CASE REPORT

Giant primary synovial sarcoma of the anterior mediastinum: A case report and review of literature

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Abstract

Primary synovial sarcoma is a very rare tumor of the mediastinum, which is unreported in the entire subcontinent of West Africa, and presents daunting challenges from diagnosis to management with lack of standard management strategies. We present a case of primary monophasic synovial sarcoma of the anterior mediastinum, in a 22-year-old Nigerian lady who presented with cough, chest pain, and pleural effusion. Chest X-ray (CXR) and computed tomography on admission showed a left-sided huge mass in the left anterior mediastinum with no metastasis to the contralateral pleural cavity. Complete resection of the mediastinal tumor was done and histologic and immunohistochemical analyses confirmed a diagnosis of monophasic synovial sarcoma. However, 10 months postoperation she represented with chest pain, productive cough and a repeat CXR showed multiple left pulmonary nodules. She received two cycles of docetaxel and gemcitabine chemotherapy, but declined further treatment until her demise 8 months later.

Key words: Chemotherapy, immunohistochemistry, mediastinal mass, surgical resection, synovial sarcoma

Date of Acceptance: 11-Jun-2015

Introduction

Primary synovial sarcoma is a very rare tumor of the mediastinum. It is a rare type of soft-tissue sarcoma, which comprise <1% of malignant neoplasms and <0.01% of all malignant thoracic neoplasms.[1] A prudent search of literature showed that it is unreported in the entire subcontinent of West Africa and pose daunting challenges from the point of diagnosis where investigations such as immunohistochemistry and cytogenetics are required to therapeutic management with the limited availability of information on standard management strategies. Complete tumor resection is the only therapy associated with long-term survival with uncertainty existing regarding the best therapeutic strategy for patients with unresectable disease.[2] External beam radiotherapy and chemotherapy are other therapeutic options that have been used as primary therapy mostly in an attempt to reduce the tumor size to achieve resectability.[2] Therapeutic combinations of surgery, chemotherapy, and radiotherapy have been used in the management of this neoplasm. Here, we report a case of this rare tumor and review the relevant literature.

Case Report

A 22-year-old Nigerian female presented in our hospital with a history of cough of 4 months, and chest pain of 1-month duration. The cough was frequent and productive of yellowish sputum, with occasional episodes of specks of hemoptysis. There was associated fever and breathlessness. The breathlessness was moderate, but the fever was high-grade and intermittent. There was also associated fatigue and anorexia, but no weight loss. The chest pain was localized to the anterior (left parasternal) and posterior chest, moderate in intensity and nonradiating. There was

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Access this article online

Quick Response Code:

Website: www.njcponline.com

DOI: 10.4103/1119-3077.175965

neither leg swelling nor orthopnea, no contact with a person with chronic cough, tuberculosis, asbestos and no prior history of chest trauma, surgery or blood transfusion. She was not a known asthmatic. There was also no history of alcohol or tobacco use and no history of similar sickness in her family. She was initially managed in a peripheral hospital with antibiotics, pleural aspiration and left tube thoracostomy drainage before referral to our center.

On clinical examination was a young lady in mild respiratory distress, afebrile, not pale, anicteric, and no pedal edema. The respiratory rate was 20 c/m, pulse rate - 90b/m and blood pressure (BP) - 90/60 mmHg. The trachea was deviated to the left and she had a thoracostomy wound at the left 5th intercostal space. There was a reduced excursion on left hemithorax with dull percussion notes at the left upper zone laterally and on the lower zone. Furthermore, a reduced vocal resonance and breath sounds at the left upper and lower zones. There were normal heart sounds with no murmurs. Examination of the abdomen was unremarkable. She was investigated, and the sputum acid-fast bacilli X3 and Mantoux tests were negative. The chest X-ray (CXR) and chest computed tomography revealed a mass in the upper left chest extending from anterior to posterior, with different densities but no mediastinal adenopathies [Figures 1 and 2]. The abdominal ultrasonography was unremarkable. She then had an exploratory left postero-lateral thoracotomy via the left 5th intercostal space while under general anesthesia with endotracheal intubation done with a 7.5 mm cuffed single lumen endotracheal tube and noninvasive monitoring of oxygen saturation, BP and heart rate. A huge encapsulated and lobulated anterior mediastinal mass measuring 20 cm × 15 cm × 15 cm was seen extending superiorly and posteriorly, and compressing on the normal left upper lung lobe. The mass was mobilized off the left upper lung zone and resected from the anterior mediastinum. With adequate hemostasis achieved and with an estimated blood loss of 2.5 L, she was transfused with 3 units of blood intra-operatively. She subsequently had an uneventful postoperative period and was discharged home on 7th day postoperation in good condition.

The gross examination of the resected specimen showed pieces of irregularly shaped greyish white tissues with the two large ones measuring 8 cm × 7 cm × 5 cm and 7 cm × 7 cm × 3.5 cm respectively and other smaller pieces aggregating to 13 cm × 12 cm × 1.5 cm. The cut surfaces were similar, solid, but with variegated colored areas. The microscopy showed a malignant mesenchymal proliferation consisting of atypical spindle tumor cells proliferating as a fairly monotonous proliferation of short spindled cells with alternating hypercellular and hypocellular myxoid areas [Figure 3]. The atypical spindle cells have vesicular blunt-ended nuclei, granular chromatin patterns and relatively thin cytoplasm with up to 8 mitoses seen per 10 high powered fields [Figure 4]. Immunohistochemistry showed that the tumor cells were completely negative for desmin, CD34, and S100. There was a focal expression in a minority of cells for calretinin, especially in the hypocellular areas [Figure 5] but no nuclear expression of WT-1. CD99 (Ewing's sarcoma marker) expression was weak and patchy [Figure 6]. There was a strong expression in a minority of cells for broad spectrum cytokeratins (AE1/3), especially in the hypercellular areas [Figure 7]. The tumor showed a varying Ki-67 index of 5–20% in different areas [Figure 8]. The histopathology report diagnosed the mediastinal tumor as having histologic and immunohistochemical features of monophasic synovial sarcoma.

She presented for follow-up at the outpatient clinic in the first 2 months postoperation in good condition and with fully re-expanded left lung on chest radiograph. However, 10 months postoperation, she represented with chest pain and productive cough, and a repeat CXR showed multiple left pulmonary nodules. She was given two cycles of

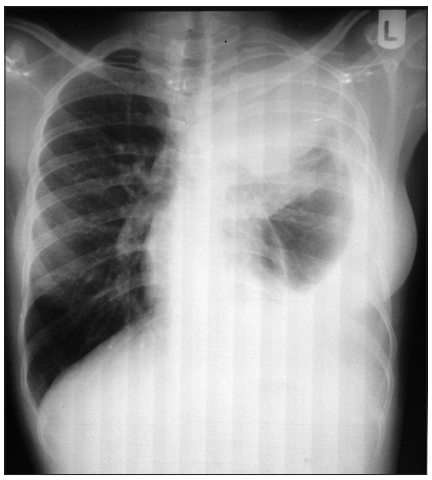

Figure 1: Chest X-ray showing a huge mass in the antero-superior mediastinum (postero-anterior view)

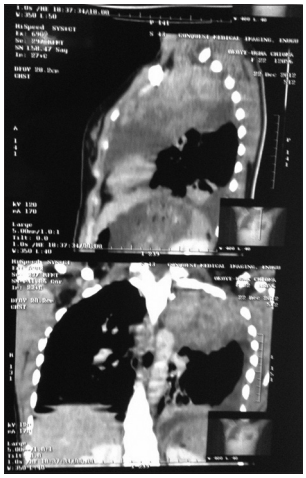

Figure 2: Computed tomography (chest) showing a huge intrathoracic mass occupying the whole upper left hemithorax with collapse of the left upper lung lobe

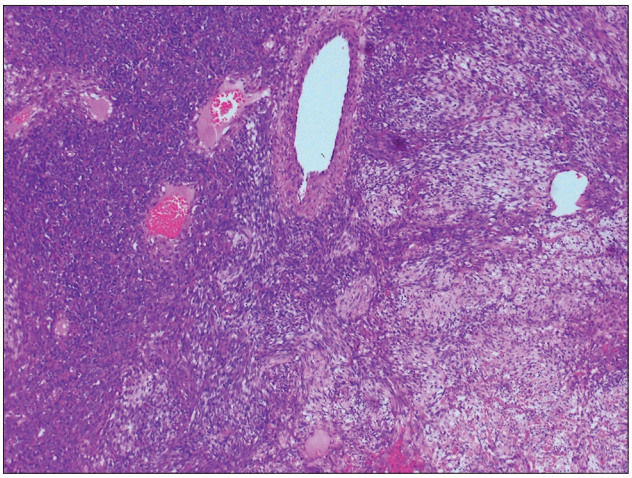

Figure 3: Photomicrograph showing atypical spindle tumor cells proliferating with alternating hypercellular and hypocellular myxoid areas (H and E, ×4 objective)

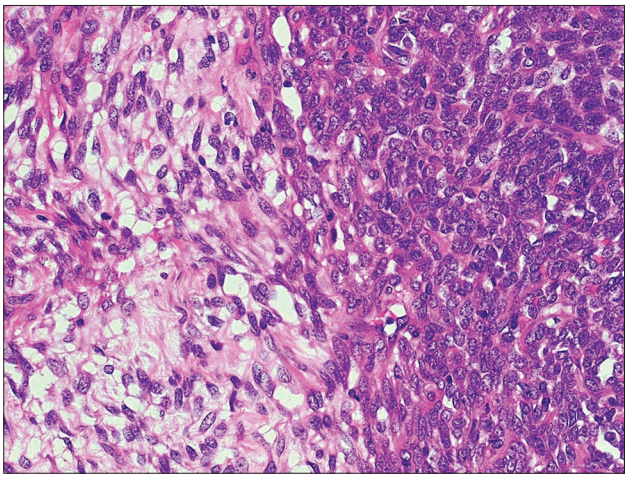

Figure 4: Photomicrograph showing atypical spindle tumor cells with vesicular blunt ended nuclei, granular chromatin patterns and relatively thin cytoplasm, proliferating in a fairly monotonous pattern (H and E, ×20 objective)

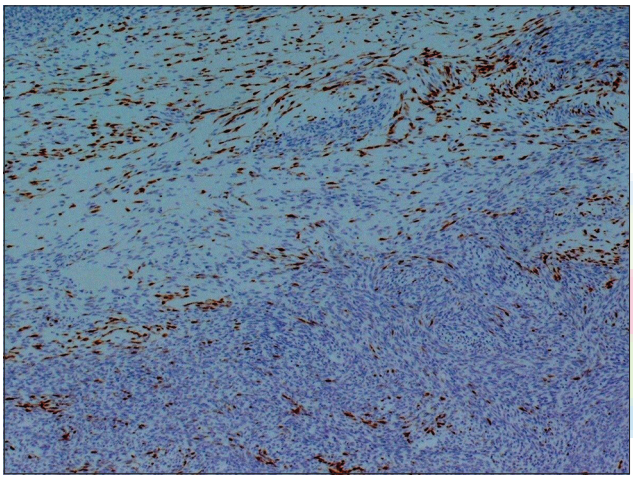

Figure 5: Photomicrograph showing focal calretinin expression in a minority of tumor cells, especially in the hypocellular areas (Calretinin, ×4 objective)

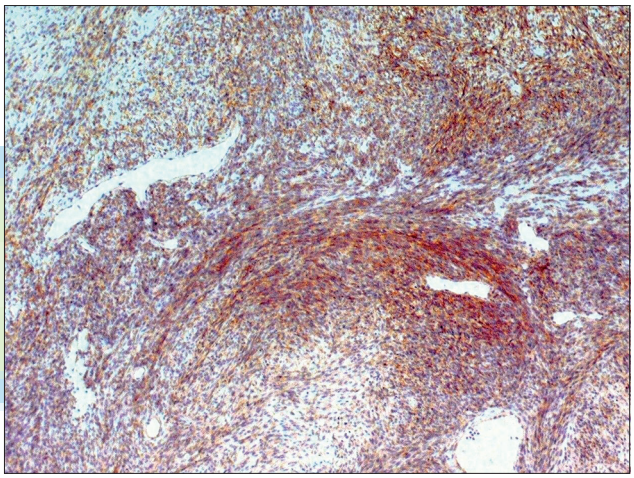

Figure 6: Photomicrograph showing a weak but patchy expression of CD99 amongst the tumor cells (CD99, ×4 objective)

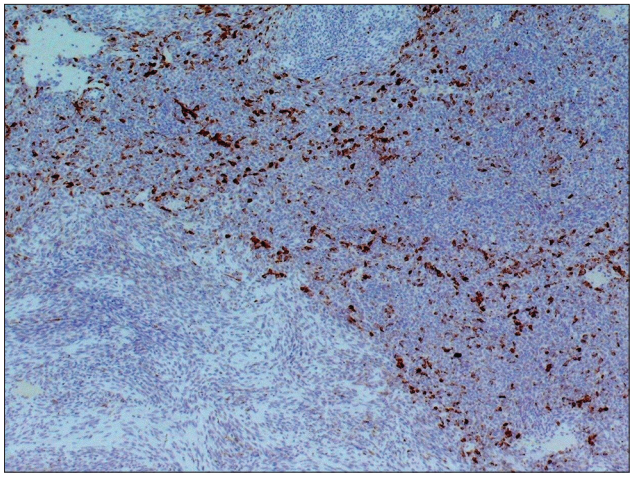

Figure 7: Photomicrograph showing a strong expression of broad spectrum cytokeratins (AE1/3) in a minority of tumor cells, especially in the hypercellular areas (AE1/3, ×4 objective)

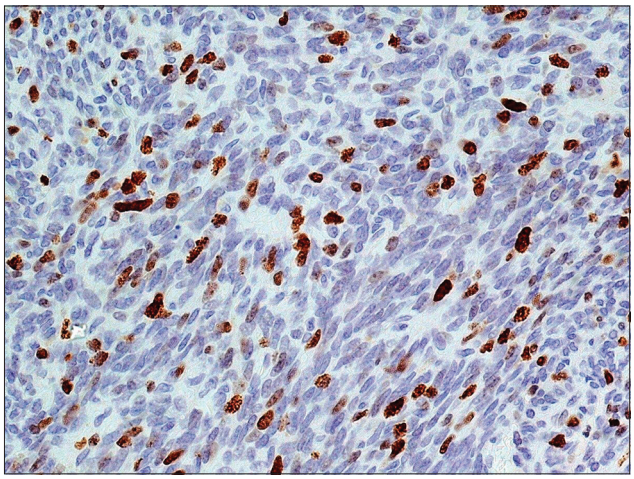

Figure 8: Photomicrograph of tumor cells showing a Ki-67 index of 5-20% (Ki-67, ×20 objective)

adjuvant chemotherapy using docetaxel (75 mg/m^2) and gemcitabine (1000 mg/m^2) and was booked for radiotherapy. She, however, declined further treatment until she died 8 months later.

Discussion

Soft-tissue sarcomas are a rare group of malignant tumors comprising <1% of malignant neoplasms and <0.01% of all malignant thoracic neoplasms.[1] Synovial sarcomas are a distinctive form of soft-tissue neoplasms, most commonly affecting the extremities of young adults and arising from the pluripotential mesenchymal cells near joint surfaces, tendons, tendon sheaths, juxta-articular membranes and fascial aponeurosis. They make up 5–10% of all soft-tissue sarcomas, and arise mainly in the extremities of young adults, in second to fourth decades of life and between 15 and 40 years of age.[3,4] Synovial sarcomas also arise in joint cavities and anywhere unassociated with a joint cavity such as the head and neck, lower back, abdominal wall, genitourinary tract, thoracic wall, and intrathoracic and other much rarer sites.[5] They can also present as a primary mediastinal neoplasm, with a morphologic appearance similar to those occurring in the extremities.[3,6] The classical histologic picture of synovial sarcoma is that of a mixture of epithelial and spindle cell components exhibiting a biphasic pattern.[4,5] However, some of these tumors show only one cell type and are classified as monophasic spindle cell type or monophasic epithelial cell type synovial sarcoma.

Our patient's tumor measured 20 cm × 15 cm × 15 cm, which is huge compared to reported mean size of 7.5 cm for similar tumors.[7] It extended superiorly and posteriorly to compress the entire upper left lung with tracheal deviation to the left. It showed only atypical spindle cells which made histological diagnosis on routine H and E stains almost impossible but for the immunohistochemical stains which ruled out other spindle cell tumors and thus made the diagnosis of monophasic synovial sarcoma. While biphasic, monophasic, and poorly differentiated types of synovial sarcoma do occur, two histological subtypes of synovial sarcoma have special clinical significance; the extensively-calcified type with a more indolent course and better prognosis, and the poorly differentiated tumors with a poor outcome.[8,9] Our patient's tumor had no areas of calcification, it was solid but had variegated colored areas.

The differentials which were considered unlikely include; malignant peripheral nerve sheath tumor (due to complete negativity with S100, no history or features of neurofibromatosis), mesothelioma (considering the age, absence of history of exposure to asbestos, weak focal expression of calretinin only in hypocellular areas and total negative with WT-1), rhabdomyosarcoma (no desmin expression), solitary fibrous tumor (the hypercellularity and negativity with CD34), and Ewing's sarcoma/primitive neuroectodermal tumours (age, and weak patchy expression of CD99).

The histopathologic diagnosis of monophasic synovial sarcoma was made on the strength of age, clinical features, and the tumor's histologic and immunohistochemical features, especially the pattern of cytokeratin expression. Additional cytogenetic and molecular assays to demonstrate the presence of typical chromosomal translocations in synovial sarcoma was however not done in this case due to financial constraints.

Synovial sarcomas, particularly mediastinal synovial sarcomas, are highly aggressive tumors, which are more likely to invade adjacent significant organs, including the heart, lung, and blood vessels, the majority of which exhibit no evident clinical features, thus highlighting challenges for diagnosis and prompt treatment.[10] Mediastinal synovial sarcoma is a rare tumor with few cases reported world over but with no case of such a rare tumor having been reported in the West African subcontinent found in the available literature.[3,5-8,10,11] The reason for this could be that, it is either rarer in West Africa or is under reported because of the unavailability of diagnostic facilities.

Surgical resection is the cornerstone of therapy for thoracic soft tissue sarcomas including those arising in the mediastinum. The complete resectability of the mass is the most important factor associated with long-term survival.[2] However, complete resection becomes a major problem in some cases, especially at late presentation. Another important factor is the presence or absence of metastasis which will also mar the prognosis. Patients with complete or repeated resections have been shown to have a better chance for long-term survival of up to 14 years.[10] Different oncologists have also used adjuvant chemotherapy and radiotherapy after either surgical resection or as neo-adjuvant therapy to reduce size of tumor, especially in unresectable diseases. However, most cases progressed locally and at distant sites shortly following completion of radiotherapy and chemotherapy and died within 2 years of diagnosis.[2] Our patient received two cycles of adjuvant chemotherapy and declined further treatment. She died 8 months after chemotherapy.

Conclusion

Primary monophasic synovial sarcoma of the anterior mediastinum is a rare tumor worldwide. More research is required in developing appropriate treatment modalities for this life-threatening condition which is hitherto unreported in our environment.

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How to cite this article: Ukekwe FI, Ezemba N, Olusina DB, Igbokwe U, Ngene C. Giant primary synovial sarcoma of the anterior mediastinum: A case report and review of literature. Niger J Clin Pract 2016;19:293-7.

Source of Support: Nil, **Conflict of Interest:** None declared.