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Case Report

Pulmonary Capillary Hemangiomatosis: A Case Report and Review of the Literature

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INTRODUCTION

Pulmonary capillary hemangiomatosis (PCH) was first described by Wagenvoort et al. in 1978.[1] Subsequently, a total of 18 cases have been described in the literature.[2-12] This condition is characterized by proliferating sheets of thin-walled capillary channels that infiltrate the walls of pulmonary blood vessels inducing a secondary pulmonary venoocclusive disease. The interlobular septa, pulmonary parenchyma, bronchioles, and pleura may also be involved. We have described an additional case of PCH associated with thrombocytopenia in a child, and it was diagnosed during life by an open lung biopsy.

CASE REPORT

A 12-year-old Syrian girl was perfectly well until 2 months prior to her referral to our hospital when she complained of cough and shortness of breath. The cough was productive of whitish sputum, but there was no hemoptysis. She was initially treated with erythromycin with suspicion of mycoplasma pneumonia because of lung infiltrates on a chest X-ray. However, she remained symptomatic and had anorexia and weight loss. There was no history of consanguinity or similar illness in the family. On examination she did not have clubbed fingers, and the only abnormality was mild respiratory distress and few scattered crepitations bilaterally.

Investigations

Her arterial blood gases at rest were normal. Her CBC revealed an Hb of 12.2 g/dL, the platelet count was 94×10^9 L^{-1}, and the differential WBC was normal. Her erythrocyte sedimentation rate (ESR) was 7 mm/hr and her reticulocyte count was 0.6%. In the peripheral blood smear there were some giant platelets. Her coagulation profile was normal, including platelet aggregation study. Her direct and indirect Coomb's tests were negative. Her hepatic, renal profile, blood sugar, LDH, and urinalysis were normal. Her qualitative immunoglobulins revealed an IgG of 1.8 g/dL, an IgA of 0.33 g/dL, and an IgM of 0.25 g/dL. T and B lymphocyte functions and number were normal. Serology for hepatitis B surface antigen and antihepatitis C antibody tests were negative. Mantoux skin tests with 5 and 10 units of PPD were nonreactive. Multiple sputum samples were negative on smear for acid-fast bacilli and TB cultures were also negative. Bone marrow aspiration and biopsy revealed normal cellularity and adequate number of megakaryocytes. There was no evidence of infiltration of the bone marrow with foreign cells. Pulmonary function tests revealed a mild obstructive pattern with an increased residual volume. Her chest X-ray revealed mediastinal widening, prominent interstitial infiltrates with well-defined Kerley's lines on the peripheral aspect of both lung fields (Fig. 1). CT scan of the chest and mediastinum showed widening of the mediastinum with a diffuse increase in mediastinal density. The vascular structures and trachea were not displaced or compressed. A small lymph node was noted at the right azygoesophageal recess. The lung fields showed diffusely distended lymphatics. No effusion was seen, but there was pleural thickening in the left paravertebral region (Fig. 2). A ventilation/perfusion scan showed mismatching, especially on the left side. Cardiac catheterization and echocardiogram revealed normal pulmonary blood flow and pressures.

In order to reach a diagnosis, a left minithoracotomy was performed. The whole left lung was very stiff and

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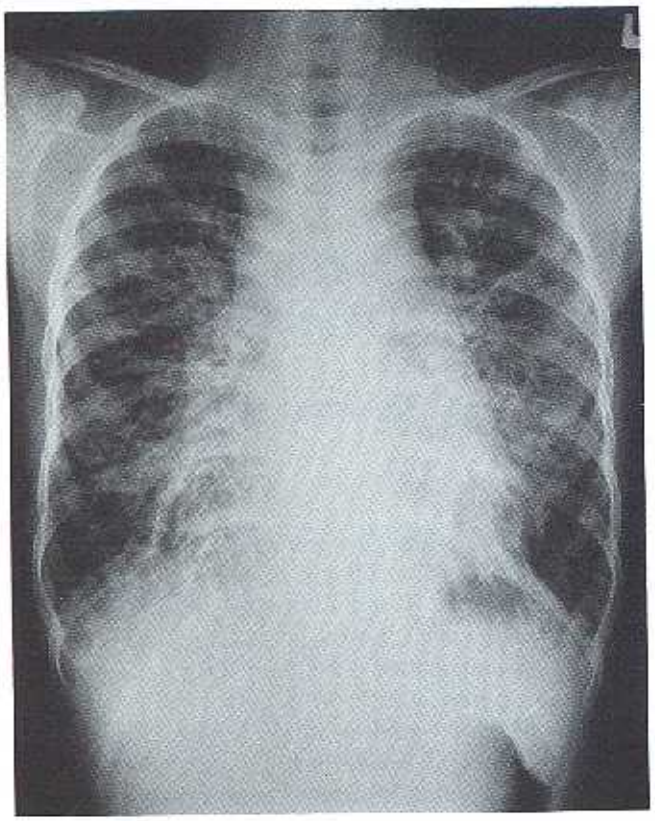

Fig. 1. Chest X-ray showing bilateral infiltrates and mediastinal widening. Note Kerley's lines.

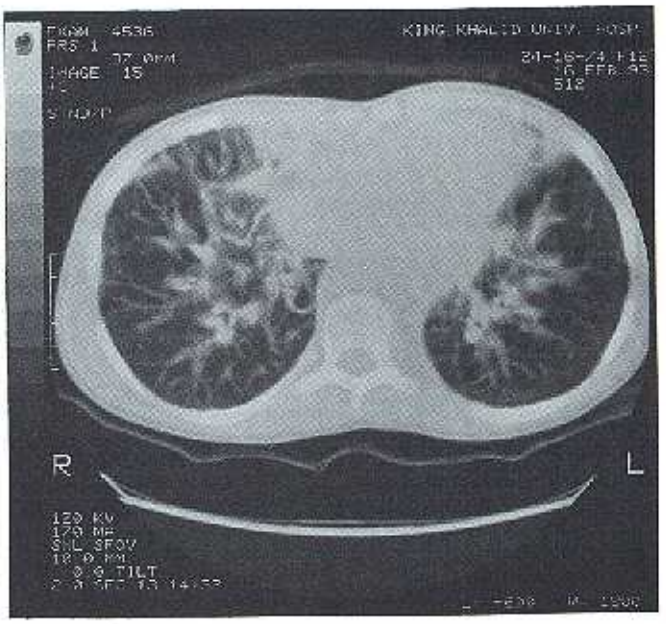

Fig. 2. CT scan of the chest showing mediastinal widening and diffuse distended lymphatics in the lung fields.

studded with numerous subpleural hemorrhagic nodules. The mediastinum was extensively infiltrated with multiple hemorrhagic masses, pink and black in color. Three biopsies were taken, two from the lung and the third from the mediastinum. The lung biopsy specimens were two fresh spongy pieces of tissue each measuring 12.5 mm long (lingula and left lower lobe). The mediastinal specimen was a piece of dark red fatty tissue 15 mm long. The tissues were fixed in 10% neutral buffered formalin, processed, embedded, and cut in the usual fashion. Sections were stained with hematoxylin-eosin (H&E), Masson's trichrome, and Verhoeff's Elastic Van Gieson stains.

Pathology

Histologically the lung parenchyma was infiltrated by sheets of proliferating thin-walled vascular channels, for most part of the size of capillaries (Fig. 3a). There was widening of the interstitium to variable degrees, creating small nodules or sheets of back-to-back capillary vessels. The vascular channels are lined by flattened inactive endothelial cells (Fig. 3b). The proliferating vessels invaded the subpleural region and the interlobular septa. In a few locations there was invasion of the walls of small pulmonary veins with associated intimal fibrosis. The venous lumen was not completely occluded by the intraluminal proliferation and venous thrombi were not seen. The pulmonary arterial and bronchial walls were also surrounded by the proliferating vascular channels, but their walls were not invaded.

The alveolar spaces contained hemosiderin laden macrophages and red blood cells. The alveolar septa were mildly thickened at the margins of the vascular tumor. In some regions the dilated lymphatic channels were prominent within the lung parenchyma. Focal interstitial lymphocytic infiltrates of the alveolar walls and bronchi were present. The mediastinal biopsy showed similar proliferation of capillary sized vascular channels in the pleura and stroma which invaded the pulmonary venous walls. The identification of these striking features led to the diagnosis of pulmonary capillary hemangiomatosis.

DISCUSSION

Pulmonary capillary hemangiomatosis is characterized by the proliferation of small vessels within the peribronchial, perivascular, septal, or pleural connective tissues.[1–12] The infiltration and compression of pulmonary veins can result in a secondary pulmonary venoocclusive disease. Within the lung, the vascular proliferation can involve the pleura, interlobular septa, bronchioles, and parenchyma. The involvement of airways probably leads to hemoptysis. In most cases, the proliferating vessels were capillary sized,[1–3,5–11] but in others they were of venule size.[4,7] There may also be extrapulmonary involvement of such structures as the mediastinum, pericar-

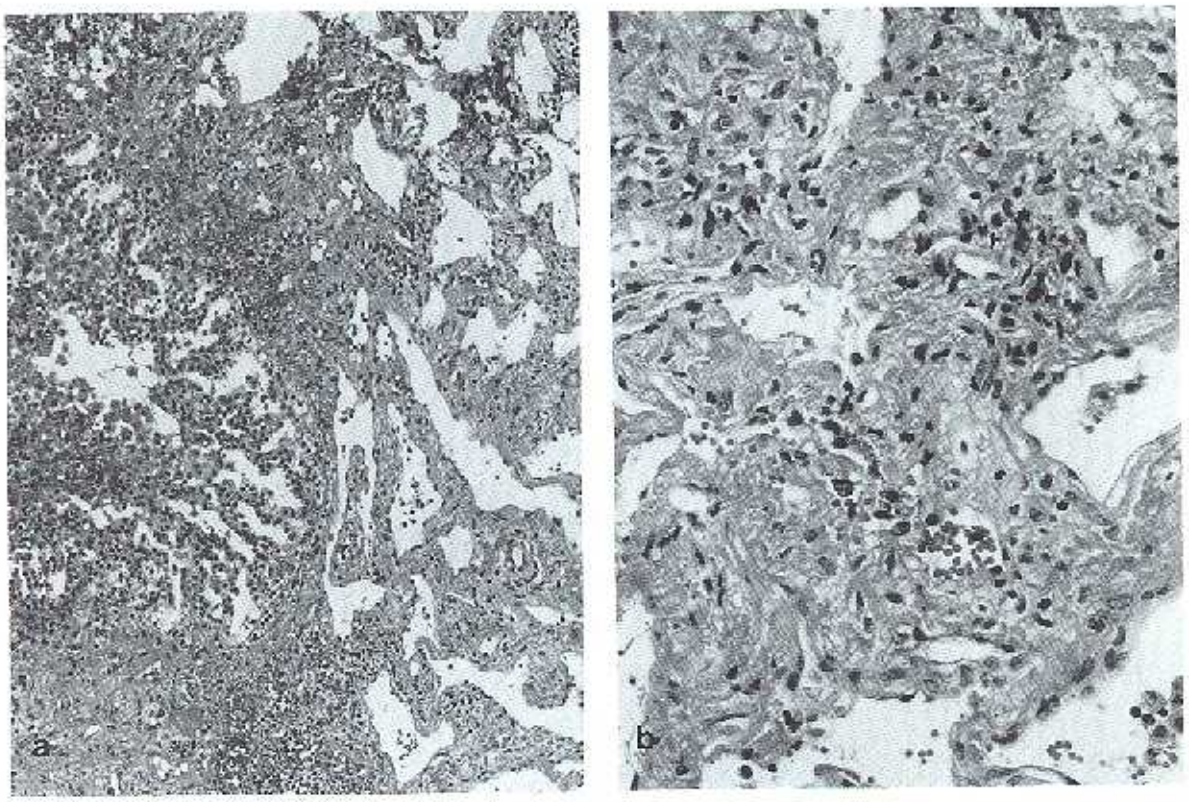

Fig. 8. (a) Photomicrograph of the histopathology of a lung biopsy showing infiltration of lung parenchyma with capillary-sized vascular channels. ×100 (H & E stain). (b) Photomicrograph of the lung biopsy showing lung parenchyma with alveoli containing histocytes filled with red blood cells. ×250 (H & E stain).

dium, thymus, and spleen.[1–11] In our patient the pathologic features of PCH were noted in the lung parenchyma, pleura, and interlobular septa with early pulmonary venous involvement. Extrapulmonary involvement was seen only in the mediastinum on both histopathology and CT scanning.

The natural history of the previously reported cases of PCH is one of progressive unrelenting dyspnea as summarized in Table 1. The ages at diagnosis of the earlier cases ranged from 12 to 71 years,[1,8,9,12] but the disease onset can be as early as 6 years of age.[8] The disease has been observed in male and female patients, and a familial association has been reported.[7] In most cases death ensues within 1 to 4 years of symptomatic presentation as the result of progressive pulmonary hypertension, cor pulmonale, pulmonary hemorrhage, or both.

The diagnosis of PCH in the living patient requires a high index of suspicion and an aggressive approach. Most patients are not recognized until signs of marked pulmonary hypertension have developed.[8,11,12] The early presentation can be indistinguishable from that of interstitial lung disease.[4] In addition to radiographic evidence of interstitial infiltrations, thickened fissures, interlobular septa, or pleura can be seen separately or in combination.[8,11,12] Although the changes seen on lung perfusion scan are not specific, they can suggest pulmonary hypertension of any cause and direct the physician to do early catheterization and pulmonary angiography to exclude pulmonary venoocclusive disease.[13] To confirm the diagnosis by histopathology, open lung biopsy is helpful but often misinterpreted. Transbronchial biopsy is contraindicated to avoid massive bleeding.[11]

Although the exact cause of PCH is not known, an uncontrolled angiogenesis in the lung appears to be the pathogenetic basis of this disease. The outcome of the disease in most of the previously reported cases is shown in Table 1. Twelve out of 19 cases died. Cases treated surgically by pneumonectomy or heart-lung transplantation[8,9] survived, and one case was treated with interferon α-2a.[10,14]

Although the finding of thrombocytopenia has been reported previously[14] in some cases of pulmonary hemangiomatosis, it was not a frequently recognized feature of PCH. However, in our case, the thrombocytopenia was very mild and with no evidence of consumption coagulopathy, and/or bleeding tendency.

TABLE 1—Previously Reported Cases of PCH[1]

No.	Sex	Age (years)	Clinical picture	Chest X-ray	Initial diagnosis	Outcome	Special features	Reference number
1	F	71	Dyspnea, hemoptysis for 1 week	Diffuse infiltrate bilaterally	Pulmonary hemosiderosis, had a trial of steroid	Died 6 months later, Dx postmortem	Hemorrhagic pleural effusion	1
2	M	15	Influenza-like illness; then progressive exercise intolerance and hemoptysis	Moderate cardiomegaly, widening of mediastinum, marked pulmonary shadowing, prominent pulmonary vessels, basal septal lines	Sarcoidosis	Died 4 years later. Dx postmortem	Infiltration of pulmonary veins and venules led to secondary pulmonary VOD	2
3	M	21	Dyspnea on exertion	Diffuse interstitial nodular pattern; prominent left hilum	Initially interstitial pneumonia; VOD after lung biopsy	Died 1 year later due to RHF. Rx steroid and cyclophosphamide	Misdiagnosed	3
4	M	14	SOB for 3 years clubbing	Fine interstitial pattern	Interstitial fibrosis after lung biopsy	Died 1 year after admission	Misdiagnosed	3
5	F	35	Pleuratic chest pain decreased exercise tolerance	Pulmonary embolism with infarction	Pulmonary embolism, then primary pulmonary hypertension	Died 5 years after presentation due to RHF	Misdiagnosed	3
6	F	38	SOB and hemoptysis	Prominent pulmonary artery	Pulmonary embolism after V/Q scan, then V/a primary pulmonary HTN	Died 1 year later. Dx postmortem		3
7	F	25	Recurrent chest infection for 12 years, progressive dyspnea, interstitial lung disease	Interstitial reticulonodular infiltrates, widening of mediastinum	Nonspecific lung fibrosis	Died of shock postpericardiocentesis, Dx postmortem	Hemorrhagic pericardial effusion and congenital scoliosis	4
8	F	35	Pleuritic chest pain, then decrease exercise tolerance 1 year later; 4 years later increasing RHF	Prominent pulmonary artery, changes in the rt. base suggestive of infarction	Multiple pulmonary emboli treated with warfarin	Died 5 years after initial presentation. Dx postmortem	Pulmonary angiography, multiple vessel obstruction with 80% loss of vasculature	5
9	M	50	Myocardial infarction and LVF	Initially pulmonary congestion due to pulmonary venous hypertension of LVF, then ill-defined pulmonary shadow later	CHF secondary to myocardial infarction	Died 1 year later due to CHF	Infiltration of pulmonary vessel with secondary VOD	6
10	F	30	Progressive dyspnea for 1 year, then pulmonary edema, transudate	Right ventricular enlargement, normal lungs	Primary pulmonary hypertension	Died of refractory heart failure 1 year after presentation. Dx postmortem		7

No.	Sex	Age (years)	Clinical picture	Chest X-ray	Initial diagnosis	Outcome	Special features	Reference number
11	M	20	Dyspnea, syncope, and progressive RVF for 1 and 1/2 year	RV enlargement prominent peripheral tapering of pulmonary vessels	Primary pulmonary hypertension	Died of RVF. Dx retrospectively at autopsy	Chronic lymphocytic thyroiditis on autopsy	7
12	F	30	Cough, hemoptysis, dyspnea for few weeks	Interstitial reticulonodular infiltrates, enlarged proximal pulmonary arteries	Primary pulmonary hypertension	Heart and lung transplantation		8
13	M	19	Hemoptysis at 11 years; left lower lobectomy, recurrent chest infection, and hemoptysis	Cardiomegaly, enlarged pulmonary arteries, reticulonodular pattern	Pulmonary hemosiderosis	Heart and lung transplantation		8
14	M	29	ASD, pulmonary HTN age 6; age 23 hemoptysis	Cardiomegaly, increased vascular marking at left base	ASD, pulmonary hypertension	Heart and lung transplantation	No ASD on pathology posttransplantation	8
15	F	12	Recurrent hemoptysis for 3 months	Interstitial pattern left base, small left lung	Not mentioned	Left pneumonectomy; improved	V/Q scan defect in left lower lobe, lingula, left upper lobe	9
16	M	12	Digital clubbing for 4 years; H/O myoplasma pneumonia 4 years ago	Bilateral interstitial infiltrates; thickened septal fissures and peribronchial thickening and superior mediastinal widening	Lung biopsy revealed pulmonary hemangiomatosis	Improved after treatment with interferon	Willebrand's factor antigen was measured with variable results	10
17	F	60	Progressive exertional dyspnea for 1 year	Bilateral interstitial infiltrate	Idiopathic interstitial fibrosis. Rx. Steroid led to temporary improvement	Died 3 years later due to RVF	Breast cancer before presentation; lung biopsy misdiagnosed as interstitial fibrosis	11
18	M	27	Progressive exertional dyspnea, hemoptysis	Coarse interstial reticulonodular pattern	Idiopathic VOD or pulmonary fibrosis	Right lung transplantation	Diagnosed antemortum but died immediately posttransplant	12
19	F	12	Cough, dyspnea for 2 months	Mediastinal widening, bilateral interstitial lung infiltrate	Mycoplasma pneumonia	Well, minimal symptoms to date	Thrombocytopenia	Present case

[1]RVF, right ventricular failure; VOD, venoocclusive disease; HTN, hypertension; Dx, diagnosed; Rx, treated; LVF, left ventricular failure; SOB, shortness of breath; CHF, congestive heart failure; V/Q, ventilation/perfusion; ASD, atrial septal defect.

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REFERENCES

1. Wagenvoort CA, Beesuri A, Spijker J. Capillary hemangiomatosis of the lung. Histopathology 1978; 2:401–406.
2. Whittaker JS, Pickering CA. Pulmonary capillary hemangiomatosis. Diagn Histopathol. 1983; 6:77–84.
3. Tron J, Magee F, Wright L, Colby T, Churg A. Pulmonary capillary hemangiomatosis. Hum Pathol. 1987; 17:1144–1150.
4. Vevaina JR, Mark EJ. Thoracic hemangiomatosis masquerading as interstitial lung disease. Chest 1988; 93:657–659.
5. Magee F, Wright JL, Kay JM, Deretz D, Donevan R, Churg A. Pulmonary capillary hemangiomatosis. Am Rev Respir Dis. 1985; 132:922–925.
6. Heath D, Reid R. Invasive pulmonary hemangiomatosis. Br J Dis Chest 1985; 79:284–294.
7. Langleben D, Heneghan JM, Batten AP, Wang NS, Fitch N, Schlesinger RD, Guerraty A, Roulcau JL. Familial pulmonary capillary hemangiomatosis resulting in primary pulmonary hypertension. Ann Intern Med. 1988; 109:106–109.
8. Faber CN, Yousem SA, Dauber JH, Griffith BP, Hardesty RL, Paradis IL. Pulmonary capillary hemangiomatosis: A report of three cases and a review of the literature. Am Rev Respir Dis. 1989; 140:808–813.
9. Wagenaar SJSC, Mulder HS, Wagenvoort CA, Van Den Bosch JMM. Pulmonary capillary haemangiomatosis diagnosed during life. Histopathology 1989; 14:212–214.
10. White CW, Sondheimer HM, Crouch EC, Wilson H, Fan LL. Treatment of pulmonary hemangiomatosis with recombinant interferon alfa 2a. N Engl J Med. 1989; 320:1197–1200.
11. Domingo C, Eneabo B, Rorg J, Lopez D, Morera J. Pulmonary capillary hemangiomatosis: A report of a case and review of the literature. Respiration 1992; 59:178–180.
12. Eltorky MA, Headley AS, Winer-Muram H, Garrett HE, Griffin JP. Pulmonary capillary hemangiomatosis: a clinicopathologic review. Ann Thorac Surg. 1994; 57:772–776.
13. Daroca PJ, Mansfield RE, Ichinose H. Pulmonary veno occlusive disease: Report of a case with pseudoangiomatous features. Am J Surg Pathol. 1977; 1:349–355.
14. White CW, Wolf SJ, Korones DN, Sondheimer HM, Tosi MF, Yu A. Treatment of childhood angiomatous diseases with recombinant interferon alfa-2a. J Pediatr. 1991; 118:59–66