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A CASE OF PLEURAL MASS PRESENTING WITH SHORTNESS OF BREATH AND REFRACTORY NON-INSULIN MEDIATED HYPOGLYCEMIA

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ABSTRACT
We report a typical case of an 80 years old male presented with severe hypoglycemia complaining of shortness of breath for the last five-six months. On investigation, he was found to have a right sided pleural mass. The patient's plain chest radiography also showed large opacity in his right hemi-thorax. His contrast-enhanced chest computed tomography (CT) revealed a lobulated mass in his right hemi-thorax. Doege-Potter Syndrome is a paraneoplastic syndrome characterized by hypoinsulinaemic hypoglycemia secondary to a solitary fibrous tumor especially in pleural cavity. This syndrome is caused by production of insulin like growth factor II (IGF-II) by the tumor cells. Although DPS is very rare, its possibility must be considered in cases of refractory hypoglycemia.

KEYWORDS: Doege-Potter Syndrome, pleural mass, paraneoplastic syndrome, hypoinsulinaemic hypoglycemia.

INTRODUCTION
Solitary fibrous tumor of the pleura (SFTP) is a rare primary tumor which arises from the submesothelial mesenchymal layer, occupying less than 5% of all pleural tumors1When hypoglycemia accompanies SFTP it is known as the Doege-Potter syndrome (DPS).[2] An incompletely processed molecule of IGF-2, is derived from the tumor and considered to be a hypoglycemic agent.[3] Our report presents a typical case of an 80 years old male who presented with shortness of breath for last five-six months. On investigation he was diagnosed to have a right sided pleural mass.

CASE
An eighty year-old Indian male was admitted to the hospital with gradual increasing shortness of breath and weakness. His initial blood sugar level was 50 mg/dL. He had no history of diabetes or any medication intake, inclusive of any hypoglycemic agent. His past medical history was significant for hypertension and he had undergone percutaneous transluminal coronary angioplasty (PTCA) of left anterior descending left anterior descending artery (LAD) in the year 2003.

On admission, his vital signs were as follows: body temperature, 37.1°C, blood pressure - 150/90 mm Hg; pulse rate - 70 per minute; and respiratory rate - 20 per minute. His initial physical examination revealed diminished breath sounds in his right middle and lower lung fields, and dullness to percussion. The patient's plain chest radiography showed large opacity in his right hemi-thorax (Figure 1). His contrast-enhanced chest computed tomography (CT) revealed a lobulated mass in his right hemi-thorax (Figure 2). Further laboratory test was performed to determine the cause of the hypoglycemia. The serum insulin and C-peptide level was suppressed (2.81 µU/mL; normal range, 4–16 µU/mL and 0.12 ng/mL; normal range, 1.07–3.51, respectively), which suggested that hypoglycemia did not result from either endogenous or exogenous hyperinsulinism. The blood cortisol, adrenocorticotrophic hormone, and growth hormone (GH) level was normal, and no insulin antibody was detected. Hence, we performed a needle biopsy of the mass and it revealed spindle cell neoplasm. Right thoracotomy revealed a large, multi-lobulated intra-thoracic mass that caused atelectasis of the right lower lobe.

We performed tumor resection and lobectomy of the right lower lobe. The tumor weighed 1,465.5 gm. and measured 15×10×4 cm in dimensions. As far as histological finding is concerned, the cells were arranged in a patternless manner , hypercellular areas were comprised of fusiform nuclei with indistinct cell border. Hypercellular areas also show area of necrosis, hemorrhage with thrombosed vessels. Mitotic activity was brisk, approximately 15-20/10 HPF. No infiltration was present in the adjacent lung. The tumor cells were immunohistochemically positive for CD34, D2-40 and Bcl-2 and negative for Cytokeratin and calretinin. Based on the microscopic appearance of the immune-histological pattern, a final diagnosis of malignant SFTP was made. The sarcomatoid changes are depicted in figure 3. After surgical resection of the tumor, the blood glucose levels became normal. The post-operative recovery was completed and the patient was discharged.

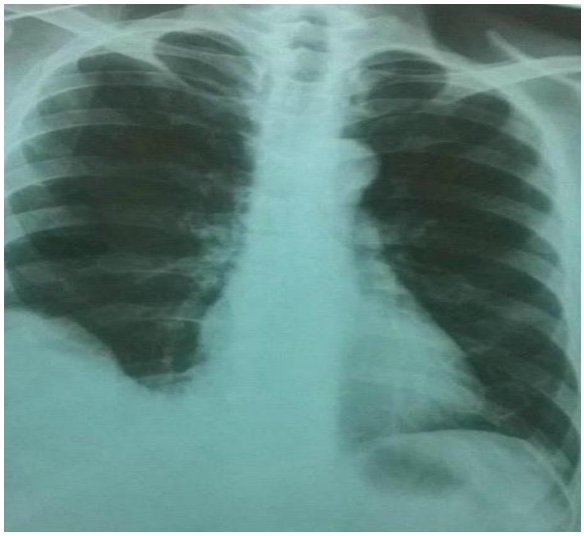

Figure 1. Plain chest radiography showed a large opacity in his right hemithorax

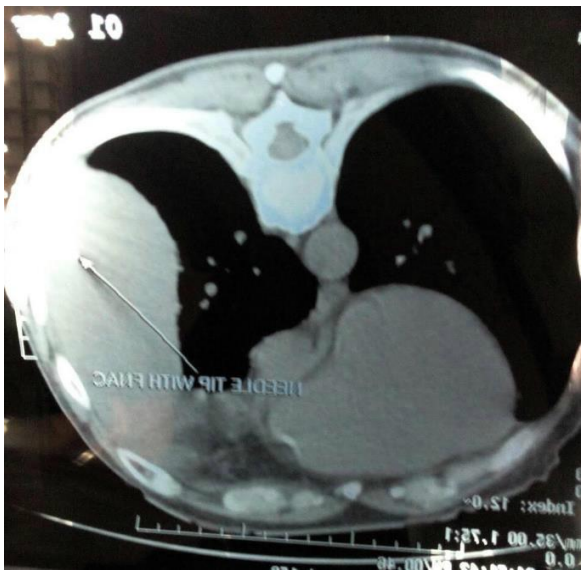

Figure 2. Contrast-enhanced chest computed tomography (CT) revealed a lobulated 15×10×4-cm-sized mass in his right hemithorax

DISCUSSION

SFTP is a rare spindle cell neoplasm derived from mesenchymal cells and it accounts for about five percent of all pleural neoplasms.[4,5,6] SFTP was first described in 1931 by Klemperer and Rabin, and since then about 800 cases of it have been reported in literature and its frequency is equal among patients of different ages, with no association with gender.[7,8,9] Tumors are usually well circumscribed with a smooth surface lobular large masses. In some cases, necrosis, hemorrhage, and calcification can be seen.[10] Diagnosis of tumor is based on histological analysis and an immunohistochemical study.[6] As far as histological analysis is concerned, SFTP consists of ovoid or elongated spindle-shaped tumor cells with varying amounts of cytoplasms.[6,10] To differentiate, SFTP from different mesenchymal tumors, sarcomatous mesothelioma, and sarcoma, immunohistochemical study is used.[1,11] CD34 is very useful and characteristic, as it is often positive in most SFT cases and negative in most other pulmonary tumors.[12] Other markers that are positive in SFTP are vimentin, Bcl-2, and CD99, and negative markers in SFTP are S-100, carcinoembryonic antigen, and smooth muscle actin.[11,13] Pathological features of malignancy as high cellularity, marked cellular atypia, significant cellular polymorphism, prominent nucleoli, and high mitotic activity (greater than 4 mitoses per high-powered field) was reported by England et al.[6,12] In our patient, the histological pattern revealed a spindle cell neoplasm. The positive CD34 finding was useful for the SFTP identification. The diagnosis of malignant SFTP was confirmed based on the criteria suggested by England et al.[12] More than 50% of benign SFPT cases are asymptomatic and appear as an abnormality in plain chest radiography.[11,14] The symptoms are correlated with the tumor size. Symptoms include cough, chest pain, and dyspnea.[1,12] Hemoptysis and obstructive pneumonitis rarely occur as results of airway obstruction.[11] Hypoglycemia is attributed to the production of the IGF-II, which lowers the blood glucose and impairs the GH's counter-regulatory response to hypoglycaemia.[15] IGF-II may also stimulate glucose uptake by the tumor itself.[16] More cases of hypoglycemia occur with malignant SFTP with diameters of 10 cm or more[12] Endocrinological test was performed to differentiate the causes of hypoglycemia. The low levels of serum insulin and C-peptide suggested not exogenous or endogenous hypoglycemia but IGF-mediated hypoglycemia. Furthermore, the blood cortisol and adrenocorticotrophic hormone levels were also within normal limits ruling out the diagnosis of adrenal insufficiency. The initial treatment goal was normalization of the blood glucose level. To avoid hypoglycemia, the patient required a high-glucose diet and continuous intravenous infusion of 50% glucose (average of 15 g/hr). When we stopped the glucose infusion, the patient suffered from hypoglycemia. To lower the glucose infusion rate, we tried glucagon injection, but it had no effect. The overnight hypoglycaemia was remarkable. Infusion of up to 50 g/hr

of glucose was needed to prevent hypoglycemia. Considering the high possibility of the association of hypoglycemia with spindle cell neoplasm, surgical treatments were recommended for the patient. In our case, the patient did not have hypoglycemia earlier, but symptomatic hypoglycemia occurred as the tumor grew, which suggest the association between the tumor size and the degree of hypoglycemia. Therapies to reduce the tumor size include surgical resection, chemotherapy, radiotherapy, brachytherapy, and photodynamic therapy. [10]Complete surgical resection is a curative therapy for both benign and malignant SFPT.[10] Thoracotomy is required in the treatment of larger tumors, but small tumors can be resected through the video-assisted thoracoscopic approach.[9,10] After the tumor resection, the patient's blood glucose level normalized without glucose infusion. The prognosis of benign SFTP with complete surgical resection is good.[9,12] In comparison, malignant SFTP has been reported to show a higher recurrence rate than benign SFTP. Most recurrences tend to occur within 24 months of the initial resection, but may happen even after more than 20 years. Thus, malignant SFTP should be followed up with computer tomography of the chest to monitor its recurrence in every two years [10,11]

Limitations

The IGF-II levels couldn't be measured due to technical problem, however it didn't alter the patient's management and the patient outcome was excellent. Recently a case study by jang et al.[17] also reported a case of solitary fibrous tumor of the pleura, where the IGF-II measurement couldn't be done but the patient was managed accordingly based on other pertinent investigations. Hence, we did not carry out the IGF-II evaluation but we strongly felt that such a problem could arise in a developing or underdeveloped nation due to lack of adequate facilities and should be communicated to medical fraternity trying to solve a human problem as it is full of challenges, keeping infrastructure centered idiosyncrasies in mind.

CONCLUSION

DPS is an uncommon paraneoplastic phenomenon with SFTP. In this case, SFTP was diagnosed based on the histological pattern and the immunohistochemical stain findings. No detailed association with IGF-II mediation was confirmed due to the lack of IGF-II measurements; but considering the large size of the malignant SFTP, the low insulin and c-peptide levels, and the normalized blood glucose level after the tumor resection, DPS was diagnosed. Although DPS is very rare, its possibility must be considered in cases of refractory hypoglycemia.

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STATEMENT OF AUTHORSHIP

All authors have given approval to the final version submitted.

CONFLICT OF INTEREST

All the authors have declared no conflict of interest to the work carried out in this paper.
Patient consent form has been procured prior to the case report study.

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