Mediastinal Hemangiomatosis — A Case Report

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Hemangiomas are benign vascular neoplasms that most commonly occur in the skin, subcutaneous tissue, mucous membranes of the oral and genital regions, and abdominal viscera. Multiple hemangiomas are defined as hemangiomatosis. The majority of hemangiomas require no intervention, however, treatment is necessary in 10% to 20% of cases, due to their location, size, or behavior. The diagnosis of life-threatening hemangiomas base on radiographic studies is challenging because the hemangiomas might mimic other lesions or carcinomas. They are typically not diagnosed until surgery. In this case, we report an 18-year-old patient who had suffered from dyspnea and chest pain for several years. Chest radiographs showed a mediastinal mass that initial CT-guided biopsy reported as a thymoma. However, the definitive diagnosis, after open lung biopsy, turned out to be mediastinal hemangiomatosis. ***(Thorac Med 2004; 19: 125-131)***

Key words: hemangiomas, hemangiomatosis, thymoma

Introduction

Hemangiomas are benign vascular neoplasms that exhibit an early and rapid proliferative phase during the first year of life. They are characterized by the canalization of hyperplastic solid masses of endothelial cells, followed by a slower involution phase that may last for years [1]. Hemangiomas most commonly occur in the skin, subcutaneous tissue, mucous membranes of the oral and genital regions, and abdominal viscera [1-3]. The majority of hemangiomas require no intervention. However, treatment is necessary in 10% to 20% of cases, due to their location, size, or behavior [4]. Diagnosis of life-threatening hemangiomas from radiographic studies is challenging: they are typically not diagnosed until surgical intervention.

Case Report

This 18-year-old boy presented with exertional dyspnea and intermittent chest pain radiating to the back for several years. No other respiratory symptoms, such as cough or hemoptysis, or systemic symptoms, such as fever or body weight loss, were noted. He went to our outpatient clinic, where chest radiography showed a widening of the upper mediastinum and increased linear opacities in bilateral basal lungs (Figure 1). He was admitted to the chest medicine division for further investigation.

In tracing the patient's past medical history, we found he had received a splenectomy at age 4 due to a splenic hemangioma causing disseminated intravascular coagulation. A recision of multiple

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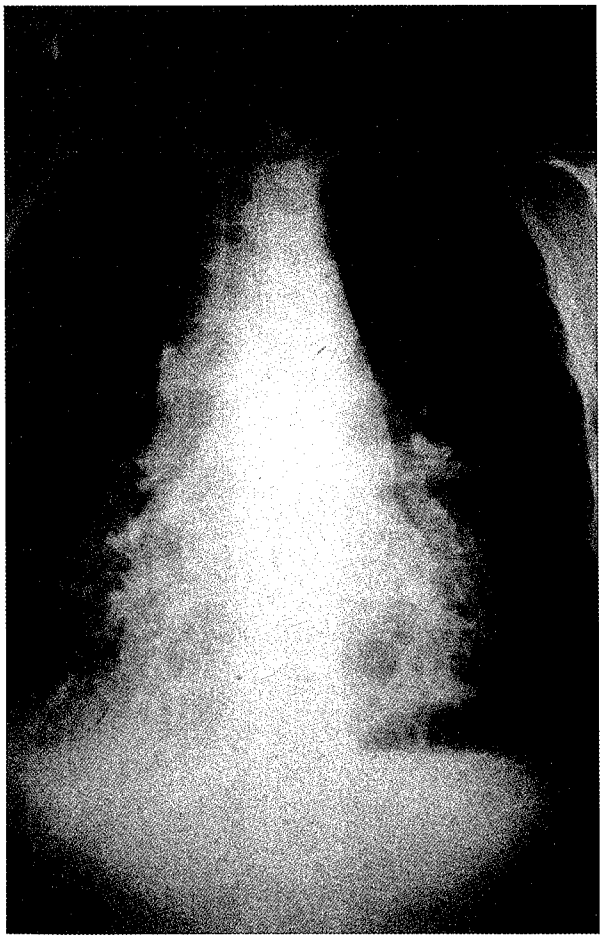

Fig. 1. Chest radiography shows a widening of the upper mediastinum and increased linear opacities in bilateral basal lungs.

hemangiomas on the occipital scalp and a hemangioma on the back was also done at age 13. He underwent a tonsillectomy and uvulopalatopharyngoplasty due to obstructive sleep apnea syndrome at age 15.

On physical examination, a decrease in breathing sounds was observed in the left chest region. The pulmonary function test reported moderately obstructive ventilatory impairment without significant bronchodilator reversibility. Sputum culture and cytologic studies showed negative findings. Chest computerized tomography (CT) revealed diffuse infiltrates of soft tissue densities in the bilateral hila and throughout the mediastinum. Multiple reticulo-nodular densities, diffuse prominent bronchovascular bundles, and interlobular septal thickening were also noted in bilateral lung fields (Figure 2). CT-guided needle biopsy of the mediastinal mass showed a nodular pattern of mixed round-shaped epithelial cells and lymphocytes, and some dilated vessels. The epithelial cells were highlighted by immunostaining with cytokeratin (AE1/AE3). The vascular channels were overlooked and the initial, although erroneous, pathologic diagnosis was thymoma. The patient was transferred for surgical intervention.

He received a minithoracoectomy in January 2003. A plaque-like lesion rather than a mass was seen in the mediastinum. Multiple engorged vascular lesions were also noted in the pulmonary parenchyma. Severe bleeding during pericardial biopsy

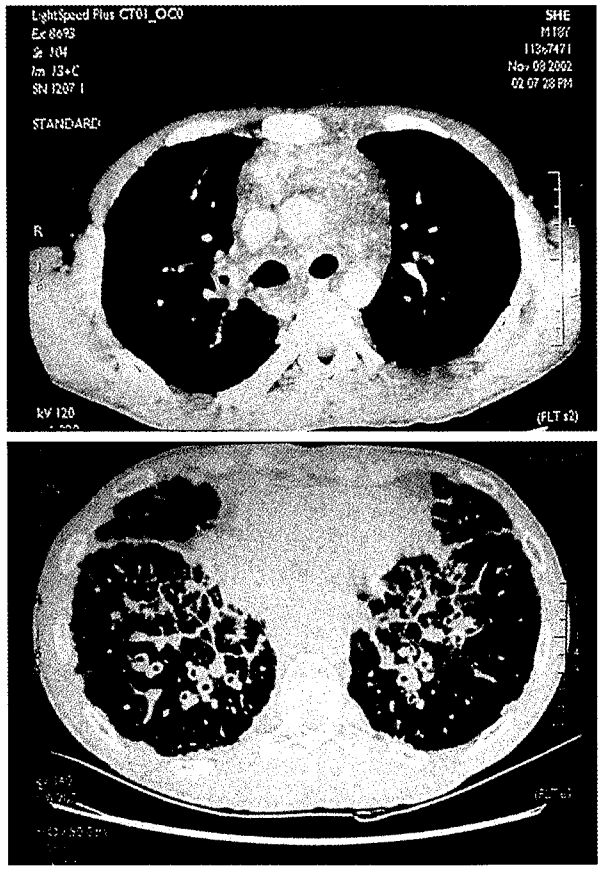

Fig. 2. Chest computerized tomography (CT) reveals: (1) Diffuse interstitial thickness and nodulation mainly in the interlobular septum. (2) Irregular thickness in the bronchovascular bundles, and subpleural surface of the bilateral lungs. (3) Widening of the mediastinum with diffuse veining opacities, consistent with hypervascularity.

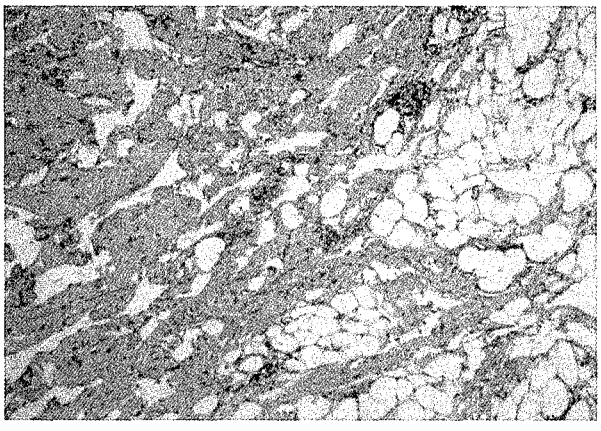

Fig. 3. Photomicrography of the pericardium shows interconnecting capillary channels within fibroadipose tissue (HE stain).

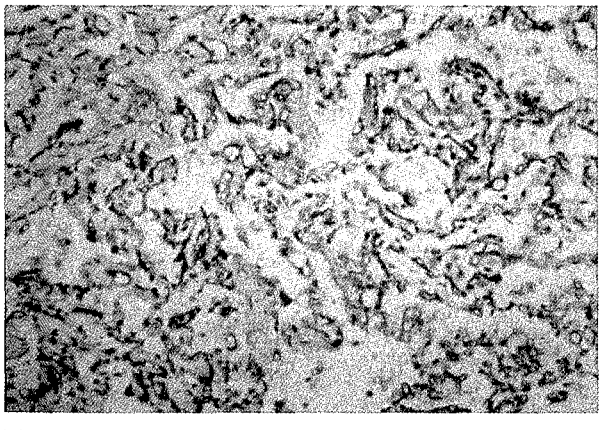

Fig. 4. Photomicrography of the pericardium stained with CD34 highlights the endothelial cells (immunohistochemical stain).

occurred. Lung wedge resections in the left upper and left lower lobes, and a pericardial biopsy, were performed. Microscopically, the specimens from the pericardium and pulmonary parenchyma showed a similar picture, that is, of a capillary hemangioma with an aggregate of capillaries with focal hemorrhage (Figure 3). The endothelial cells were highlighted with CD34-immunostaining (Figure 4). The definitive diagnosis was hemangiomatosis.

The patient was then referred to the oncology division for further radiation treatment.

Discussion

Hemangioma is a primary tumor of the microvasculature in which angiogenesis is initially excessive, followed by a regression of the newly formed vessels. Their histological components include capillary endothelial cells along with an accumulation of macrophages, plasma cells, pericytes, and mast cells [4]. Hemangiomas have a predilection toward females rather then males, at rate of 3:1, and occur in nearly 1-2% of newborns and 10-12% of infants by one year of age [1,5-7].

Hemangiomas limited to the skin have a good prognosis since they usually undergo involution within the first 2 years of life. Fifty percent of the lesions resolve themselves by 5 years of age, and 70% by 7 years of age [1,5,8-9]. The most commonly affected sites are the head and neck, followed by the trunk and limb. When hemangiomas occur in the orbit or adnexa, the complications include astigmatism, anisometropia, amblyopia, and strabismus [1,5-6]. If the subglottalic region is involved, the patient will most probably suffer from respiratory failure, especially infants of 6 to 12 weeks old. Hoarseness and stridor are the signs of subglottalic hemangiomas [5-6]. If the hemangiomas involve the visceral organs, the morbidity and mortality rates are high (40-80%), because of the complications of high-output cardiac failure, gastro-intestinal bleeding, anemia, obstructive jaundice, seizures, hydrocephalus, and consumptive coagulopathy [1-2,5-6, 8,10-11]. Multiple congenital hemangiomas that affect the skin and viscera have been defined as diffuse neonatal hemangiomatosis [1-2,8]. The most commonly involved visceral organ is the liver (60-100%), followed by the lung (52%), brain (52%), and intestine (52%) [1-2,8,10-11]. Hemangiomas also involve the lymph nodes, spleen, kidney, iris, retina, salivary glands, heart, thymus, bladder, gallbladder, pancreas, and adrenal gland [1].

The diagnosis of hemangiomatosis by radiographic imaging can determine the extent and location of the involvement [9]. Ultrasonography with Doppler studies demonstrates the high flow pattern that is the characteristic of hemangiomas [6]. On CT scanning, hemangiomas appear as a homogeneous mass [6]. Magnetic resonance imaging of hemangiomas has shown well-circumscribed,

densely lobulated masses, with an intermediated signal intensity on T_1 -weighted images [6,9]. However, the diagnosis of hemangiomas of the internal organs by radiographic imaging or CT-scan is somewhat challenging, since the hemangiomas might mimic other lesions or carcinomas. Raymond et al. mentioned that internal hemorrhoids, adenomatous polyps, carcinoma, inflammatory bowel disease, and proctitis, might all mimic diffuse cavernous hemangiomas [12].

In this case, we mistook the mediastinal mass for a thymoma, and lymphangitis carcinomatosis was also suspected, base on the CT findings. However, the specimen from the open lung biopsy showed plaque-like lesions rather than a mass. Severe bleeding was also noted during pericardial biopsy, with multiple engorged vascular lesions in the pulmonary parenchyma. Thus, mediastinal hemangiomatosis was highly suspected.

From the past medical history, we knew that the patient had had splenic hemangioma and multiple cutaneous hemangiomas in the past. The pathologic results this time showed hemangiomatosis of the pericardium and lung. We believe that this 18-year-old boy has diffused neonatal hemangiomatosis (DNH), a rare condition characterized by multiple benign cutaneous and visceral hemangiomas.

As mentioned above, the diagnosis of hemangiomas in the visceral organs, using radiography only, may occasionally be difficult. In this case, the mediastinal mass was misdiagnosed as a thymoma initially, using CT-guided biopsy, because the cytokeratin stain highlighted the thymic epithelial cells which mimicked a thymoma; besides, the thymoma is the most common tumor of the anterior mediastinum. After surgical intervention, we reviewed the previous CT-guided biopsy specimen again. Microscopically, multiple small vascular channels lined with endothelial cells were present between the hyperplastic thymic tissue and thymic epithelial cells, admixed with small lymphocytes. Thus hyperplasia of the thymic tissue can be misinter-preted as a thymoma.

Our patient had dyspnea, and his chest films showed a widening of the upper mediastinum and increased linear opacities in bilateral basal lungs, mimicking bronchiectasis. Chest CT scanning showed multiple nodularities with diffuse bronchovascular bundles and interlobular septal thickening in the bilateral lung field. These findings were quite similar to pulmonary capillary hemangiomatosis (PCH) and pulmonary veno-occlusive disease. The characteristic anatomic abnormality in pulmonary veno-occlusive disease is obstruction of the pulmonary veins and venules by intimal fibrosis, cellular proliferation, and muscularization [13]. Pulmonary capillary hemangiomatosis is characterized by thin-walled microvessels infiltrating the peribronchial and perivascular interstitium, lung parenchyma, and septal or pleural connective tissue [13-14]. Secondary pulmonary veno-occlusive disease might occur, resulting in the infiltration and compression of the pulmonary vein by these microvessels [13]. Following a slow, progressive clinical course, PCH will lead to pulmonary hypertension, hemoptysis, and right heart failure [14-15].

The pathogenesis of hemangiomas is unclear, and is believed to be related to hormonal influences and cellular markers of angiogenesis [5-6,11]. Vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF), transforming growth factor-β (TGF-β), and interleukin-6 (IL-6) are the regulators of angiogenesis, and may be involved in the proliferation and involution of hemangiomas [4].

The majority of hemangiomas need no intervention. Treatment is considered based on the location and size of the lesions, the presence of complications, the rate of growth or involution of the lesions, and the age of the patient [1,5-6]. When hemangiomas interfere with important structures and their functions, active treatment is necessary [1]. There are various therapeutic modalities, including systemic corticosteroids, interferon-α-2a, arterial embolization, surgical excision, cryotherapy, cytotoxic agents, laser treatment, and radiation [1-2,4-5]. High-dose systemic or intralesional steroid is the first-line treatment, and a dramatic response has been observed in 30% of cases [1,4]. Interferon-α-2a, an inhibitor of angiogenesis, is recommended for the treatment of life-threatening

hemangiomas that fail to respond to corticosteroid therapy [5-6,9]. The mechanism of action of interferon-α-2a is the inhibiting of the response of endothelial cells, smooth muscle cells, and fibroblasts to their respective growth factors [2]. So the proliferation and migration of endothelial cells is inhibited [14]. Arterial embolization is used to treat cutaneous hemangiomas that have not responded to medical therapy [6]. Cryotherapy and laser treatment are used for the treatment of superficial hemangiomas [5-6]. Radiation was the primary treatment used for hemangiomas during the 1940s and 1950s [5-6]. Surgical excision could be considered for hemangiomas that are life-threatening or impair function, and for which pharmocologic therapy is not effective or well tolerated. However, the benefits and risks of the surgery must be weighed carefully. There might be a high risk of bleeding, and the scar formation may be worse than the result of a spontaneous involution [5-6].

In our case, the patient was referred to the oncology department for radiation therapy. The dyspnea on exertion had resolved by the time of the later follow-up. The mediastinal hemangiomatosis lesions had been restricted and mildly reduced in size. His condition became satisfactory, and he received regular outpatient follow up.

Conclusions

Hemangiomas are benign vascular neoplasms and usually regress spontaneously. Multiple congenital hemangiomas that affect the skin and viscera, known as diffuse neonatal hemangiomatosis, may be fatal. As in our case, hemangiomatosis may involve the lungs, mediastinum, and pericardium, mimicking a mediastinal tumor and lymphangitis carcinomatosis in the radiographic findings. Since the important traits of hemongiomatosis are multiple and recurrent, tracing past medical history is mandatory. The definitive diagnosis relies on histological findings through surgical intervention.

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縱膈血管瘤病—病例報告

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血管瘤是良性的血管贅瘤，通常好發於皮膚、皮下組織、口腔及生殖器官的黏膜、以及腹腔內臟。多發性血管瘤被定義為血管瘤病。大部份的血管瘤不需要積極治療，然而基於血管瘤的位置、大小及狀態，約有一成至二成的病例是需要進行治療的。使用放射線學來診斷血管瘤是有困難的，因為血管瘤會表現得類似其他的病灶或腫瘤。除非經由手術，否則通常是無法輕易把血管瘤診斷出來。

我們報告的這個病例是一位18歲患者，主訴有數年的呼吸困難及胸痛。胸部X光片顯示有一縱膈腫瘤，電腦斷層導引的切片報告則為胸腺瘤。然而經由開胸肺切片之後，最終診斷報告確定為縱膈血管瘤病。*(胸腔醫學 2004; 19: 125-131)*

關鍵詞：血管瘤，血管瘤病，胸腺瘤

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