KL-6-producing Invasive Thymoma

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Abstract

We report a patient with KL-6-producing invasive thymoma. A 58-year-old man was admitted complaining of dyspnea and fatigability. Computed tomography of the chest revealed interstitial pneumonia and an anterior mediastinal tumor. The tumor was surgically extirpated and diagnosed as invasive thymoma. Serum KL-6 levels later increased further and another tumor was found in the liver. That liver tumor was resected and histologically diagnosed as a metastasis of thymoma. Following resection, the serum KL-6 level decreased. Tumor cells of both primary and metastatic lesions exhibited positive reactivity to immunohistochemical staining for KL-6. A review of this case is presented.

(Key words: liver metastasis, mucin-like high-molecular-weight glycoprotein, MUC1, tumor marker, interstitial pneumonia)

Introduction

Thymoma is the most common primary neoplasm of the anterior mediastinum, and can generally be cured by complete surgical extirpation. However, about one-third of patients demonstrate extensive growth, and lymph node or hematogenous metastasis, which may occur in both encapsulated and invasive types (1). The sites of hematogenous metastasis include lung, liver, bone, and others (2). In this case, both primary and metastatic lesions of thymoma were surgically extirpated and exhibited positive reactivity to immunohistochemical staining for KL-6.

KL-6 is a mucin-like high-molecular-weight glycoprotein that generally indicates the degree of fibrotic and destructive changes of lung structure (3). However, it is reported that the increased expression of MUC1 mucin, into which KL-6 is classified, is associated with metastatic potential and poor prognoses of malignant tumors (4–7). When serum levels of KL-6 increase, the existence of malignant tumors such as invasive thymoma may need to be considered even if the patient appears to be suffering from interstitial pneumonia.

Case Report

A 58-year-old man, who had been clinically diagnosed with interstitial pneumonia in June 1998 at another hospital, was admitted to our hospital in July 1998, complaining of dyspnea and fatigability. His medical history showed gout, thrombophlebitis, hypertension and colon cancer (left hemicolectomy had been performed in 1995). Physical examination revealed crepitant rales in bilateral lower lung fields. Radiography of the chest revealed a reticular shadow, predominantly in bilateral lower lung fields and an anterior mediastinal mass (Fig. 1). Computed tomography of the chest also revealed a reticular shadow in bilateral lower lobes of the lung and an anterior mediastinal mass (Fig. 2). Transbronchial lung biopsy revealed possible non-specific interstitial pneumonia. Administration of oral glucocorticosteroid (initiated at 40 mg/day then tapered to 20 mg/day) resulted in improvement of symptoms.

Two months later (September 1998), computed tomography of the chest was again performed and the same anterior mediastinal mass was revealed. The absence of change in the mass over the two-month period suggested a diagnosis of non-invasive thymoma. However, because the tumor had invaded the right lung and pericardium, total thymectomy and partial resection of the right middle lobe of the lung with pleura and pericardium was performed in October 1998. Histopathology showed the polygonal epithelial cells of the tumor disposing in solid sheets and invading the peripheral adipose tissue through the capsule. For these reasons, this tumor was diagnosed as invasive thymoma (epithelial type).

Ultrasonography of the abdomen for general screening examination in February 2000 and subsequent computed tomography (also in February 2000) revealed a space-occupying lesion in the left lobe of the liver (20 mm in diameter, Fig. 3). Since the lesion had not been enhanced by administration of the contrast material, metastasis from the colon cancer (resected...
Figure 1. Radiography of the chest, demonstrating the reticular shadows predominantly in bilateral lower lung fields. The lateral view revealed anterior mediastinal mass (arrowhead). A: front view. B: lateral view.

Figure 2. Computed tomography of the chest on admission, illustrating an anterior mediastinal mass (arrowheads).

Figure 3. Computed tomography of the abdomen performed 15 months after the resection of primary lesion, illustrating a space-occupying lesion in the left lobe (the fourth segment) of the liver (arrowheads).

Figure 4. Slides of the primary (A, B) and metastatic (C, D) lesions of tumors. Polygonal epithelial cells were disposed in solid sheets. Immunoperoxidase stain for KL-6 demonstrates positive reactivity in some tumor cells of both primary and metastatic lesions. A: HE stain of primary lesion in the thymus (×100). B: immunoperoxidase stain for KL-6 of primary lesion in the thymus (×100). C: HE stain of metastatic lesion in the liver (×100). D: immunoperoxidase stain for KL-6 of metastatic lesion in the liver (×100).

in 1995) was initially suspected. Partial hepatic resection was performed in May 2000. However, the resected lesion was histologically diagnosed as metastatic thymoma.

In October 2000, computed tomography of the abdomen revealed multiple liver metastases. Radiotherapy and chemotherapy were considered inappropriate options because of the patient's underlying interstitial pneumonia, and methods of best supportive care were selected.

Immunohistochemistry

Serum levels of KL-6 increased to 2,000–3,000 U/ml (2,360 U/ml in July 1999, 3,060 U/ml in October 1999, 1,920 U/ml in December 1999; normal range <500 U/ml) without exacerbation of interstitial pneumonia before the liver tumor was identified. Following resection of the tumor, serum levels of KL-6 decreased to 939 U/ml. A KL-6-producing tumor was therefore suspected and immunohistochemical staining was performed. As both primary and metastatic lesions exhibited positive reactivity to anti-KL-6 staining (Fig. 4), this case was diagnosed as KL-6-producing invasive thymoma with liver metastasis.

Discussion

Thymoma is the most common primary neoplasm of the anterior mediastinum. Patients with benign thymomas, which show no histological invasion of the capsule, can be cured by complete surgical extirpation. However, invasive thymoma
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exhibits extensive invasion through the capsule, and frequent lymph node or hematogenous metastases (1, 2). About one-third of patients demonstrate extensive growth, and lymph node or hematogenous metastasis (1). Okumura et al (8) reported that in 273 patients with thymoma who had experienced surgical resection of tumors, 124 were diagnosed as non-invasive thymoma which was defined as stage I by the classification system of Masaoka et al (9).

In this case, the tumor cells of the primary lesion invaded the surrounding adipose tissue through the capsule, providing support for diagnosis of the tumor as invasive thymoma. One year after extirpation of the primary lesion, elevated serum levels of KL-6 (up to 3,060 U/ml in October 1999) decreased (to 939 U/ml in April 2000) following resection of the metastatic lesion. The relation between the primary lesion and serum levels of KL-6 was uncertain because we did not examine the KL-6 level before and immediately after resection of the primary lesion. As the possibilities of not only exacerbation of the interstitial pneumonia but also a KL-6-producing tumor were suspected, we performed immunohistochemical staining. Since the primary and metastatic lesions both exhibited positive reactivity to anti-KL-6 staining, we diagnosed the tumor as KL-6-producing invasive thymoma. When further metastatic lesions were identified in October 2000, serum levels of KL-6 did not increase. This may be due to the heterogeneity of the tumor lineage, as some cells in the initial anti-KL-6 staining did not exhibit positive reactivity.

KL-6, a mucin-like high molecular weight glycoprotein, is classified as "Cluster 9 (MUC1)" of lung tumor and differentiation antigens, according to the findings of immunohistochemical and flow cytometry studies (10). Since KL-6 is predominantly expressed on type 2 pneumocytes and respiratory bronchiolar epithelial cells, its serum levels are used as an indicator of disease activity in interstitial lung diseases (3). Actually, the area of interstitial pneumonia from the lung of this patient resected at the thymectomy exhibited positive reactivity to immunohistochemical staining for KL-6 (Fig. 5). But the possibility that the non-KL-6-expressing cells of the thymus or thymoma cells express KL-6 is still uncertain. In this patient, because not all tumor cells express KL-6, we suppose that the non-KL-6-expressing cells of the thymus were transformed into thymoma cells and some of those cells further acquired the character of metastasis accompanied with an increased expression of KL-6.

In conclusion, we reported the case of KL-6-producing invasive thymoma. While this patient had been diagnosed as interstitial pneumonia, the invasive thymoma was thought to be a contributing factor to the increased serum level of KL-6. This occurrence, the invasive thymoma along with the increased level of KL-6, suggests the possibility that KL-6 could be used as an indicator of the invasiveness of thymoma. So, when serum levels of KL-6 increase, the existence of malignant tumors such as invasive thymoma may need to be considered even if the patient appears to be suffering from interstitial pneumonia.

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References


