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Primary Pulmonary Synovial Sarcoma: Case Report and Literature Review

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***Abstract*—Primary pulmonary synovial sarcoma is an extraordinarily rare tumor among the primary malignancies of lung with an unknown cause. The establishment of diagnosis of PPSS entails clinical, radiological and pathological investigations for confirmation and exclusion of alternative primary tumours and metastatic sarcomas of lung.**

We report the case of a 56-year-old man who presented with a mass in the right lung on a chest X-ray and CT scan. Thoracoscopic right middle and lower lobectomy yielded a diagnosis of monophasic PPSS according to the histological examination and immunohistochemistry. 10 months after the thoracic surgery, he developed extensive disease judged inoperable; therefore, doxorubicin and ifosfamide systemic chemotherapy was administered.

***Index Terms*—Primary Pulmonary synovial sarcoma, lobectomy, immunohistochemistry, chemotherapy.**

I. INTRODUCTION

Synovial sarcoma (SS) is an uncommon highly malignant spindle-cell tumor accounting for approximately 5.8% of all sarcomas and 10 % of soft tissue sarcomas [1].

SS is usually located in soft tissue, especially near large joints of the extremities [2], however, any anatomic site including head and neck region, abdominal wall, intra-abdominal and intrathoracic organs can be affected [3].

Lung is the most preferred site of metastasis in soft tissue sarcomas and Primary pulmonary synovial sarcoma (PPSS) is extremely rare, comprising less than 0.5% of all lung malignancies [4].

The diagnosis is established after metastatic extra-thoracic sarcoma and other primary lung malignancies have been excluded.

PPSS requires multimodality treatment with surgery, radiation therapy, and chemotherapy.

This tumor is thought to be more locally aggressive and associated with a poorer prognosis than soft tissue synovial sarcoma [5]. Survival of patients with advanced SS is reported to range between 18 and 19.7 months [6, 7].

Only a few cases of the thoracic involvement of synovial sarcoma have been reported in the literature.

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Here, we report the case of a 56-year-old man who presented with locally advanced recurrence and liver metastases of primary synovial sarcoma of lung 10 months after primary pulmonary surgery.

II. CASE REPORT

A 56-year-old male presented with the complaints of right-side chest pain and dry cough. Patient's history was unremarkable. There is no history of smoking or alcohol intake. Examination of respiratory system revealed dull percussion note, diminished vesicular breath sound and vocal resonance on right side. Examination of other systems revealed no abnormality.

Complete hemogram and blood biochemistry were within normal limits.

A chest X-ray showed large opacity on right side wich was further confirmed on computed tomography (CT) scan as heterogeneous tumor mass measuring 10 cm in diameter in the right lower and middle lobe of lung. Lymphadenopathy and metastases were not observed.

Because a CT-guided percutaneous lung biopsy failed to establish a definitive diagnosis, the patient underwent right middle and lower lobectomy of lung, for both diagnosis and treatment.

Histologic examination of the specimens revealed a cellular spindle cell tumor in long fascicles. The cells had hyperchromatic nuclei and scant cytoplasm, with increased mitotic activity and necrosis.

The differential diagnosis narrowed to carcinoid sarcoma, sarcomatoid mesothelioma, solitary fibrous tumor and fibrosarcoma.

Immunohistochemically, neoplastic cells were positive for vimentin, TLE-1, epithelial membrane antigen (EMA), CD99 and Bcl-2, and negative for CD34, S-100 and cytokeratin 7 (CK7).

Unfortunately, we could not perform cytogenetic study using reverse transcriptase-polymerase chain reaction on this patient; we lack the molecular platform in our instruction.

We retained the final diagnosis of monophasic synovial sarcoma of lung based on above characteristics and after eliminating the differential diagnosis.

10 months after surgery, the patient presented with locally advanced recurrence and liver metastases (figure 1), therefore, we initiaed palliative chemotheray with doxorubicin and ifosfamide every 21 days, considering the extensive and the progressive nature of the disease.

Following three cycles of chemotherapy, patient reported worsening of symptoms and progression of tumor size was noted in evaluation CT scan. He refused further treatment and lost to follow-up.

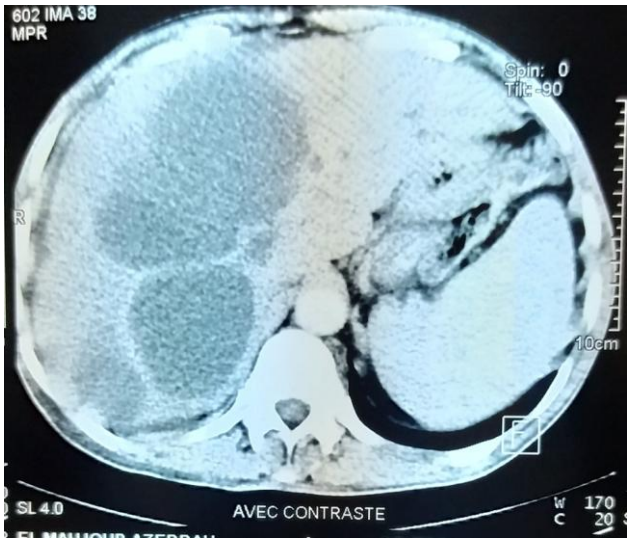

Figure 1: Abdominal CT scan showing metastases to the liver of primary pulmonary synovial sarcoma

III. DISCUSSION

Synovial sarcoma (SS) is a high grade tumor which accounts for 10% of all soft-tissue sarcomas (STS) [1].

SS occur not only in the para- articular tissues of extremities, but also in the lung, head and neck, mediastinum, heart, kidney, prostate, esophagus, and vulva [3].

Primary pulmonary synovial sarcoma (PPSS) was first described by Zeren *et al.* in 1995 [8] and It's uncommon highly aggressive malignant neoplasm with an unknown cause. It may arise from the parenchyma, tracheobronchial tree or pulmonary artery [9].

PPSS chiefly affects young and middle-aged adults with no sex predilection and mostly nonsmokers [2].

The clinical symptoms of PPSS may be associated with the histological type, region, size and degree of differentiation of the tumor [10]. These tumors are mostly centrally located and frequently cause respiratory symptoms with effusion secondary to invasion of pleura. Patients with primary synovial sarcoma of the lung may present as chest wall pain, cough, dyspnea, or hemoptysis [11]. Low-grade fever and weight loss are less frequent presentations [12]. Incidental detection of PPSS in asymptomatic individuals is not uncommon [13].

Local recurrence of PPSS is frequent and commonly metastasizes to bone, liver, skin, brain, contralateral lung, spleen, abdomen, and subcutaneous tissue [13].

The diagnosis of PPSS requires clinical, radiological, pathological, and immunohistochemical investigations to exclude alternative primary tumors and metastatic sarcoma [11].

The radiologic manifestations of PPSS are no different from bronchogenic carcinoma, metastatic, or other primary lung tumors. On chest X ray, it appears as a homogenous opacity in the lung, often accompanied by ipsilateral pleural effusion. It may appear as a consolidation or a complete opacification of the hemithorax or as a pleural thickening [11, 14]. Rarer presentations may include pneumothorax. Significant mediastinal adenopathy is usually not seen in PPSS and argues more in favor of bronchogenic carcinoma.

On CT scan, it appears as a well-defined heterogeneously mass, often with calcifications and mass effect, that enhances heterogeneously on contrast with areas of fluid indicating necrosis or hemorrhage. Bone involvement is extremely rare [13].

One differentiating feature between PPSS and soft tissue sarcoma is the presence of triple sign (bright, dark, and gray) representing tumor, hemorrhage, and necrosis on magnetic resonance imaging (MRI). MRI aids in more accurate localization and is useful to know the extent of tumor invasion [15].

Apart from extent of disease and involvement of other sites, PET-CT imaging does not help to narrow the differential diagnosis [16].

The term 'Synovial sarcoma' is actually a misnomer because the tumor does not originate from the synovium; it only resembles synovial tissue in light microscopy [17]. Synovial sarcoma is a spindle cell malignant tumor originating from mesenchymal tissue with variable epithelial differentiation. Like other soft tissue sarcomas, synovial sarcoma's diagnosis is also difficult to establish purely on the basis of histological appearance.

There are four histologic subtypes commonly reported: monophasic fibrous, monophasic epithelial, biphasic, and poorly differentiated subtypes [18]. The most commonly observed subtype is monophasic, and the biphasic subtype is easily diagnosed on the basis of the presence of both epithelial and spindle cells.

Differential diagnoses of monophasic subtype are fibrosarcoma, hemangiopericytoma, leiomyosarcoma, and spindle cell variant of squamous cell carcinoma as all are spindle cell neoplasms [19]. Hence, to differentiate monophasic subtype of synovial sarcoma from others, immunohistochemistry is essential. Synovial sarcomas are generally positive for cytokeratin 7 and 19, EMA, Bcl-2, CD99 and vimentin, and usually negative for S-100, CD-34, desmin, actin and vascular tumor markers [20-22].

Recently, histology and immunohistochemistry have also been supplemented by molecular testing. Cytogenetic study by reverse transcriptase-polymerase chain reaction (RT-PCR) helps differentiate monophasic and biphasic form. Synovial sarcoma is associated with a specific t(X;18) (p11;q11) translocation that involves SS18 (also known as SYT) and SSX1, SSX2, or SSX4. A balanced reciprocal translocation is found in over 90% of synovial sarcomas. As a result, the *SYT* gene on chromosome 18 is fused with the *SSX1* or *SSX2* gene on the X chromosome [23]. SYT–SSX 1 gene is associated with biphasic subtype and prognosis is bad, whereas monophasic subtype may have either one of two fusion transcripts, SYT–SSX 1 or SYT–SSX 2. Despite its high sensitivity, molecular testing is

not required if the diagnosis of synovial sarcoma is certain or probable on the basis of clinical, histological, and immunohistochemical evaluations [24].

PPSS is thought to be more aggressive than that of soft tissue origin, and in a retrospective study, 46% of pulmonary and mediastinal synovial sarcoma patients died within 5 years and only 26% of them were alive with no evidence of disease after several treatments [5].
Factors predicting a worse prognosis for patients with PPSS include failure to achieve a complete resection, tumor size, extensive tumor necrosis, higher histological grade, male gender, mitotic rate, neurovascular invasion and, recently, the SYT-SSX1 variant [24].

Due to the rarity of PPSS, there are no guidelines on its optimal treatment. Wherever feasible, wide surgical resection with tumor-free margins remains the preferred modality of treatment followed by chemotherapy and/or radiotherapy [25]. Adjuvant chemotherapy for soft tissue sarcoma is controversial [22, 26].
In advanced or unresectable tumors, doxorubicin and ifosfamide based chemotherapy can be used [27] as synovial sarcoma is chemosensitive to both ifosfamide and doxorubicin [28]. This combination may be used for rapid symptom relief and in patients planned for curative resection of metastases.
Undoubtedly, there is a serious need for an ideal therapeutic agent in synovial sarcoma that is more effective and less toxic. Several novel potential therapeutic targets under research are *SS18-SSX* fusion oncogene, epidermal growth factor receptor (EGFR), and vascular endothelial growth factor receptor (VEGF-R) [29, 30].

IV. Conclusion

Primary synovial sarcoma of lung is a very rare tumor, with poor prognosis. This tumor have been increasingly reported as a result of growing awareness and improved diagnostic capabilities. The most appropriate management is surgical excision with negative margins, whenever feasible. Adjuvant chemotherapy and radiotherapy have limited role. Synovial sarcoma is relatively chemosensitive, and ifosfamide-based regimen showed improved survival in metastatic disease.

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