

Fibrous Pleural Tumor with Hypoglycemia:

Case Study

NAEEM ADHAMI, M.D.¹, RAEES AHMED, M.D.², PATRICK A. LENTO, M.D.³, MONA SHIMSHI, M.D.⁴, STEVEN D. HERMAN, M.D.⁵, AND ALVIN S. TEIRSTEIN, M.D.⁶

Abstract

Many neoplastic tumors exhibit paraneoplastic syndromes manifested by endocrinopathy. This is particularly true of intrathoracic tumors such as lung cancers, thymomas, carcinoid tumors and mediastinal germ cell neoplasm. Fibrous tumors of the pleura are rare intrathoracic tumors, which are usually benign and often grow to huge size. A subset of these neoplasms present with the syndrome of hypoglycemia. Although first reported more than 70 years ago, the diagnosis is rarely considered when a patient presents with syncope and hypoglycemia. This article reports a patient who presented with a large pleural mass and a hypoglycemic syndrome. (The disease was surgically cured.) The probable mechanism of hypoglycemia is discussed.

Key Words: Pleura, tumor, hypoglycemia.

Case Report

A 62-YEAR-OLD WHITE MALE presented in 1996 with left-sided pleuritic chest pain, cough and fever. He had psoriasis and hypertension well controlled with nifedipine. He was an ex-smoker. Physical examination was normal except for dullness to percussion and decreased breath sounds over the left inferior hemithorax. Chest X-rays showed a left pleural effusion. Thoracentesis revealed an exudate of unknown etiology. A chest tube was inserted and intravenous antibiotics administered, with improvement. Subsequent chest CT scan revealed a left pleural mass.

Closed biopsy of the pleura was negative for malignancy, revealing only nonspecific connective tissue. The patient refused thoracoscopy.

Two years later, in 1998, the patient experienced recurrent syncopal attacks, light-headedness and generalized weakness, usually upon awakening or about 5–6 hours after his last meal. Repeated tests of blood glucose level during these episodes revealed hypoglycemia. Blood glucose on one occasion was 32 mg/dL; it rose to 125 mg/dL with oral glucose administration. Physical examination revealed hypertension, psoriasis and dullness to percussion, with decreased breath sounds over the left hemithorax. Chest X-rays showed a huge pleural mass occupying the left lateral lower hemithorax (Fig. 1). Serum insulin level was low (4 μ U/mL) (normal fasting 5–20), insulin-like growth factor I (IGF-I) was 39 ng/mL (normal 152–494), IGF II was 661 ng/mL (normal 98–444). Thyroid function, liver function and serum cortisol were within normal limits.

A left thoracotomy was performed. A large lobulated mass, occupying the posterior and inferior portions of the entire left hemithorax, was encountered. There were dense adhesions to the parietal pleura. The left lower lobe and

From the ¹Department of Intensive Care Unit, King Fahad National Guard Hospital Riyadh, Kingdom of Saudi Arabia; ²Department of Pulmonary and Critical Care Medicine, King Abdulaziz National Guard Hospital, Kingdom of Saudi Arabia; and ³Department of Pathology, ⁴Division of Endocrinology, ⁵Division of Cardiothoracic Surgery, and ⁶Division of Pulmonary and Critical Care Medicine, Mount Sinai School of Medicine, New York, NY.

Address all correspondence to Alvin S. Teirstein, M.D., Box 1232, Mount Sinai School of Medicine, One East 100th Street, New York, NY 10029.

Supported by the Catherine and Henry J. Gaisman Foundation.

Accepted for publication January 2004.



Fig. 1. Chest radiograph on admission to hospital showing a large pleural mass occupying the lower two-thirds of the left hemithorax.

the diaphragm were adherent to the mass. Multiple vessels entered the tumor (Fig. 2). Removal of the pleural mass required left lower lobectomy and diaphragm resection and repair. The resected mass measured 17×15×9 cm and weighed approximately 4 kilograms. Pathologic examination revealed a highly cellular spindle cell tumor, with rare mitoses. Many tumor cells were positive for CD34 immunoperoxidase stain. These findings were consistent with the diagnosis of solitary fibrous tumor (Fig. 3). The postoperative course was uncomplicated. In the seven years following surgery, there were no hypoglycemic symptoms and blood glucose was 90–100 mg/dL on several occasions. Immediate post-resection IGF-I was 191 ng/mL

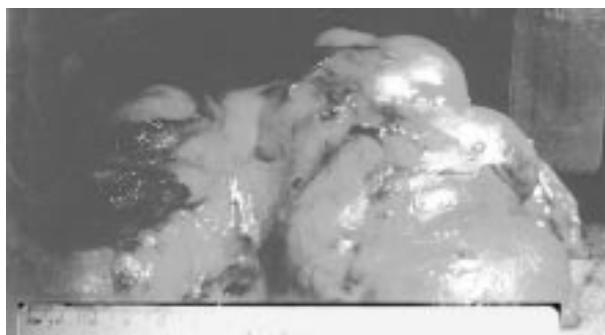


Fig. 2. Photograph of the resected huge pleural fibroma measuring 17×15×9 cm and weighing approximately 4 kilograms.

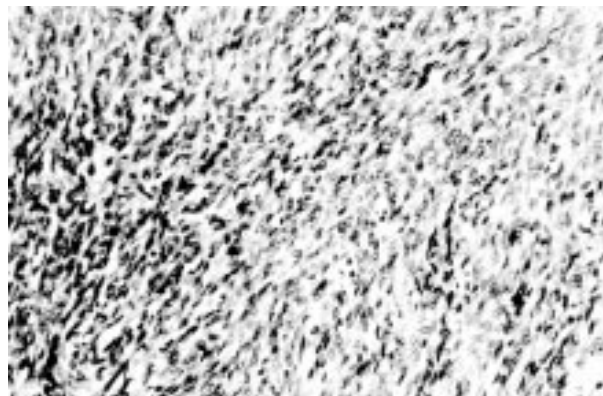


Fig. 3. Microscopy of resected pleural tumor demonstrating high cellularity, spindle cells and few mitotic figures, which showed positive staining with CD34. Consistent with a solitary fibrous tumor of the pleura. (H+E, 50x original magnification).

and IGF-II was 515 ng/mL. Subsequent IGF-I and IGF-II levels were normal: 114 ng/mL and 355 ng/mL, respectively.

Discussion

Solitary fibrous tumors (SFT) are spindle cell neoplasms. They are usually benign, but may be malignant. Klemperer and Rabin described benign fibrous tumors of the pleura (1). Most authors believe they arise from submesothelial connective tissue (2, 3). In the thorax, they usually involve the pleura, but can be intrapulmonary or mediastinal. Histologically, they show a variety of arrangements, from a “patternless pattern” to a hemangiopericytoma-like or diffuse sclerosing appearance, and stain positive for CD34 and vimentin (4). Smooth muscle tumors and malignant peripheral nerve sheath tumors show occasional positivity with this antibody, but these spindle cell tumors usually can be identified with an immunohistochemical panel using specific markers such as actin, desmin and S-100 (5).

Most solitary fibrous pleural tumors cause minimal symptoms despite growth to huge proportions. When present, the most common symptoms are cough, chest pain, dyspnea and pulmonary osteoarthropathy. Hypoglycemia is rare (6, 7). Malignant pleural tumors may metastasize. Most neoplasms associated with hypoglycemia are pancreatic β -cell tumors. Doege reported the first patient with an intrathoracic fibrous tumor associated with hypoglycemia in 1930 (8). In 1981, Briselli et al. reviewed 360 cases of solitary pleural fibrous tumors reported since 1942. Four percent had

symptomatic hypoglycemia (9); one instance of hypoglycemic coma was fatal (10).

Several mechanisms for hypoglycemia associated with solitary fibrous tumors have been proposed (11–13); these include secretion of insulin-like growth factor II (IGF-II or big IGF-II), increased utilization of glucose by the huge tumor, insulin receptor proliferation mediated by the solitary fibrous tumor, decreased gluconeogenesis, and decrease in effective glucagon secretion.

Secretion of IGF by the tumor is the most widely accepted mechanism for hypoglycemia in fibrous masses (14–16). Stuart et al. reported an increased number of insulin receptors in these large tumors (17). The finding of increased IGF-II with hypoglycemia before resection and decreased IGF-II with abatement of hypoglycemia after resection, as in our patient and a similar patient reported by Filosso et al. (18), supports this hypothesis. Further evidence in favor of tumor production of IGF is the high concentration of messenger RNA for IGF-II in an excised mesenchymal tumor reported by Daughady et al. (19).

Our patient had hypoinsulinemic hypoglycemia and suppressed serum pituitary growth hormone and IGF I levels, and a high concentration of IGF II. After resection the concentrations returned to normal. Baxter et al. suggested that there is an overexpression of IGF II, which is responsible for hypoglycemia in solitary fibrous tumors (20). IGF I and IGF II are arranged in a ternary complex with IGF binding protein. Failure to form a ternary complex is thought to explain the enhanced hypoglycemic activity of circulating IGF-II in these patients. This failure to form a ternary complex may occur because these complexes are pituitary-growth-hormone dependent and most of these patients have a subnormal level of pituitary growth hormone (16, 21).

Conclusion

When confronted with a patient with hypoglycemia and suppressed insulin levels, non-islet cell hypoglycemia should be considered. The case reported here demonstrated that a solitary fibrous pleural tumor should be considered in the differential diagnosis. Hypoglycemia due to an imbalance of circulating IGF I and IGF II caused by the tumor may be the primary clinical feature of these patients. Surgical resection of the tumor is curative. Rarely, the pleural tumor is malignant and recurs locally or at a metastatic site.

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