

Giant Mediastinal Haemangiopericytoma: An Uncommon Case

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Abstract

Haemangiopericytoma is a rare soft tissue tumour characterised by tightly packed tumour cells situated around thin walled endothelial lined vascular channels, ranging from capillary sized vessels to large gaping sinusoidal spaces. The tumour cells are surrounded by reticulin and are negative for muscle, nerve and epithelial markers. The diagnosis of extra-pulmonary intra-thoracic, extra-pleural mediastinal mass is difficult. It constitutes only 6% of all primary tumours and cysts of the mediastinum. We report the rare occurrence of primary intra-thoracic, extra-pulmonary mediastinal haemangiopericytoma of mesenchymal origin with perivascular localisation. The patient underwent right postero-lateral thoracotomy and post-operatively received chemotherapy with adriamycin (60 mg/m²) on day 1 and ifosfamide (1.5 g/m²) on day 1 to 3. Thirty-seven months after the operation, the patient has been well with evidence of a single recurrence in the left lower lobe.

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Key words: Haemangiopericytoma, Thoraco-mediastinal tumours.

Introduction

Primary intra-thoracic, extra-pulmonary mediastinal haemangiopericytomas (HPCs) are rare tumours. In these tumours, a consistent HPC pattern is evident throughout the entire tumour with reticulin surrounding individual cells (everywhere), muscle, nerve sheath and epithelial markers are negative but CD34 and vimentin are positive. One fourth of them are benign.^{1,2} These constitute only 1% of all vasoformative tumours of the body, 6% of mediastinal tumours and 3%-5% of all soft tissue sarcomas.³ Only six cases of HPC of the thorax out of 17165 cases are documented.³ Prolonged chemical exposure, radiation therapy, rarely burns or scars, trauma and steroid therapy have been linked with aetiology. Because of its rarity, it practically never enters into clinical differential diagnosis of giant intra-thoracic tumours. Biologic behaviour of HPC varies from benign to malignant depending on the tumour site, size, degree of cellularity and necrosis. It is currently no longer considered a specific entity, but is a growth pattern because morphological characteristic of moderate cellularity, monotonous appearance and a well-defined branching staghorn vascular pattern is shared by unrelated benign or malignant lesions like (i) solitary fibrous tumour, (ii) several types of true sarcomas including synovial sarcoma, and (iii) benign neoplasms with myoid differentiation which is related to smooth muscle neoplasms and glomus tumours.³⁻⁶ We report an unusual case of primitive, giant, voluminous, intra-thoracic, extra-pleural mediastinal HPC with an aggressive clinical course.

Case Report

A 22-year-old woman presented with progressive shortness of breath with chest pain, cough and intermittent fever for 18 months. Physical examination revealed tachypnoea, use of accessory respiratory muscle, the percussion note was dull on the right, and breath sounds were diminished to absent on the right side. Laboratory studies revealed haemoglobin of 8.2g/dL, haematocrit 28% and hypochromic microcytic anaemia. Blood urea nitrogen, serum creatinine were normal. Pulmonary function study showed a restrictive defect only.

Chest radiograph (Figure 1) showed a homogeneous opacity occupying the medial two-thirds of the right hemithorax. Computed tomography (CT) of the chest showed a mass in the right hemithorax (16cm × 11cm) causing compression atelectasis of the lung. The lesion showed no signs of infiltration and was non-homogeneous on contrast enhanced computerised tomography (CECT) (Figure 2). Bronchoscopy revealed compression and crowding of the right upper, middle and lower lobes but no intraluminal growth. Gun biopsy specimen disclosed only spindle cell tumour.

The patient underwent right postero-lateral thoracotomy along the fifth intercostal space. Intra-operatively a huge, well-circumscribed, vascular mass (20cm × 14cm) which appeared to be attached to posterior mediastinum with adhesions to surrounding structures (Figure 3). The surrounding lung parenchyma was compressed by the tumour and

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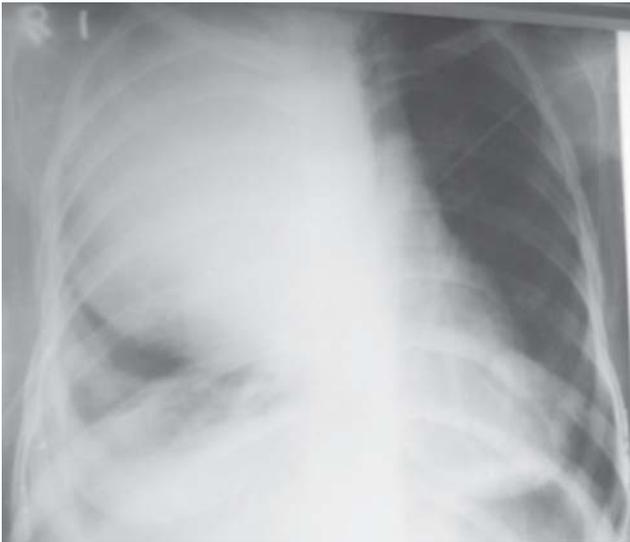


Figure 1. Pre-operative chest radiograph (PA view) showing a large mass on the right side of the chest with displacement of the lung.

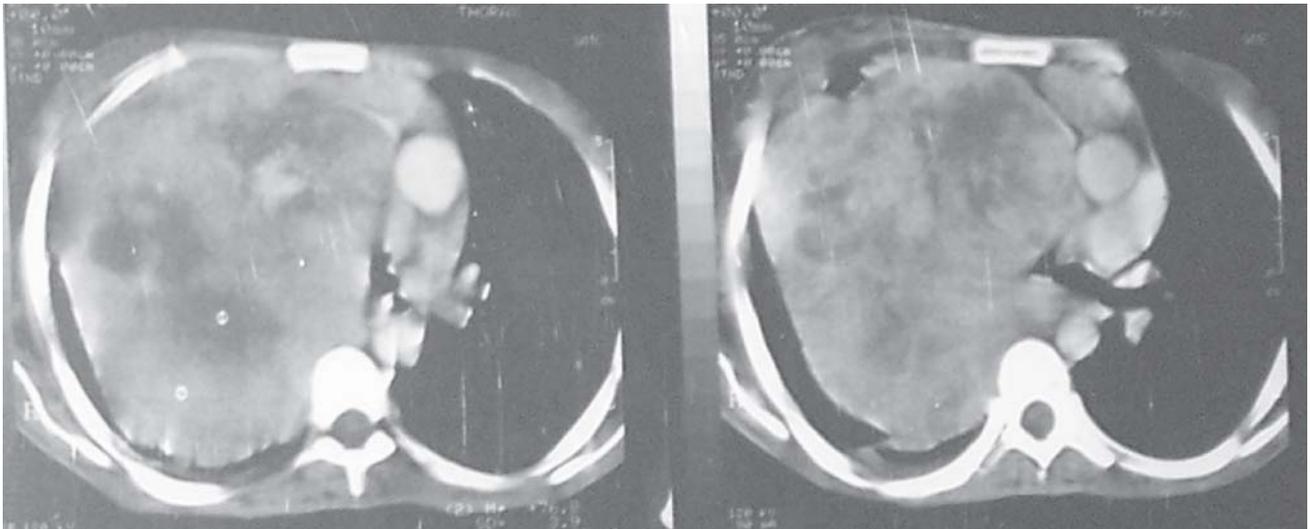


Figure 2. Pre-operative CECT of the chest demonstrating a hypodense tumour mass located in the mediastinum on the right side with a smooth outline and compressed adjacent lung tissue.

there was no involvement of vital mediastinal structures. The tumour was resected totally by morcelment despite persistent bleeding; 130 mL of sanguinous fluid was aspirated. The mass weighed 2.2Kg. Microscopically the mass was characterised by round and spindle cells with a network of branching irregular vascular spaces around which tumour cells were arranged in a concentric or radial pattern, separated from the flat endothelial cells by a basement membrane, giving a staghorn or moose antler appearance (Figure 4). The mitotic activity was low (3-4 per 10 hpf) but necrosis could be observed. The silver reticulin stain demonstrated the extra-vascular position of these cells about the small vascular spaces. This was typical of low grade malignant haemangiopericytoma. The tumour cells were immunoreactive for vimentin and CD34.

Endothelial markers, anti-smooth muscle actin (A-SMA), S-100, cytokeratin and desmin were negative. The post-operative period was uneventful and the patient was discharged on 13th post-operative day. Post-operatively the patient was treated with adriamycin (60mgm/m²) on day 1 and ifosfamide-based (1.5gm/m²) on day 1 to 3 chemotherapy. Thirty-seven months after the operation the patient has been well with evidence of a single recurrence or metastasis in the left lower lobe.

Discussion

We diagnosed this case by structural feature of the mass, spindle-shaped cells surrounding the endothelial lined vascular spaces observed on histopathology and the mass was positive for CD34 and vimentin, and negative for CD99, bcl2, desmin, cytokeratin, S-100, epithelial membrane antigen and A-SMA.

Intra-thoracic mediastinal HPC is a rare mesenchymal tumour with pericytic differentiation



Figure 3. Operative photograph revealing a huge, mass which is highly vascular.

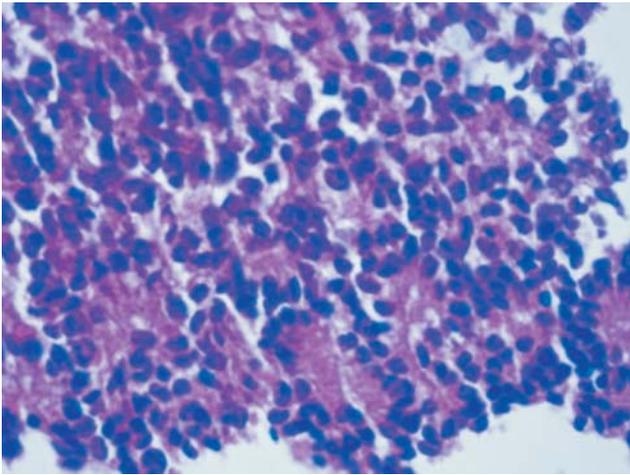


Figure 4. Photomicrograph showing round and spindle cells surrounded by thin walled endothelium lined vascular spaces, giving a staghorn appearance to the vessels as typically seen in haemangiopericytoma (Haematoxylin and Eosin \times 200).

with few cytoplasmic organelles in adults. On review of the literature, 29 cases most of them case reports could be retrieved. The age range is wide (3 to 81 years, mean 45 years) with an equal distribution in the gender. Intra-thoracic primary HPC was first described by Schmidt in 1937 but documented by Feldman and Seaman in 1964,⁷ though Stout and Murray coined the term HPC in 1942.³ These are rare compared to tumours of pulmonary origin. These present as a well-defined mass containing solid and cystic components with extreme hypervascularity in the solid component with uniform positivity for CD34 and vimentin. About half of the patients are asymptomatic but chest pain, cough and haemoptysis can be associated. Pre-operatively diagnosis can be difficult. Para-neoplastic syndromes like hypoglycaemia produced by insulin like growth factor II (IGFII), and osteoarthropathy producing clubbing are described. Lesion mimics hamartoma. The differential diagnosis includes solitary fibrous tumour, synovial sarcoma, carcinoid tumour, benign clear cell tumour, malignant melanoma, mesothelioma and thymoma class 1A (spindle cell).⁸⁻¹⁰

In adult cases, a benign course is noticed which is associated with massive growth of the mass but 20% to 30% do behave in a malignant fashion. In infantile cases, there is marked similarity between infantile myofibromatosis.^{9,11,12} Chest radiograph reveals a homogeneous, soft tissue density mass with a smooth lower margin. Unenhanced CT shows soft tissue mass lesion with a smooth margin, ground glass appearance and occasionally tumoural calcification, and after contrast an inhomogeneous mass with areas of low attenuation due to necrosis.⁸ Magnetic resonance imaging (MRI) shows intermediate signals on T₁ weighted images and increased signal on T₂ weight image.⁸ A triple sign (bright, dark and grey) representing tumour, haemorrhage and necrosis is noticed on MRI.

Macroscopically it appears to be a well-defined, voluminous, expansive mass having a fibrous pseudocapsule which compresses the surrounding structures with areas of necrosis and haemorrhages. The mass is well demarcated and solid. It can be asymmetric, lobulated, nodular, soft, spongy, firm or friable. The cut-surfaces are red brown with visible vascular spaces with extreme hypervascularity in the solid component.^{9,11}

Microscopically cells are spindle-shaped, highly cellular with abundant cytoplasm, oval nuclei located eccentrically with small nucleoli. A frame-work of silver stain reticulin fibers, surrounding individual spindle cells is a characteristic diagnostic feature. The diagnostic criteria of aggressiveness include size more than 6.5cm, anatomic location, recurrence of tumour, presence of immature or pleomorphic cells, presence of more than 4 mitotic figures per 10 high power field, foci of haemorrhage or necrosis. No single clinical, histopathologic feature, or deoxyribonucleic acid (DNA) ploidy allows prediction of biological behaviour.^{2,9,10,13} Haemangiopericytomas pattern occurs in fibrous histiocytoma (storiform pattern and inflammatory cells), phosphaturic mesenchymal tumour (calcification and osteoclast like giant cells), angiosarcoma, mesothelioma, thymoma (express cytokeratin and very sparse reticulin) solitary fibrous tumour (fibrosis, fascicular form, vimentin, CD34, CD99 and bcl2 immuno-reactivity), synovial sarcoma (biphasic pattern, epithelial membrane antigen and cytokeratin), mesenchymal chondrosarcoma (islands of mature cartilages), infantile fibrosarcoma,¹⁰ (herringbone pattern) myopericytoma, infantile myofibromatosis and low grade endometrial stromal tumour.

Immunohistochemically, HPCs are known to show a positive response to antibodies against vimentin and type IV collagen, and a negative response to factor VIII related antigen, S-100 protein, neuron-specific enolase, carcino-embryonic antigen, desmin, laminin and cytokeratins AE1/AE3.^{6,8,9,14} The immunohistochemical examination demonstrated the tumour is non-epithelial (vimentin positive and cytokeratin negative) and has CD34 antigens, a marker of pericytes and hematopoietic progenitors. The CD34 and vimentin are characteristics of mesenchymal origin and identify neoplastic progenitor cells surrounding vascular spaces. The KI-67 immunocytostain may determine proliferative rate which is upto 39% with a median value of 10%, and vein structure stained with actin upon which characteristic vascular structure with staghorn configuration is noticed. In addition vascular endothelial growth factor (VEGF-A) is up-regulated in tumour cells. Solid fibrous tumour has also above immunocytoreactivity but CD34, CD99 and bcl2 reactivity is very specific for this.¹⁴ In a recent World Health Organization classification of soft tissue tumours, HPCs and solid fibrous tumours are considered as a single entity with a morphological continuum among them.⁵ The CD34 positivity in

apparent HPC is now called solitary fibrous tumour when CD34 expression is strong and diffuse.^{4,6} In the absence of pericytic differentiation most HPCs are considered morphological forms of solitary fibrous tumour.^{2,6} Cytometric studies showed near diploid and breakpoints in 12q13, 12q24 and 19q13 seem to be common with t(12;19) (q13;q13) being a recurrent translocation but such observation are not consistent.^{10,14} In HPC, t(1:3) (q22;q11), t(7:12) (p22; q13), t(12:19) (q13; q13:3), t(13:21) (q22;q11) is observed.^{10,14}

Wide surgical excision of the HPC either by thoracotomy or by thoracoscopy is the treatment of choice. Pre-operative radiotherapy or embolisation^{12,13,15} has been utilised to reduce the vascularity and size of the large tumour. It is important to look for invasion to the lung, or to the surrounding chest wall at the time of resection. Pre-operative and post-operative radiotherapy and adjuvant chemotherapy with adriamycin has been recommended to prevent local recurrence of the tumour or superior vena cava obstruction. Now a P₆ protocol which consists of high doses of chemotherapy, debulking operation, cytoreduction surgery, radiation therapy, haematopoietic stem cell transplantation, and radiofrequency ablation is followed.⁴

The five-year survival rate of HPC is reported to be 85%⁸ and that of thoracic pulmonary origin is 30% to 35%, with 5- and 10-year-acturial-survival rates of 80% to 47%, respectively; local recurrence is about 50% within two years while distant metastasis occurs in about 11% to 56% (average 22%) of cases. Overall survival and disease-free survival is worse on necrosis, high P53, metastasis and de Perrot staging. Lymph node metastasis is rare. Latency period upto 33 years has been reported. Recurrences are usually found in the thorax either in the pleura or in the lung parenchyma. All intra-thoracic, extra-pulmonary mediastinal HPCs, are potentially malignant and a combination of complete surgical excision, chemotherapy (adriamycin) and radiotherapy is the treatment of choice.^{4,6,9,10} The combination temozolomide bevalizumab, and tyrosine kinase inhibitors (imatinib, sorafenib and sunitinib) are showing promising results.³

References

1. Cakir E, Findik G, Hosgun D, Demirag F. Primary mediastinal haemangiopericytoma: an unusual cause of massive haemoptysis in a young woman. *Acta Chir Belg* 2010;110:235-7.
2. Yucel O, Kavakli K, Genç O, Gunnah O. Hemangiopericytoma located in the mediastinum: a case report. *Turkish J Thorac Cardiovasc Surg* 2010;18:74-7.
3. Stout AP, Murray MR. Hemangiopericytoma a vascular tumor featuring Zimmermans pericytes. *Ann Surg* 1942; 116:26-33.
4. Penal N, Amela EY, Decaniar G, Robin YM, Berard PM. Solitary fibrous tumours and so called hemangiopericytoma. *Sarcoma* 2012;
5. Fletcher CD. The evolving classification of soft tissue tumours: an update based on the new WHO classification. *Histopathology* 2006;48:3-12.
6. Gengler C, Guillou L. Solitary fibrous tumour and hemangiopericytoma: evolution of a concept. *Histopathology* 2006;48:63-74.
7. Feldman F, Seaman WB. Primary thoracic haemangiopericytoma. *Radiology* 1964;82:998-1009.
8. Kusumoto S, Nakamura R, Mizoguchi N, Ono S, Watanabe K. Primary intrathoracic extrapulmonary hemangiopericytoma: CT and MR findings. *Clin Imag* 1997;21:51-3.
9. Chnaris A, Barbetakis N, Efstathiou A, Fessatidis I. Primary mediastinal hemangiopericytoma. *World J Surg Oncol* 2006; 4:23-8.
10. Espat NJ, Lewis JJ, Leung D, Woodruff JM, Antonescu CR, Shia J. Conventional hemangiopericytoma: modern analysis of outcome. *Cancer* 2002;95:1746-51.
11. Hiraki A, Murakami T, Aoe K, Matsuda E, Haedat Umemori Y, Ueoka H. Recurrent superior mediastinal primary haemangiopericytoma 23 years after the complete initial excision: a case report. *Acta Med Okayama* 2006; 60:197-200.
12. Morandi U, Stefani A, Desantish M, Paci M, Lodi R. Preoperative embolization in surgical treatment of mediastinal hemangiopericytoma. *Ann Thorac Surg* 2000;69:937-9.
13. Jalal A, Jeyasingham K. Massive intrathoracic extrapleural haemangiopericytoma: deployment of radiotherapy to reduce vascularity. *Eur J Cardiothorac Surg* 1999;16:378-81.
14. Sanguenza OP, Requena L, Walse SH. Perivascular cell neoplasms. *Pathol Case Rev* 2008;13:247-57.
15. Findir S, Akah H, Baris BD, Satici AG, Uzum O, Erkan L. Preoperative embolization in surgical treatment of a primary hemangiopericytoma of the rib: a case report. *J Korean Med Sci* 2005;20:316-8.