

Case Report

Metaplastic thymoma with CD56 and S-100 expression in spindle cells: report of a case indicating the utility of CD56 and S-100 for discriminating spindle tumors

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Abstract: Metaplastic thymoma is a subtype of thymoma with a biphasic structure comprising polygonal cells and spindle cells, and is extremely rare. Although expression of the neural marker S-100 has previously been observed in only two patients, we encountered a valuable case in which both CD56 and S-100 were expressed in spindle cells. We report our findings here. A 33-year old man visited our hospital with cough and bloody phlegm. Chest computed tomography (CT) revealed a microlobulated mass measuring 5.4×4.4 cm in the anterior mediastinum. The patient underwent thymectomy with median sternotomy. Pathological examination revealed a biphasic pattern of epithelial and spindle cells. On immunohistochemistry, spindle cells were negative for AE1/AE3, but positive for EMA and vimentin. The most interesting immunohistochemical finding was that the spindle cells were diffusely positive for both CD56 and S-100. Numerous spindle cell-containing tumors exhibit a biphasic pattern, and differential diagnosis can be difficult with morphological diagnostic methods or immunostaining using existing markers. No reports to date have conducted a detailed investigation of expression levels of CD56 and S-100 in metaplastic thymoma, and accumulation of data in additional patients is therefore necessary. Nonetheless, the present findings suggest that immunohistochemical findings in which CD56 is expressed in spindle cells, S-100 shows markedly greater expression in spindle cells, and CD20 is absent from both components may be useful in differentiating between metaplastic thymoma and other tumors containing spindle cells.

Keywords: Metaplastic thymoma, CD56, S-100, CD20, spindle cells

Introduction

Metaplastic thymoma is a tumor that exhibits a biphasic pattern of polygonal cells and spindle cells. This entity is known to express epithelial markers such as cytokeratin in the polygonal cells, and mesenchymal markers such as vimentin in addition to epithelial markers in the spindle cells. However, numerous types of spindle cell-containing tumors exhibit a biphasic pattern, and differential diagnosis can be difficult when based on morphological diagnosis or immunostaining with existing markers. Few cases of neuroendocrine marker-positive metaplastic thymoma have been reported, including only two S-100-positive cases. We encountered a case in which the spindle cells of metaplastic thymoma showed expression of both CD56 and

S-100. We report our findings herein, as expression of CD56 and S-100 in spindle cells may be useful in differentiating between metaplastic thymoma and other tumors containing spindle cells.

Case

A 33-year-old man visited our hospital due to cough with bloody phlegm. Chest X-ray and computed tomography (CT) revealed a mass measuring 5.4×4.4 cm in the anterior mediastinum (**Figure 1**). The mass showed a microlobulated margin and no apparent invasion to adjacent organs. Anti-acetylcholine receptor antibody (Ach-R) levels were normal. Under a presumptive diagnosis of thymoma, the patient underwent thymectomy through a median ster-

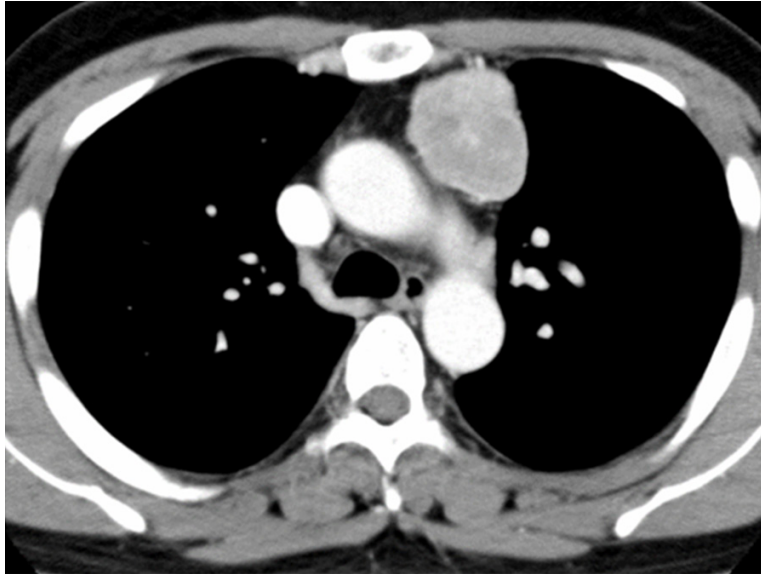


Figure 1. Chest computed tomography (CT) revealed a microlobulated mass that measured 5.4×4.4 cm in the anterior mediastinum.

notomy. The mass was well encapsulated and separated easily from the pericardium. The postoperative course was uneventful and the patient was discharged from hospital on day 14 after surgery. As of the time of writing, he remains free of recurrence. Pathological examination revealed a biphasic pattern consisting of epithelial cells with polygonal or oval nuclei and spindle cells without nuclear atypia (**Figure 2A, 2B**). The tumor showed slight invasion beyond the capsule. No metastatic lymph nodes were detected. Immunohistochemical examination showed the epithelial islands were positive for AE1/AE3, E-cadherin and p63, while negative for epithelial membrane antigen and vimentin. Conversely, the spindle cells were negative for AE1/AE3, E-cadherin and p63, but positive for epithelial membrane antigen and vimentin (**Figure 3A, 3B**). These findings confirmed the diagnosis of metaplastic thymoma (pathological stage, pT2N0M0 stage II). In addition to these typical findings of metaplastic thymoma, the most interesting finding from immunohistochemistry was that the spindle cells were diffusely positive for CD56 and S-100 (**Figure 3C, 3D**), but negative for chromogranin A and synaptophysin.

Discussion

We encountered a case in which spindle cells from metaplastic thymoma showed strong, dif-

fuse expression of CD56 and S-100. Few reports have described expression of neural markers in metaplastic thymoma, and, to the best of our knowledge, this represents the first to demonstrate CD56 expression in metaplastic thymoma (**Table 1**). Although accumulation of data on additional patients and further investigations are necessary, we postulate that immunohistochemical findings of CD56 expression in spindle cells, S-100 expression especially in spindle cells, and absence of CD20 in both components may be useful in differentiating between metaplastic thymoma and other spindle cell-containing tumors.

Metaplastic thymoma is a rare mediastinal tumor with a tissue morphology presenting a biphasic structure comprising polygonal epithelial cells and spindle cells, and is known to account for 1-2% of all thymomas. Typically, the epithelial cells of metaplastic thymoma are positive for AE1/AE3 and p63, partially positive for epithelial membrane antigen, and negative for vimentin according to immunohistochemical staining examinations. In contrast, spindle cells are negative or partially positive for AE1/AE3, negative for p63, locally positive for epithelial membrane antigen, and positive for vimentin [1]. Disorders that must be differentiated from metaplastic thymoma include type A and type AB thymoma, which are thymomas primarily comprising spindle cells, and sarcomatoid carcinoma, synovial sarcoma, malignant mesothelioma, and malignant peripheral nerve sheath tumor (MPNST), as higher-grade tumors exhibiting atypical spindle cells. In particular, type AB thymoma morphologically exhibits a biphasic pattern and can also present similar to immunohistochemical findings to metaplastic thymoma, leading to potential difficulties in differentiating these two types of thymoma. In general, spindle cells in type AB thymoma, similar to spindle cells in type A thymoma, are positive for AE1/AE3 and E-cadherin and negative to partially positive for epithelial membrane antigen. However, Miki et al. [2] reported a “metaplastic subtype” of spindle

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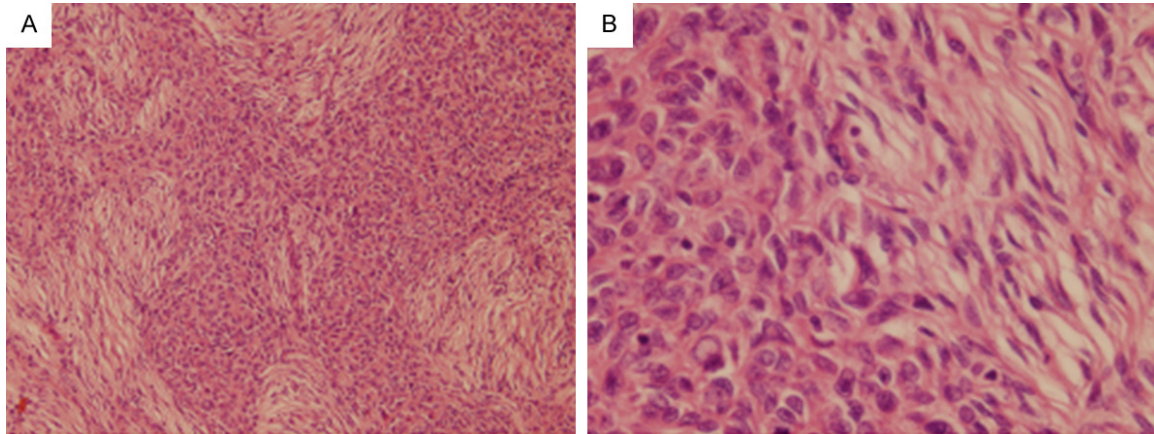


Figure 2. A, B. Tumor showed a biphasic pattern consisting of epithelial cells with polygonal or oval nuclei and spindle cells without nuclear atypia.

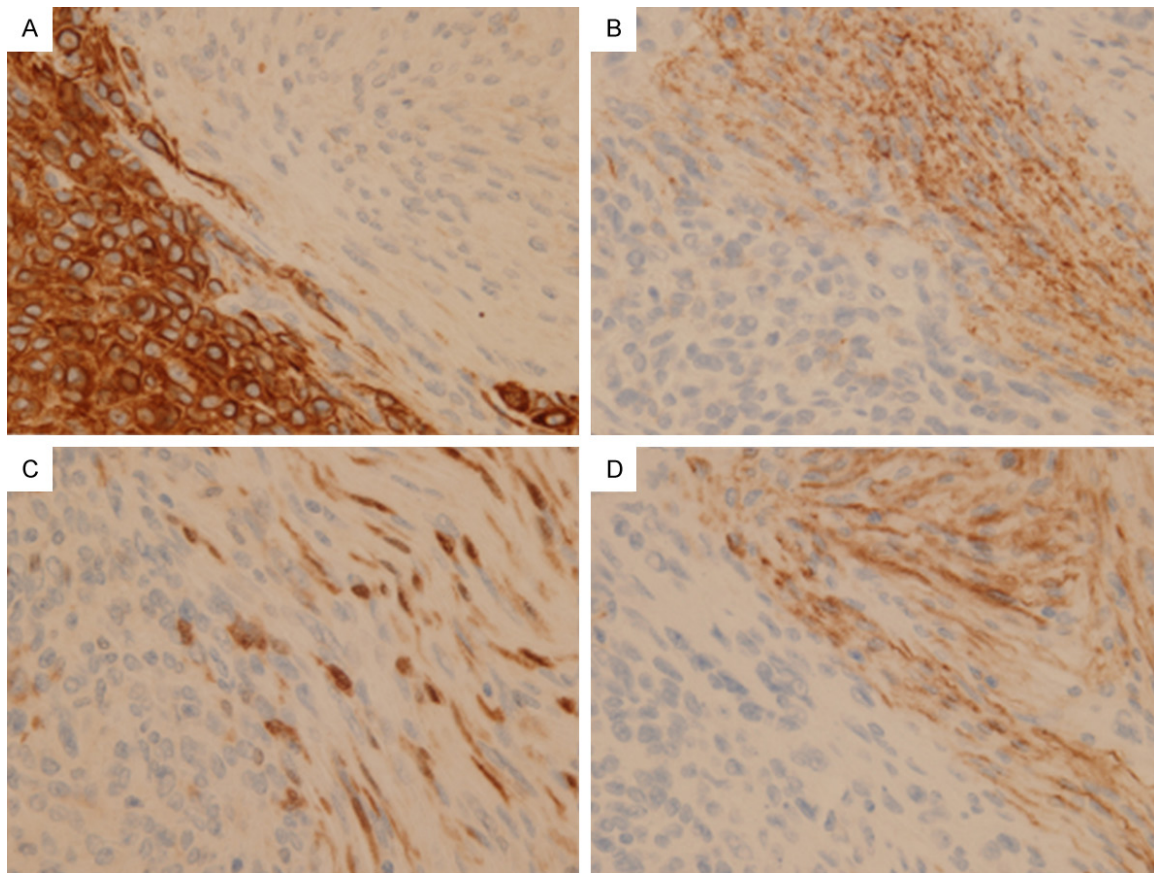


Figure 3. Immunohistochemical examination showed (A) AE1/AE3 was positive in the epithelial islands, while negative in the spindle cells. (B) Epithelial membrane antigen was negative in the epithelial islands, but positive in the spindle cells. (C) CD56 and (D) S-100 were diffusely positive in the spindle cells.

cells in type AB thymoma, in which AE1/AE3 and E-cadherin are negative and vimentin and epithelial membrane antigen are positive, similar to spindle cells of metaplastic thymoma.

They also reported this as a major subtype (14/19 cases, 74%) of type AB thymoma. Differentiating between these two types can be difficult with existing immunostaining markers,

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Table 1. The number of cases that expressed CD56, CD57, S-100 and CD20 in metaplastic thymoma

	CD56	CD57	S-100	CD20
Suster et al. 1997	-	-	1/6 in spindle cells	-
Yoneda et al. 1999	-	0/4	1/4 in both component	-
Lu et al. 2011	-	-	0/1	-
Liu et al. 2012	-	0/7	0/7	0/7
Our case	1/1 in spindle cells	-	1/1 in spindle cells	0/1

(-); not stained.

and the discovery of new markers that are useful in differentiation is highly desirable.

CD56, known as a neural cell adhesion molecule, is a neuroendocrine marker similar to chromogranin and synaptophysin, and is expressed in tumors such as small cell carcinoma, large cell carcinoma, and carcinoid. Although no previous reports have described expression of CD56 in metaplastic thymoma, high expression was evident only in the spindle cells in our case. In addition, although no previous reports have summarized CD56 immunostaining findings in thymoma, both components of thymoma, including type AB thymoma, are known to stain positively for CD57, an uncommonly available marker similar to commonly available CD56, but only in a few scattered cells [3]. Both components would also presumably be positively stained with CD56 in a scattered fashion. If it can be established that, unlike type AB thymoma, metaplastic thymoma expresses CD56 in spindle cells alone by accumulating CD56 immunostaining data from both thymoma types in additional patients, CD56 could become a more accessible marker for differentiating between these distinct types of thymoma.

S-100 is a neural marker that is positively expressed in cells such as a neurogenic tumor. Thymomas including type AB are generally negative for S-100 [4]. However, in the present case, spindle cells were strongly positive for S-100. Positive S-100 expression in metaplastic thymoma is observed on rare occasions. Suster et al. [5] reported a case in which S-100 was expressed only in spindle cells, similar to our case. In addition, Yoneda et al. [6] reported S-100 as diffusely and weakly positive in both components in a patient. S-100 expression is sometimes detected in metaplastic thymoma, especially in spindle cells, albeit at a low frequency (3 of 19 cases (16%) including the pres-

ent case) [5-8]. Determining expression levels may assist in diagnosis when difficulties are encountered in differentiating between metaplastic thymoma and type AB thymoma.

In addition, CD20 is a prominent B-cell marker that is known to be positive in both components in type AB thymoma. In the present case, both components were negative for CD20. Biao et al. [7] studied CD20 expression in 7 patients with metaplastic thymoma and reported CD20 as absent in both epithelial and spindle cells. By determining expression levels of CD20 in metaplastic thymoma and type AB thymoma through the accumulation of additional data, the combination of the absence of CD20 in both components together with CD56 and S-100 results may prove useful in diagnosing metaplastic thymoma when differentiation from type AB thymoma is difficult.

Conclusion

We encountered a patient with metaplastic thymoma that positively expressed both CD56 and S-100. Reports on metaplastic thymoma that exhibits expression of CD56 and S-100 are scarce and more data must be accumulated. Nonetheless, using CD56 and S-100 along with CD20 in an integrated manner may prove useful in diagnosing metaplastic thymoma.

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Disclosure of conflict of interest

None.

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