Special Communication: Clinical Quiz

A patient with hypoxemia and a normal chest radiograph

Abdullah F. Al-Mobeireek, MRCP, FCCP, *Mohamed A. Babatin,* MBBS, ABIM.

ABSTRACT

The case of a young patient with hypoxemia and a normal chest radiograph is presented in the form of a clinical quiz, followed by a discussion of the differential diagnosis, investigative methods and a brief review of the final diagnosis.

Saudi Med J 2001; Vol. 22 (10): 924-927

Case Presentation

An 18-year-old male patient presented with dyspnea on exertion for one year, which had progressed recently, occurring even at rest. There was no history of orthopnea, paroxysmal nocturnal dyspnea, wheeze, cough or expectoration. He did report, however, recurrent bouts of hemoptysis, epistaxis, dizziness and generalized fatigability. His past medical history and family history were not contributory. On examination, his vital signs were within normal limits. A photograph of the patient's eyes is shown in Figure 1. He had peripheral and central cyanosis and digital clubbing. On cardiovascular examination, heart sounds were normal and no added sounds or cardiac murmurs were heard. Chest examination showed equal chest expansion, normal vesicular breathing, and no adventitous sounds. Examination of other systems was unremarkable. Investigations showed the following: arterial blood gas on room air: pH 7.44, PCO_2 31mmHg, PO_2 56mmHg, HCO_3 24 mmol/L and oxygen saturation 88%. Chest radiograph was reported normal. Hemoglobin was 18.9 g/dL and hematocrit was 62%. Spirometric values were: forced expiratory volume in one second (FEV_1) 4.36 L (113% of predicted), forced vital capacity (FVC) 4.63L (104% of predicted), FEV_1/FVC 94%, and diffusing capacity (DLCO) was 86% of predicted. Twelve lead electrocardiogram was normal. Echocardiography with a doppler study was reported to be normal, and specifically showed no evidence of pulmonary hypertension, valvular lesions or septal defects. Computed tomography (CT) scan of the chest was performed and a cut through the lower lung field is shown in Figure 2. Computed tomography of the brain showed a small density in the right cerebral hemisphere, most likely representing an infarct.

Questions

1. Mention the possible causes of hypoxemia with a normal chest radiograph and state which one is the most likely in this patient, justifying your choice?

2. The patient went on to have a CT scan of the chest. A cut is shown in Figure 2. Interpret the CT image.

From the Department of Medicine, College of Medicine, King Saud University, Riyadh, Kingdom of Saudi Arabia.

Received 17th March 2001. Accepted for publication in final form 30th May 2001.

Address correspondence and reprint request to: Dr. Abdullah Al-Mobeireek, Department of Medicine (38), College of Medicine, King Saud University, PO Box 2925, Riyadh 11461, Kingdom of Saudi Arabia. Tel. +966 (1) 467 1521. Fax. +966 (1) 467 2686. E-mail: mobeireek@yahoo.com

**** This is a special communication, which will not be a regular format in the Journal. Please send your review for the Editors if you think this is a useful exercise.***

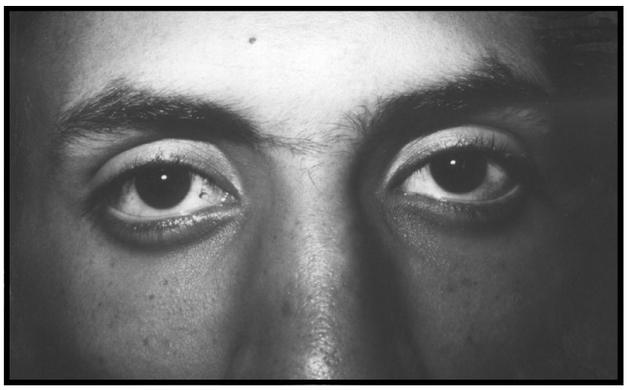

Figure 1 - Eyes of the patient.

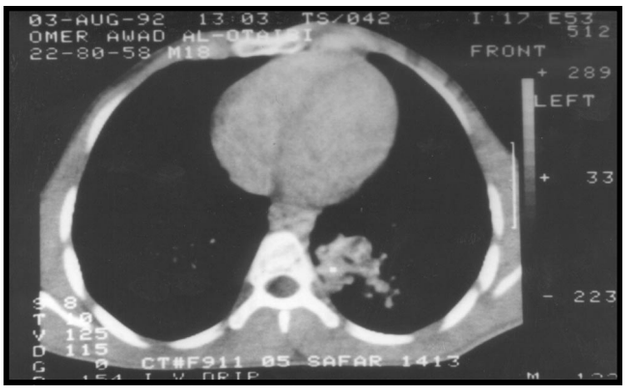

Figure 2 - A selected image of computed tomography of the chest.

3. What are the potential complications of this disorder?

Answers

1. Common causes of in a patient with normal or near normal chest radiograph are shown in Table 1. Normal pulmonary function tests rule out airway, interstitial and chest wall disorders as a cause, and normal pCO_2 excludes the hypoventilation syndromes (neuromuscular or central). Normal electrocardiographic and echocardiographic studies make a cardiac cause unlikely. In pulmonary vascular disease spirometry may be normal, but DLCO is reduced and there would be evidence of pulmonary hypertension. In pulmonary arteriovenous malformation (PAVM), however, there is no pulmonary hypertension and DLCO is normal or slightly reduced,[1,2] which was the case in this patient. The patient had the classical triad originally described in association with PAVM (clubbing, cyanosis and polycythemia).[1,2] A normal chest radiograph is unusual, but can be rarely seen in patients with PAVM when the lesions are tiny,[1] endobronchial or if they are located in the retrocardiac region, which was the case in our patient. In such situations, CT may help to establish the diagnosis, particularly when the feeding vessels are identified.

The patient also had telangiectasia in the conjunctiva shown in Figure 1. This raises the possibility of hereditary hemorrhagic telangiectasia (HHT). A consensus statement of the Scientific Advisory Board of the HHT Foundation International, Inc. on the diagnosis of HHT was recently published.[3] This has suggested that out of the 4 recognized criteria (epistaxis, telangiectasia, visceral lesions and positive family history) 3 would make the diagnosis definite, 2 possible and one unlikely. Accordingly, the diagnosis of HHT seems highly likely in our patient, despite the lack of family history. Recent discoveries on genetic abnormalities in HHT are expected to facilitate the task of definitive diagnosis and screening for HHT.

Table 1 - Causes of hypoxemia and a normal or near normal chest radiograph.

1. Pulmonary vascular disease: pulmonary hypertension either idiopathic (primary) or secondary (such as thromboembolic, cardiac).
2. Pulmonary arteriovenous malformation (cogenital or acquired, such as cirrhosis).
3. Obstructive airway disease (upper and lower, such as vocal cord dysfuntion, emphysema).
4. Early interstitial lung disease, (including fibrotic and granulomatous disorders).
5. Hypoventilation syndromes (neuromuscular, central).
6. Methemoglobinemia and carbon monoxide poisoning.*
*PaO_2 may be normal, but measured oxygen saturation is reduced.

Table 2 - Common complications of pulmonary arteriovenous malformations.

1. Neurological: Strokes, transient ischemic attacks, migraine, brain abscess, seizures.
2. Thoracic: Hemoptysis and hemothorax
3. Hematological: polycthemia and anemia
4. Cardiac: Infective endocarditis

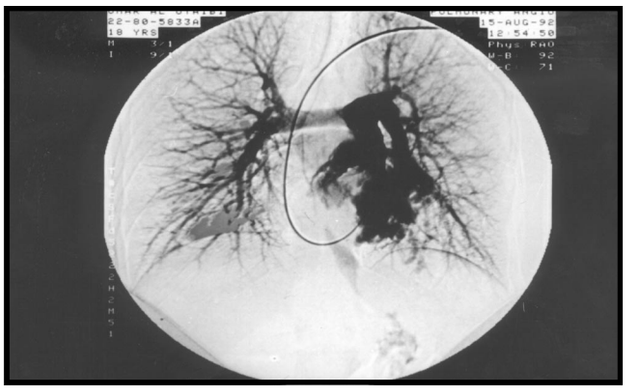

Figure 3 - Pulmonary angiogram showing a large arteriovenous malformation in the left lower lobe.

2. Computed tomography of the chest shows a well-defined enhancing nodular racemose opacity in the left lower lobe posteriorly which is highly suggestive of PAVM. The diagnosis was confirmed with pulmonary angiography which is shown in Figure 3. If surgery is being contemplated it is mandatory to perform bilateral pulmonary angiogram to rule out other co-existing PAVMs, which occur in nearly a quarter of patients.[1,2]

3. The most common complications are neurological (Table 2). Our patient had a small asymptomatic infact, which was evident on CT scan of the brain. Patients should also receive prophylaxis for infective endocarditis

Discussion

Pulmonary arteriovenous malformation (PAVM) or fistula was first described in 1897 by Churton and consists of an abnormal aneurismal vascular communication between a pulmonary artery and vein.[2] This leads to a right to left shunt and predisposes to paradoxical embolization to the systemic circulation. Although uncommon, they are an important consideration in the differential diagnosis of hypoxia and pulmonary nodules on the chest radiograph. They may present as solitary or multiple lesions usually in the lower lobes, or less commonly appear as a diffuse form.[1] The majority of these lesions are either congenital or developmental, but acquired causes may be occasionally encountered, as a result of chest surgery, correction of heart disorder, penetrating chest trauma, actinomycosis, schistosomiasis, cirrhosis, metastatic carcinoma, and mitral stenosis.[1,2] Pulmonary arteriovenous malformation occur more frequently in women and the mean age of presentation is between 36-41 years and tends to increase in number and size over time.[1,2,4] Pulmonary arteriovenous malformation can be confined to the lungs or in association with AVM or fistula in other organs, such as skin, mucous membrane, gastrointestinal tract, liver, or brain. In such cases HHT (also known as Rendu-Osler-Weber syndrome) should be suspected. More than half of PAVM are associated with HHT and approximately 10%-15% of patients with HHT have PAVM.[1,2,4] In patients with HHT, cutaneous telangiectasia or episodes of epistaxis often present before age 20, while PAVMs appear later in life. The recent discoveries regarding the genetics of HHT may be relevant to the etiology of PAVM with or without HHT. Endoglin has been identified as the gene product for HHT type 1 on chromosome 9, while activin receptor-like kinase 1 is the gene product for HHT type 2 on chromosome 12.[5] These proteins are necessary for the binding of a transforming growth factor-β and activin, which are needed for vascular development.

Exertional dysponea is a common symptom, occurring in 30 to 60% of patients and correlates with a degree of right to left shunt. Dyspnea may improve on reclining (platypnea), due to a decrease in blood flow through PAVM in the supine position. Hemoptysis occurs in 10%-15% of patients and occasionally can be massive and fatal.[4] Epistaxis is a common complaint among patients with HHT. In addition, patients can present with any of the complications listed above in Table 2. Clues in physical examination that are suggestive of PAVM include cyanosis, finger clubbing, and a continuous murmur audible over the lesion, and superficial telangiectasia in patients with HHT. All these signs were present in our patient, including a murmur that was overlooked in the initial examination. Treatment of PAVMs is either embolization or surgery. The objectives are to improve symptoms related to hypoexmia and to prevent hemorrhage and neurological complications. Embolization is preferred as it obviates the need for thoracotomy and general anesthesia, and as it can preserve functioning lung tissue especially when multiple lesions have to be dealt with. It is performed by using coils or other intravascular devices like detachable balloons.[6] Surgical resection may be necessary in certain situations, such as serious bleeding, intraplural rupture of PAVM, or failure of embolotherapy. Because of recurrent and significant hemoptysis, our patient underwent surgical resection of the left lower lobe. Following this his symptoms improved and his PaO_2 rose to 95 mm Hg and O_2 saturation to 97%. A month later his hemoglobin fell to 13.7 g/dL. On a follow up visit a year later, the patient continued to be well and his clubbing had disappeared. Other family members were advised to consult their

physician regarding screening for PAVM.

Final Diagnosis

Pulmonary arteriovenous malformation associated with hereditary hemorrhagic telangictasia and complicated with a cerebral infarct (old).

Acknowledgment. The authors are grateful to Prof. F. Al-Kassimi for revising the manuscript.

References

1. Fraser RG, Peter Pare JA, Pare PD, Fraser RS, Genereux GP. Pulmonary arteriovenous fistula. In: Diagnosis of diseases of the chest. Philadelphia (PA): WB Saunders Co; 1989. p.752-755.
2. Chilver ER. Clinical and physiological aspect of pulmonary arteriovenous malformation. Br J Hosp Med 1988; 39: 188-193.
3. Shovlin CL, Guttmacher AE, Buscarini E, Faughnan ME, Hyland RH, Westermann CJ et al. Diagnostic criteria for hemorragic herditary teleangectasia (Rendu-Osler-Weber syndrome). Am J Med Genet 2000; 91: 66-67.
4. Swanson KL, Prakash UBS, Stanson AW. Pulmonary arteriovenous fistulas: Mayo clinic experience 1982-1997. Mayo Clin Proc 1999; 74: 671-680.
5. Berg JN, Guttmacher AE, Marchuk DA, Porteous ME. Clinical hetrogenity in heritary haemorragic teleangectasia: are pulmonary arteriovenous malformation more common in families linked to endoglin? J Med Genet 1996; 33: 256-257.
6. White RI Jr, Pollak JS, Wirth JA. Pulmonary arteriovenous