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Five years four months old girl with cyanosis and clubbing of the fingers

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Case

A five-year and four-month old female patient was referred to an external hospital with a complaint of thickening and cyanosis in the tips of the fingers and toes which was noted for the last two months. She was referred to our clinic for further investigation and treatment with a prediagnosis of malignancy because of multiple nodular lesions found on chest x-ray and thoracic tomography.

Her personal history revelaed no pathology except for occasional epistaxis.

At presentation her physical examination revealed the following: her general status was well, her consciousness was open, she was cooperated, her weight and height were between the 5-25-50th percentile, cyanosis was observed in her tounge, lips, oral mucosa and finger tips. In addition, clubbing was present in her finger tips. Telengiectasies were found on her face. Examination of the respiratory system was normal. Her apical heart beat was found to be 130/min and her blood pressure was found to be 90/70 mmHg. Cardiac sounds were found to be normal.

Examination of the gastrointestinal and nervous systems was normal.

However, she had an articulation disorder for a few words.

White blood cells: 11900/mm^3, hemoglobin: 15.1 g/dL, hematocrite 45.7%, platelet count: 405000/mm^3, LDH: 263 U/L. Other laboratory findings were found to be normal.

Echocardiography was found to be normal.

The patient was referred to our clinic with a prediagnosis of malignancy-metastasis when bilateral diffuse nodular lesions were found on chest x-ray (Picture 1) and multiple nodular lesions with various localizations and sizes were found diffusely in both lungs on high-resolution lung tomography with the largest one in the superior segment of the lower lobe in the right lung with a size of 14x11 mm and additionally consolidation areas including air bronchograms were found in the anterobasal segments of the lower lobe in the right lung and posterobasal segments of the lower lobe in the left lung.

The laboratory findings in our hospital were as follows: hemoglobin: 13.7 g/dL, hematocrite: 41.3%, erythrocyte count: 5,44/mm^3, white blood cells: 14500/mm^3. Acute phase response, PT, aPT, INR, creatinine, ALT, AST, fasting blood glucose, electrolytes and methemoglobin levels were found to be normal. LDH was found to be 506 U/L.

Capillary oxygen saturation was found to be 69% in room air and no increase in capillary oxygen saturation was observed when 100% oxygen was inhaled (beginning: 69%, final: 72%).

The patient who had normal echocardiography findings had a normal caridothoracic index on telegraphy.

Further investigations were decided to be performed.

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Diagnosis: Osler-Weber-Rendu syndrome

It was thought that the patient might have pulmonary arteriovenous malformation or fistula because of presence of central cyanosis, recurrent epistaxis and telengiectasies on the face, absence of pathology in the heart and exclusion of methemoglobinemia. Echocardiography performed using contrast material revelaed the right atrium and right ventricle were filled with bubbles initially and the left atrium was filled with bubbles in the second cycle. Contrast-enhanced lung tomography was ordered. Nodular lesions showing multiple dense contrast uptake in bilateral lung paranchymes with the larger one with a size of 6x25 mm in the basal segment of the lower lobe of the right lung were observed on contrast-enhanced lung tomography and arteriovenous malformation was considered when the supplying artery and draining vein were noted clearly in the lesion which was especially large in the right lung. Highly diffuse arteriovenous malformations especially prominent in the lower lobes were observed with selective pulmonary artery injections performed seperately in both pulmonary arteries during cardiac catheterization (Figure 2A, 2B). Especially two arteriovenous malformations were observed to have multiple supplying arteries and direct filling into the pulmonary vein from these arteries was observed.

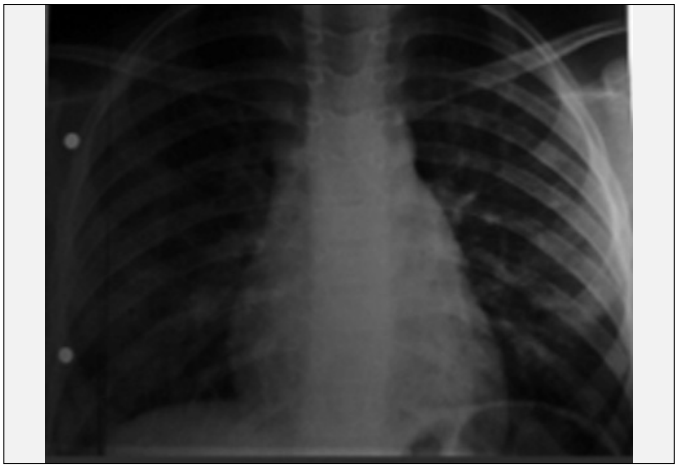

Figure 1. Bilateral nodular lesions on chest x-ray

Hyperechoic nodular lesions containing internal vascularization surrounded by a hypoechoic moon were found in the center of the liver with dimensions of 18x15x12 mm adjacent anteriorly to the main portal vein and 33x6x24 mm in the 6th segment on abdominal ultrasonography performed in terms of possible involvement in other internal organs.

Abdominal magnetic resonance imaging revealed a vascular lesion was observed with dimensions of 17x16 mm in the center of the 4-8th segment of the liver and 31x30 mm in the 6th segment of the liver showing mild hyperintense appearance on T2a examination and mild hypointense appearance on T1a examination and intense contrast uptake on post-contrast examination. This was considered as an arteriovenous malformation. Cranial magnetic resonance imaging was found to be normal.

According to Curacao criteria (1) a diagnosis of Osler-Weber-rendu syndrome was made with spontaneous, recurrent epistaxis, mucocuteneous telengiectasia and arteriovenous malformations in the organs (lung and liver).

Discussion

Osler-Weber-rendu syndrome is a familial autosomal dominant vascular dysplasia characterized by telengiectasies and mucosal bleedings. The incidence of the disease ranges between 1/5000 and 1/8000. The most common pathologic finding is telengiectasies which lead to mucocutaneous bleedings and epistaxis is frequently the first finding in the childhood. The second most common finding is arteriovenous malformations (AVM) in the internal organs. The most common localizations include lung, brain and hepatic circulation (1,2,3).

The diagnostis criteria in Osler-Weber-Rendu syndrome include spontaneous recurring epistaxis, mucocutaneous telengiectasies, AVM's in the internal organs and presence of Osler-Weber-Rendu syndrome in the first-degree relatives. The diagnosis is made with presence of at least three criteria (1). The

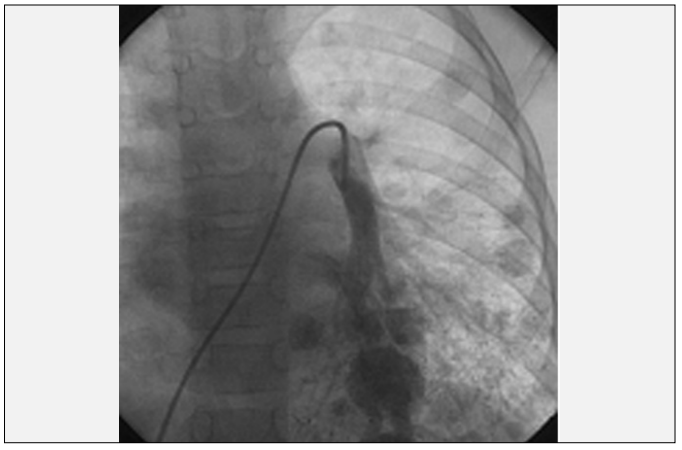

Figure 2A- Anastomoses between lobular arteries and pulmonary veins in the left lung

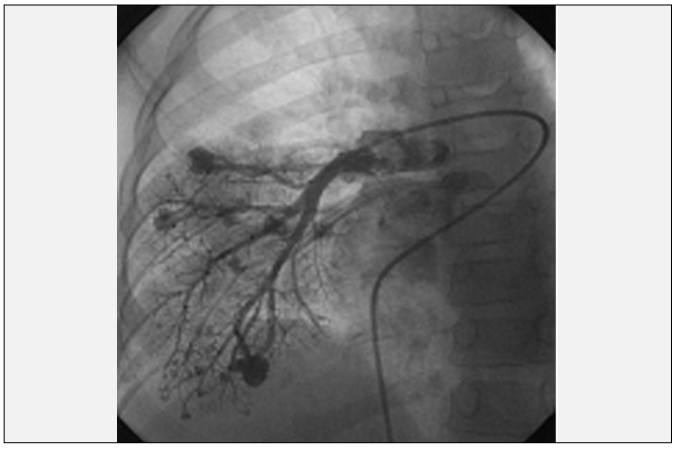

Figure 2B- Anastomoses between lobular arteries and pulmonary veins in the right lung

diagnosis of arteriovenous malformations is possible with contrast-enhanced echocardiography, contrast-enhanced CT and angiography (4). The fact that mucocutaneous findings are not prominent especially in the first ten years and recurrent epistaxis which is the most common finding is associated with trauma, upper respiratory infection and allergic diseases in children makes the diagnosis difficult (5). Considering all age groups recurrent epistaxis is observed in 90-95% of the patients (6,7) and gastrointestinal bleedings are observed in 10-33% of the patients (8,9) due to mucosal involvement.

Considering internal organ involvement AVM's are observed in the lung in 30-40% of the patients and in the brain 15-20% of the patients, while the frequency in the liver is not exactly known. Rarely, AVM's may also be observed in the spleen, coronary arteries, eye and genitourinary tract (3,10,11,12). AVM in the lung may be observed in a single lung or as a single lesion in both lungs or may be diffuse (13,14,15). Diffuse AVMs in both lungs and two AVMs in the liver were found in our patient and there was no AVM in the brain.

Patients who have AVM in the lungs may stay asymptomatic for a long time. In symptomatic patients, respiratory complaints, exercise intolerance and cyanosis are obsevred commonly (3). Our patient had clubbing in the fingers ans cyanosis. Cyanosis was related to lung involvement.

Since the first finding in undiagnosed patients may sometimes be life-threatening lung bleeding, stroke due to righ-to-left shunt or brain bascess, early diagnosis and treatment is important (3,13).

To diagnose arteriovenous malformations contrast-enhanced studies should be performed (4,13,14,15). If nodular lesions are observed on chest x-ray amd thoracic CT in patients with cyanosis, contrast-enhanced studies should be performed for internal organs (4,13,14,15). Our patient is a good example for this. Otherwise, malignancy-metastasis may be considered incorrectly in presence of nodular lesions as in this patient. This may lead to loss of the patient before the diagnosis is made as a result of diagnostic biopsy of the nodular lesion or as a result of spontaneous acute hemorrhage.

In treatment, manuel transcatheter embolization aimed at local AVMs or surgery is performed. In patients with highly diffuse AVMs, lung transplantation is recommended (3,4,15). Embolization and surgical intervention were not performed in our patient, since the AVMs in the lungs were bilateral and diffuse. However, the patient and parents were informed that treatment consisted of lung transplantation. The patient is stil being followed up in the outpatient clinic of pediatric cardiology and lung diseases.

Conclusively, history and physical examination findings should be evaluated carefully in patients with central cyanosis and nodular lesions in the lung. AVM should be investigated using contrast-enhanced radiologic studies in internal organs, if necessary and the diagnosis of Osler-Weber-Rendu syndrome should be excluded.

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