limit.

Fine needle aspiration biopsy (FNAB) of the mass was done. Microscopic examination of specimen obtained from FNAB showed polymorphic clustered and dispersed cells with moderate to no cytoplasm, big nuclei, some of them more than one, with coarse chromatin. There were also tubular or rosette pattern. The background showed many erythrocytes and lymphocytes (FIGURE 1). The diagnosis of malignant thymoma was determined based on microscopic examination of specimen obtained from FNAB.

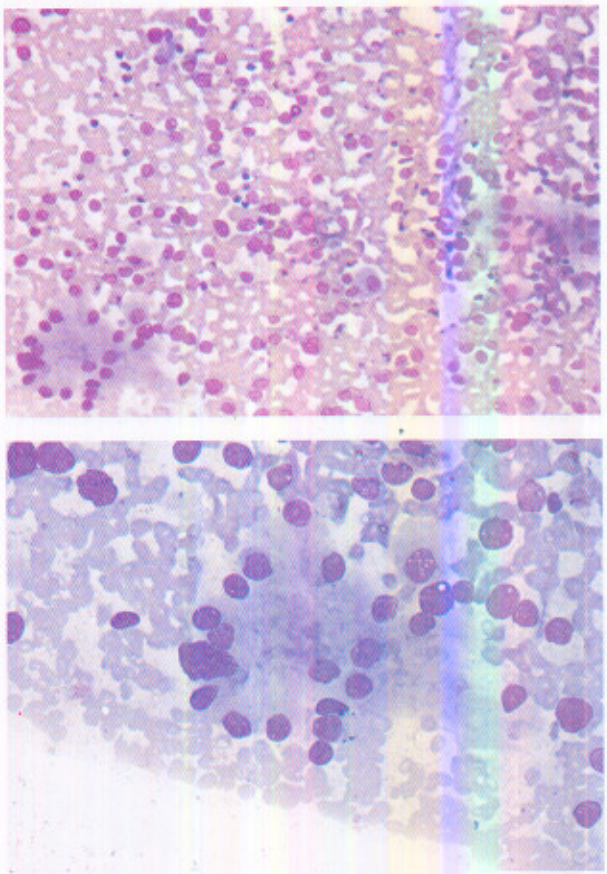

FIGURE 1.Smear obtained from FNAB showed polymorphic clustered cells forming tubular or rosette pattern in the background of many lymphocytes (1a.Giemsa staining, 100 X, 1b.Giemsa staining, 200X)

Biopsy of the sternal mass was done. Macroscopic examination revealed two brown fragments of tissue each measured 1 x 0.5 x 0.2 cm with rubbery consistency.

Histological examination from the biopsy specimen showed a tumor, composed of epithelial cells and arranged in nests, solid, partly tubular and glandular structures. The tumor cells were polymorph with moderate to abundant eosinophylic, granular, oncocytic, and partly clear cytoplasm. The nuclei were varied round to oval with coarse and clumping chromatin and conspicuous nucleoli. Mitotic figure was moderate. Morphological pattern considered a thymic carcinoma with differential diagnosis of a poorly differentiated adenocarcinoma (FIGURE 2).

PAS staining was positive (FIGURE 3) and PAS diastase was negative, considered that the cytoplasm contained glycogen. The tumor cells showed expression of polykeratin (CAM5.2, TTF-1, and CD10). FIGURE 4 and 5 showed TTF-1 and CD10 positivity. Neurogenic and neuroendocrine markers (S100, CD56, CD57), mesothelial markers (calretinin, EMA), and mesenchymal markers (vimentin, CD68, desmin, SMA) are negative. The impression was metastatic adenocarcinoma. In case of metastatic one could consider a metastasis of a lung adenocarcinoma or thyroid carcinoma (TTF-1+, but CD10 expression did not fit) and renal cell carcinoma (CD10+, but TTF-1 did not fit). The final diagnosis was poorly differentiated adenocarcinoma: metastasis from the lung, thyroid, or renal cell carcinoma was considered.

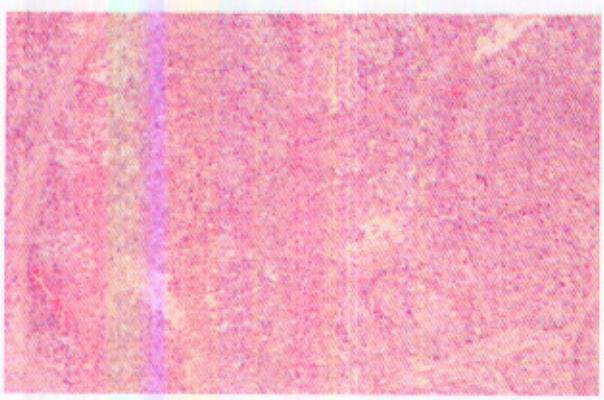

FIGURE 2a.Microscopic feature of presented case showed a tumor composed of epithelial cells and arranged in nests, solid, partly tubular and glandular structures. (HE staining, 100X)

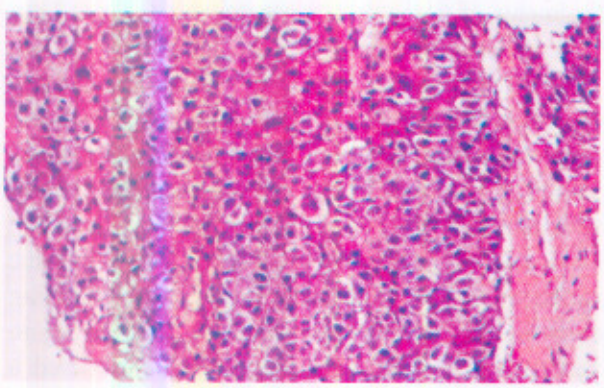

FIGURE 2b.Microscopic feature of presented case showed polymorph tumor cells with moderate to abundant eosinophylic, granular, oncocytic, and partly clear cytoplasm. (HE staining, 200X)

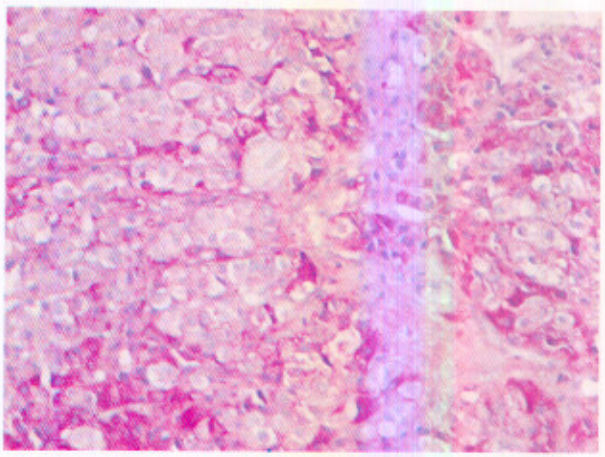

FIGURE 3. PAS staining of the presented case was positive (200X)

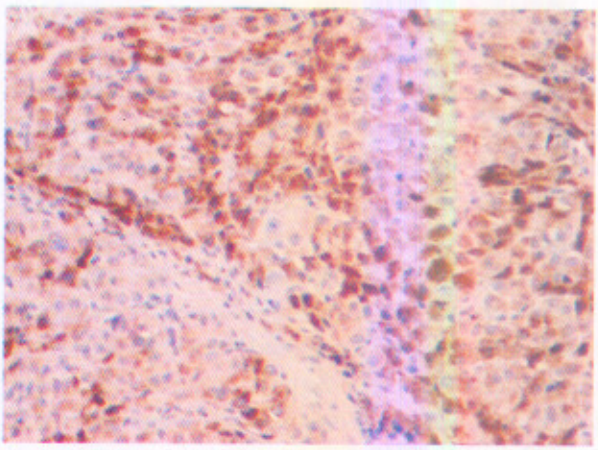

FIGURE 4. Positive expression of TTF-1 showed cytoplasmic brown staining

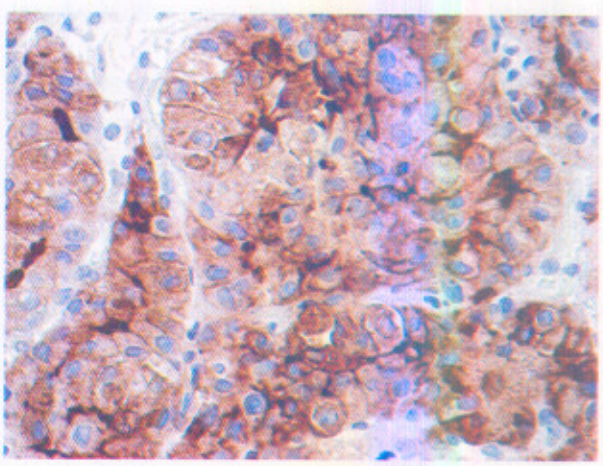

FIGURE 5. Positive expression of CD10 showed cytoplasmic brown staining

DISCUSSION

Various cancers have been reported to metastasize to the sternum as a solitary tumor, including breast, lung, thyroid, renal cell, colon, and endometrial carcinomas.[3-8] Metastatic tumors present symptomatically earlier because of their increased doubling time.[9-12] The chief complaint of this presented case was a painful sternal mass that was becoming larger since 6 months before hospitalized accompanied by decreasing in appetite and body weight, but without complaining of difficulty of breathing, urination, and defecation. The sternal mass grew rapidly and reached diameter of 10 cm. History taking and clinical examination gave impression of a primary tumor of the sternum or invading tumor from anterior mediastinum with progressive growth. Additional examination including chest X ray, chest CT scanning, abdominal USG, and complete laboratory examination supported a primary tumor of the sternum or invading tumor from anterior mediastinum with a suspicion of metastasis to liver.

Fine needle aspiration biopsy suggested a malignant thymoma. The presented case considered a malignant thymoma from anterior mediastinum that invading sternum, supported by cytological features and clinical evidence that the most common lesion in anterior mediastinum are thymoma and thymic cyst.[13] Primary tumors of the sternum are uncommon. Of 2000 primary bone tumors in a series at the Mayo Clinic reported by Pascuzzi and colleagues[14] in 1957, only 126 (6%) occurred in the ribs and 18 (1%) were in the sternum. Nearly half of all chest wall tumors originate in cartilaginous tissue[15] and the most common primary malignant tumour of the chest wall is chondrosarcoma.[16]

Microscopic pattern on HE staining of the tumor considered a thymic carcinoma with differential diagnosis of a poorly differentiated adenocarcinoma. Thymic carcinoma usually presents in 4th to 6th decade[17]. It is defined as a thymic epithelial tumor exhibiting clearcut cytologic features of malignancy.[18,19] It displays a relatively large variety of microscopic patterns. They differ from all other types of thymomas in the following respects. Firstly, they are very rarely associated with myasthenia gravis or any other immune-mediated systemic diseases. Secondly, they generally lack all of the ancillary features of thymoma seen with one or another of the other types, such as perivascular space, foci of medullary differentiation, abortive Hassal's corpuscles, rosettes, or gland-like spaces. Thirdly, they lack immature T lymphocytes.[13] Thymic carcinomas lack all of the morphologic and functional attributes of the other thymoma types. Their appearance is instead similar to and sometimes indistinguishable from that of corresponding carcinoma types in other organs, and their specific identification as thymic neoplasms can therefore be difficult or impossible. The diagnosis is often one of exclusion, in the presence of a malignant epithelial tumor located in the thymic region in the absence of disease in the lung or any other organ. In this presented case, the morphological pattern considered a thymic carcinoma, but the presence of tubular and glandular space made the possibility of a poorly differentiated adenocarcinoma.

There are some immunostains that can be of great of assistance in differentiating between thymic carcinoma and other carcinoma from other organs, such as TTF-1 and CD10.

Human thyroid transcription factor-1 (TTF-1) is a single polypeptide of 371 amino acids. It is expressed at the onset of lung and thyroid organogenesis and is essential for the normal development of these organs.[20,21] The exclusive expression of TTF-1 in thyroid follicular epithelial cells, pulmonary type II cells, and Clara cells makes it a useful diagnostic epitope to identify adenocarcinomas arising from or expressing differentiation toward these cell types. It is also a useful marker in differential diagnosis of primary tumor of lung and thyroid versus metastases from other organs.[22] TTF-1 is expressed in 80-100% of thyroid neoplasms[23] and 70-100% of adenocarcinoma of lung.[22] TTF-1 is very rarely expressed in nonpulmonary and nonthyroid adenocarcinomas. TTF-1 was not expressed by thymic carcinoma.[13]

In the presented case, the tumor cells showed expression of CAM5.2 considered an epithelial origin. The expression of TTF-1 indicated that the tumor was not thymic carcinoma, but a metastatic tumor from lung or thyroid. Thymic carcinoma of

papillary type resembles papillary thyroid carcinoma by virtue of the complex arborizing structure and the presence of psammoma bodies.[24] However, it lacks optically clear nuclei, it is positive for CD5, and it shows no reactivity for thyroglobulin or TTF-1.[25]

CD10 antibodies recognize a 90 – 10-kDa cell surface glycoprotein CALLA that is present in a variety of cell types including some epithelial cells (liver canaliculli, renal tubules, enterocytes), and hematopoietic cells including lymphoid cells and granulocytes.[26] Despite the wide range of tumors which stain with CD10, in some situations it is useful as a clear renal cell carcinoma marker since other renal cell carcinoma subtypes, with the exception of papillary renal cell carcinoma, usually do not show CD10 positivity.[27,28] Clear cell renal cell carcinoma stains with CD10 in 94% of cases, while chromophobe renal cell carcinoma is consistently negative, and oncocytoma is positive for CD10 in only one-third of cases.[27]

In the presented case, the tumor expressed CD10 considered a metastatic of renal cell carcinoma. The presence of large amounts of glycogen-rich, clear cytoplasm, in the tumor cells of thymic carcinoma of clear cell type resulted in a striking resemblance with renal cell carcinoma.[13]

The final diagnosis in this presented case was poorly differentiated adenocarcinoma, metastasis from the lung, thyroid, or kidney was considered. There was diagnostic confusing because double expression of TTF-1 and CD10. In these presented case, immunohistochemical staining (IHC) had limitation, could not solve the diagnostic problem.

Certain practical limitations of IHC should be noted. While IHC stains may be of great value in the identification of the lineage of a cell (and the derivative neoplasm), their value is much more limited with regard to distinguishing normal tissue from neoplastic, or separating benign from malignant neoplasms. In marking these distinctions, heavy reliance still is placed upon traditional morphology, although IHC stains that are useful within this context are beginning to make an appearance. However, these stains generally are not helpful in making distinctions among lesion that already have been characterized as anaplastic malignancies on morphologic grounds, and their utilization and interpretation is deferred to those organ system chapters where they do find application.[22]

In this presented case, determining the definitive diagnosis relied on further clinical information to check for possibilities of tumor of lung, thyroid, and kidney. Unfortunately, the patient was loss of follow up because of an earthquake in Yogyakarta in 2006. In a difficult case such as the presented case, good morphologic evaluation must be done by pathologist for excluding the differential diagnosis. A definitive diagnosis will not be determined without further clinical information and good morphologic evaluation.

CONCLUSION

A difficult case of metastatic poorly differentiated adenocarcinoma of the sternum in which immunohistochemical staining could not solve the morphological diagnostic problem was reported. Considering that immunohistochemical staining was not always able to solve the diagnostic problem, clinical information and good morphologic evaluation is very important to determine the definitive diagnosis in a difficult case.

ACKNOWLEDGMENT

We would like to thank also Pathology Anatomy Installation, Dr. Sardjito Hospital for giving permission to take histopathology data of the patients.

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