

Case  
Report

## Solitary Fibrous Tumor of the Pleura Suddenly Induced Hypoglycemia before Surgical Treatment

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**We present a case of a solitary fibrous tumor of the pleura with sudden onset, recurrent hypoglycemia. A 76-year-old smoking male with type-II diabetes mellitus admitted to our hospital for dyspnea and general malaise. Radiological findings revealed a large tumor occupying the right hemithorax. After bronchoscopic examination, the patient developed a fever and began to wheeze. Treatment with antibiotics and several other drugs improved his symptoms. Percutaneous needle biopsy confirmed the diagnosis. After these medical interventions, the patient suddenly developed recurrent hypoglycemia. After the right pneumonectomy, the patient never experienced hypoglycemia again. We should consider the possible relation between hypoglycemia and solitary fibrous tumor of the pleura, even when the patient is not hypoglycemic during the initial examination.**

**Key words:** solitary fibrous tumor, pleural tumor, hypoglycemia, insulin-like growth factor II

### Introduction

A solitary fibrous tumor is a mesenchymal tumor which has been increasingly recognized these days. Although occurrence in extrathoracic organs such as the kidney, urinary bladder, uterus, upper respiratory tract, spinal cord, and soft tissue has been reported lately,<sup>1–3)</sup> the pleura is the most common site of solitary fibrous tumor.<sup>4, 5)</sup> About 80% of solitary fibrous tumors of the pleura (SFTP) originate from the visceral pleura, and the remaining, from the parietal pleura.<sup>6)</sup> The tumors are generally pedunculated and have benign morphological

features.<sup>7)</sup> However, one-third of SFTP are malignant,<sup>6, 8–12)</sup> and lead to death through local recurrence or distant metastasis. Symptoms of SFTP usually include cough, chest pain, and dyspnea, which are associated with an increase in tumor size.<sup>6, 8–12)</sup> Hypoglycemia is a rare, though well-known paraneoplastic syndrome of solitary fibrous tumors. Hypoglycemia occurs in 3 to 5% of patients with SFTP,<sup>6, 7, 11)</sup> and is more common in patients with large tumors.<sup>1, 3–5)</sup> The tumors reportedly produce insulin-like growth factor II (IGF-II),<sup>3–5, 9, 10)</sup> which decreases blood glucose instead of insulin.

We had the opportunity to treat SFTP in a patient with long-term type II diabetes. The patient had never displayed any signs of hypoglycemia before admission; however, recurrent hypoglycemia unexpectedly occurred after several invasive diagnostic procedures.

### Case Presentation

A 76-year-old smoking man was admitted to our hospital with progressive dyspnea and general malaise for a month. He had no history of asbestos exposure, and he regularly took antidiabetics (voglibose and glimepiride) for type II diabetes mellitus. Eight years earlier, he had a

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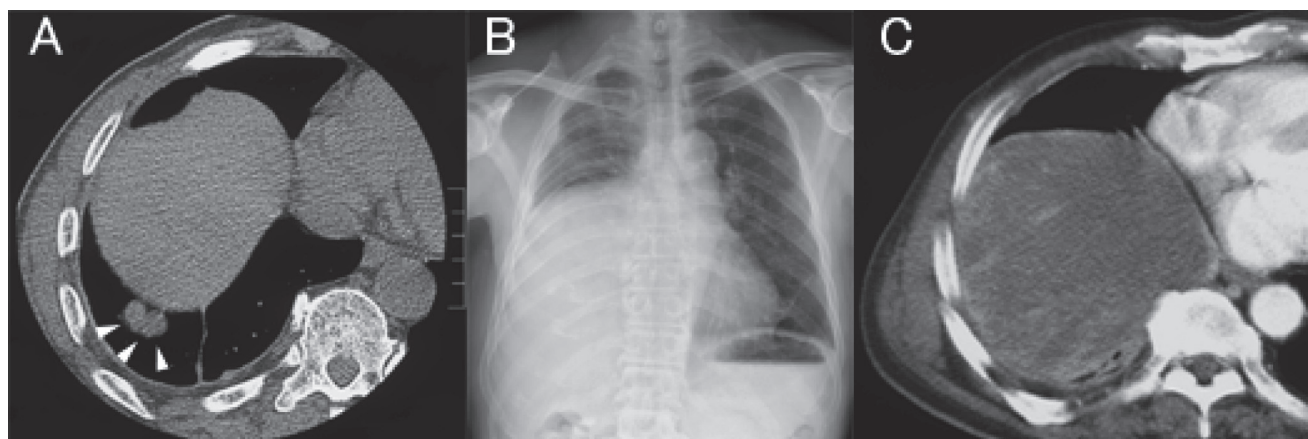
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Received: February 19, 2010; Accepted: April 15, 2010

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**Fig. 1** (A) Chest computed tomography 8 years before admission indicating a walnut-sized mass (arrow heads) with notching at the right posterior costophrenic space. (B) Chest roentgenogram on admission revealing a large mass occupying more than half of the right lower hemithorax without tracheal shift. (C) Contrast enhanced CT scan on admission showing a large, well-delineated mass in the right hemithorax with heterogeneity.

right lung abscess, and computed tomography (CT) revealed a walnut-sized tumor on the right diaphragm (**Fig. 1A**). Gradually, the tumor had enlarged; nevertheless, he had refused any invasive diagnostic procedures or resection of the tumor.

Physical examination on admission revealed that the patient had clubbed fingers, and there were weak breath sounds and absence of normal resonance over the right lower part of the chest. Blood analysis indicated a blood glucose of 120 mg/dL, and an HbA1c of 6.3%, which were otherwise normal. A chest roentgenogram showed a large mass obscuring the right diaphragm and more than half of the right lower hemithorax (**Fig. 1B**). Chest CT with contrast medium indicated that a well-delineated large tumor filled the posterior costophrenic space with slight heterogeneity (**Fig. 1C**).

The patient underwent a bronchoscopic examination; however, brushing cytology and transbronchial biopsy could not confirm the diagnosis. The day after the examination, he developed a fever and began to cough and wheeze. Although antibiotic administration resolved his fever, he wheezed with impaired oxygenation. A 3-day administration of steroid and then treatment with theophylline and a long acting anti-cholinergic inhalant gradually diminished his symptoms. Finally, percutaneous large-bore needle biopsy confirmed the diagnosis of SFTP; however, severe hypoglycemia repeatedly occurred thereafter (**Fig. 2**). Blood glucose decreased as low as 30 mg/dL early in the mornings, even though the patient discontinued taking antidiabetics immediately after the first hypoglycemic attack.

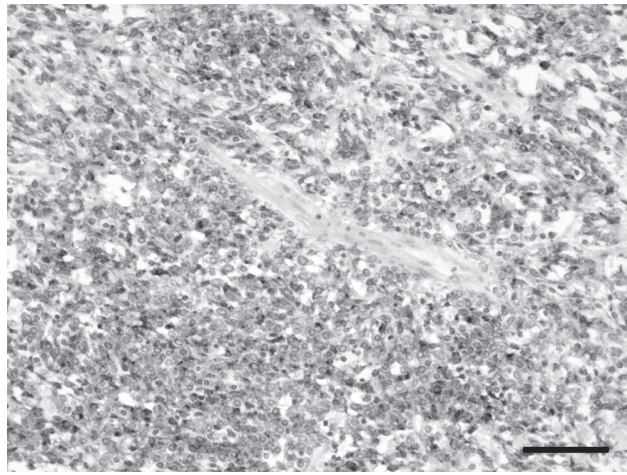
A right standard thoracotomy revealed severe inflammatory pleural adhesions throughout the right thoracic cavity. A large encapsulated tumor infiltrated the right upper and lower lobes with firm adhesion to the diaphragm, and the middle lobe was completely collapsed. Eventually, right pneumonectomy was performed to remove the tumor.

The tumor was a solid, elastic, soft mass, with dimensions of  $16 \times 12.5 \times 7$  cm and weight of 694 g. Sectioning revealed a lobulated, gray parenchyma with areas of hemorrhage and necrosis. Microscopically, spindle cells with oval nuclei arranged in collagenous bundles and fascicles. Tumor cells showed mild polymorphism with high mitotic rate. They were immunoreactive for CD34, bcl-2 and p53; moreover, 25% of them were immunoreactive for MIB-1. These findings confirmed the diagnosis of malignant SFTP. Additionally, most of the tumor cells showed distinct immunoreactivity for IGF-II (**Fig. 2**).

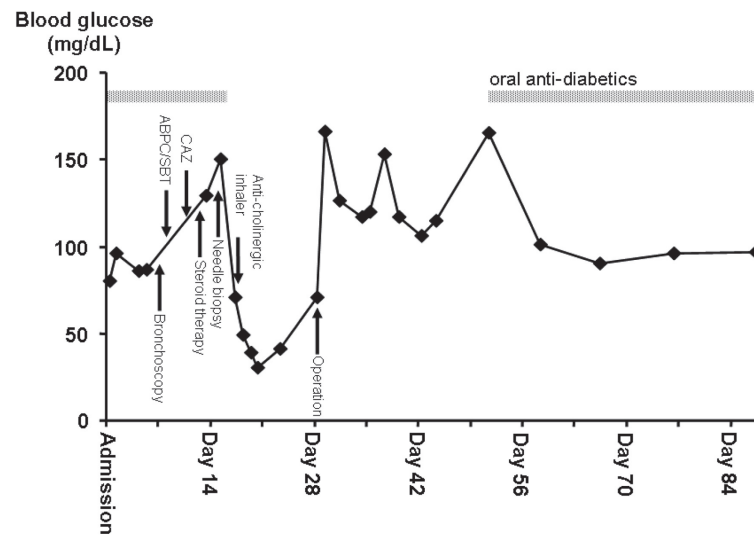
The patient experienced no further hypoglycemia after surgery (**Fig. 3**), so he resumed taking oral antidiabetics. He has been free from hypoglycemia and any signs of tumor recurrence for 26 months after the operation.

## Discussion

Compared to other patients who had severe hypoglycemia on admission,<sup>1, 3-5)</sup> the patient described here is unique because he had no hyperglycemia on admission, though he did have recurrent episodes of hypoglycemia after preoperative diagnostic procedures or medical



**Fig. 2** Imuunohistochemical analysis of the resected specimen showing distinct immunoreactivity for IGF-II in most of the tumor cells. A scale bar indicates 100  $\mu$ m.



**Fig. 3** Clinical course of the patient. Blood glucose decreased suddenly after medical interventions and increased remarkably after excision of the tumor.

interventions. To the best of our knowledge, this is the first report in English describing the onset of recurrent hypoglycemia in a patient with SFTP.

The production of IGF-II in solitary fibrous tumors is considered to be the cause of the hypoglycemia, and elevated levels of serum IGF-II have been reported in patients with SFTP.<sup>4,5</sup> Unfortunately, we could not demonstrate an elevation in the level of serum IGF-II. However, the level of insulin was suppressed despite of severe hypoglycemia. After surgical removal of the tumor, the blood glucose and insulin level returned to normal.

Moreover, tumor cells were markedly immunoreactive for IGF-II. Thus, we can conclude that there was no pathological insulin production in the patient, and the tumor was likely responsible for the hypoglycemia.

Although the exact mechanisms for the sudden onset of recurrent hypoglycemia in the present case have not been clarified, we should be aware of a possible onset of hypoglycemia in patients with SFTP, even if they had never been hypoglycemic before. The flare-ups occurred after the bronchoscopic examination and treatments with antibiotics, theophylline, hydrocortisone, and an

anticholinergic inhaler. Then he underwent the percutaneous needle biopsy. We discontinued his antidiabetic medication immediately after the first hypoglycemic attack; however, recurrent hypoglycemia continued. None of medications listed above has been reported to decrease blood glucose. Some physical or inflammatory stimuli raised by the diagnostic procedures could presumably modify the patient's glucose metabolism to cause hypoglycemia. Considerable care must be taken in the preoperative management of patients with SFTP.

Complete resection of the tumor is the mainstay of treatment for all benign and malignant SFTP.<sup>9)</sup> From our experience, we strongly recommend early surgical intervention. Complete resection could be achieved easily on a small or pedunculated tumor under video-assisted thoracoscopic surgery,<sup>13)</sup> while a large tumor, sessile or infiltrating into lung parenchyma, sometimes requires lobectomy or pneumonectomy under standard thoracotomy.<sup>9)</sup> As in the present case, as the tumor grows, morbidity of the patients increases. In addition, poor prognosis is associated with larger tumors.<sup>7)</sup> Early surgical intervention would allow us to perform a complete resection in a safe and easy manner, and ensure less morbidity and better prognosis for the patients with SFTP.

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