CASE REPORTS

Progressive fatigue and central cyanosis due to severe pulmonary arterial hypertension as the initial manifestation of systemic lupus erythematosus in a boy: A case report

Feng Zhang, Prasad Shrestha Arnav, Jinquan Lao, Bingbing Ye, Xiaofei Peng, Deo Mandal Krishna, Liu Luo, Zhifeng Cao, Yusheng Pang*

Department of Pediatrics, the First Affiliated Hospital of Guangxi Medical University, Nanning, China

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ABSTRACT

Severe pulmonary arterial hypertension of systemic lupus erythematosus (SLE) in pediatrics is rarely seen, especially in boys. Sometimes SLE may only present as progressive fatigue and central cyanosis that may be diagnosed initially as cardiovascular diseases, which makes harder the diagnosis of SLE. We present a 13-year-old boy with a month of progressive fatigue and central cyanosis, diagnosed only as severe idiopathic pulmonary arterial hypertension. The boy was finally diagnosed as severe pulmonary arterial hypertension of systemic lupus erythematosus. Due to different choices of therapy, underlying cause of pulmonary arterial hypertension should be diagnosed and searched thoroughly.

Key Words: Systemic lupus erythematosus, Pulmonary arterial hypertension, Pediatric

1. INTRODUCTION

Systemic lupus erythematosus (SLE) is a debilitating autoimmune disease involving multi-organs. Articular, cutaneous, and renal systems are the most common areas of involvement,[1] and it almost affects females (90.9%-92.9%).[2,3] Common presenting symptoms are fever, malaise, fatigue and anorexia, which are all nonspecific. Pulmonary arterial hypertension (PAH) is one of the most serious complications of SLE and other connective tissue diseases as well.[4] It may be present in the patients of SLE in advanced of their diagnosis of SLE.[5] Severe PAH as the initial manifestation in pediatric is rare, especially in boys. We hereby elaborate a rare case of SLE whose initial features were progressive fatigue and central cyanosis due to severe PAH.

2. CASE PRESENTATION

A 13-year-old boy, height 151 cm (P_{50}, 153.4), weight 36 kg (P_{50}, 39.5),[6] presented to our pediatric department with progressive fatigue and lip cyanosis for one month, and dry cough for 15 days. His medical history was not significant. He visited a doctor in a clinic before and was diagnosed as common cold, but the manifestations above were not effectively controlled after treatment for cold. On our department arrival, we had some tests and laboratory results showed WBC count of 3.95 $\times$ $10^{-9}/\mu$l, platelet count of 40.50 $\times$

*Correspondence: Yusheng Pang; Email: pangyush@163.com; Address: Department of Pediatrics, the First Affiliated Hospital of Guangxi Medical University, Shuangyong Road 6, Nanning, Guangxi Zhuang Autonomous Region, China.

$10^{-9}/\mu$l, and normal level of C-reactive protein and Troponin-l. The 12-lead ECG showed sinus tachycardia with right axis deviation, and electrical alternans. Enlarged cardiac silhouette with obvious pneumonia patches were present in chest x-ray. The ultrasound cardiogram revealed severe pulmonary hypertension (estimated systolic pulmonary artery pressure of 95 mmHg, severe idiopathic PAH to be doubted). Mild pericardial effusion was present but without any chamber compression.

On arrival at pediatric Department, the vital signs were body temperature of 36.8°C , heart rate of 108 bpm, rapid respiratory rate of 35 breaths per minute, blood pressure of 140/88 mmHg. On physical examination, he had mild cyanosis of the lips, multiple dermal purpura hemorrhagica and staled petechiasis in his abdominal region and both lower extremities. A loud S2 and a prominent P2 without audible murmur in every auscultatory valve area and engorged jugular vein were noted. Patient had Hepatomegaly and splenomegaly, measured 4 cm and 6 cm below the right and left costal margin respectively. Under this condition, the laboratory results showed ESR of 26 (Normal, 0-15 mm/h), low platelets count of 29.10, WBC count of 2.94, decreased C3 of 0.347 (Normal, 0.790-1.520 g/L) and C4 of 0.035 (Normal, 0.160-0.380 g/L), high 24 h urine protein of 634.8 (Normal, < 500 mg). The arterial blood gas analysis and cardiac enzyme were not found abnormal. Anti-Smith antibody was week positive and anti-double stranded DNA antibody and antinuclear antibody were both positive (Normal, negative). Mild to moderate pericardial effusion pericardial effusion, doubted idiopathic PAH, and portal hypertension were also showed but thromboembolism in pulmonary vasculature was not found in computed tomography. Patient had serositis, hematologic disorder, immunologic disorder, antinuclear antibody and abnormal renal function which fulfilled the criteria of American Rheumatism Association for Diagnosis of SLE.[1] He received methylprednisolone, hydroxychloroquine and bosentan treatments. The symptoms got better significantly after two weeks. For better understanding the situation of PAH, he underwent right heart catheterization which showed mean pulmonary arterial pressure of 40 (Normal, < 25 mmHg) and pulmonary vascular resistance (PVR) of 5.47 WU (Normal, < 3 WU).[7] At that time some main tests of SLE showed normal or almost normal. But Anti-double stranded DNA antibody and antinuclear antibody both remained positive. He was discharged after one-month of hospitalization. During follow-up, he had no obvious discomfort. Anti-double stranded DNA antibody and anti-Smith antibody turned to be both negative and pulmonary arterial pressure almost had no changes. But antinuclear antibody was positive still (see Table 1).

Table 1. Laboratory assessment of SLE and PAH at admission, in hospital and at follow-up 1 or 3 months later showing serologic phenotype and response to therapy

Test parameter	Reference range	Admission value	Pre-SPT value	Pre-discharg e value	Post-discharge follow-up value (1 M)	Post-discharge follow-up value (3 M)
ESR (mm/h)	0-15	26	45	10	6	9
CRP (mg/L)	0.00-10.00	< 10.00	< 10.00	< 10.00	< 10.00	< 10.00
PLT count (10-9/μl)	125.00-350.00	29.10	43.20*	83.90	110.00	128.00
WBC count (10-9/μl)	5.00-12.00	2.94	1.34	3.75	4.70	4.90
C 3 (g/L)	0.790-1.520	0.347		0.394		
C 4 (g/L)	0.160-0.380	0.035		0.034		
Anti-dsDNA Ab titer (IU/L)	Negative (0.00-7.00)	Positive, 1:40	Positive, 1:40 (111.00)	Positive, 1:40 (42.15)	Negative	
Anti-Smith Ab	Negative	Mild positive			Negative	
ANA titer	Negative	Positive, 1:320#	Positive, 1:320#	Positive, 1:1000#	Positive, 1:1000#	Positive, 1:1000#
24 h UP (mg)	< 500	634.8		89.8		
SPAP (mmHg)		95（UCG）	79 (UCG)	60 (RHC)	63 (UCG)	67 (UCG)
MPAP	< 25			44 (RHC)		
Pericardial effusion	None	Mild to moderate		Mild	None	

#Granular pattern. *After received PLT 4 times (the lowest count of PLT: 10.00); Ab: antibody; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; PLA: plantlet; WBC: white blood cell; UP: urine protein; ANA: antinuclear antibody; dsDNA: double-stranded DNA; SPT: steroid pulse therapy; SPAP: systolic pulmonary arterial pressure; MPAP: mean pulmonary arterial pressure; UCG: ultrasound cardiogram; RHC: right heart catheterization.

3. DISCUSSION

SLE is a diffuse connective tissue disease mainly manifested for autoimmune-mediated autoimmune inflammation and female has got higher incidence. Serum antinuclear antibody as the representative of a variety of autoantibodies and multisystem involvement are the two main clinical features of it. With the increasing levels of diagnosis and treatment of SLE, prognosis of the disease is getting better. But PAH leading to a progressive increase in PVR is a rare complication of SLE, occurring in 0.5% to 17.5% of patients with SLE.[5, 8, 9] One report shows its prevalence rate (3.8%) is lower than lupus nephritis (47.4%), joint involvement (54.5%), hematologic involvement (56.1%), and even neuropsychiatric lupus (4.8%).[2] In view of underlying diseases leading to organ damage with SLE, it was the third cause of death second to neuropsychiatric lupus and lupus nephritis, and when patients had SLE for more than three years, PAH was the leading one of death.[10] So rheumatic, cardiac and respiratory physicians should be involved and consulted to solve the following problems.

PAH usually presents with mild and nonspecific clinical manifestations, such as only fatigue on sports and chest distress. Hypoxia, respiratory failure or heart failure can also lead to PAH. Making a diagnosis of the basis of these symptoms would be very difficult as they are also present in conditions such as myocarditis, pneumonia, and severe sepsis. So most of the cases are diagnosed late, when PAH is already moderate to severe or symptomatic, such as lip cyanosis and syncope. It is also highly unusual for combined acute pericarditis and decreased platelets to be the initial manifestation of SLE, just as in above-mentioned case of the boy. Methods used to diagnose PAH are using ultrasound cardiogram and the gold standard of RHC.[7] Someone with worsening dyspnea, progressive fatigue, and rapid palpitation should have loud S2, hepatomegaly, and raised Jugular Venous Pressure in physical examinations to be diagnosed.

Several studies have shown early-targeted treatment for PAH is favorable for long-term prognosis; otherwise the opportunities will be lost and cardiac function will be decreased and hard to recover. In general, multi-systems involvement of SLE can provide early diagnosis of PAH of SLE on account of rash, arthritis, nephritis and other system damage. But for this boy, it's not. So if the diagnosis of PAH is confirmed but there is doubt in involvement of connective tissue, Cardiologists should be not satisfied with that diagnosis and pay more attention to the performance of the system examination and screening of SLE and make a clear diagnosis of SLE with the consultation of rheumatology doctor.

We should justify the clinical classification of the patients. Early diagnosis and severity assessment is to develop more precise treatment to improve the prognosis and quality of patient lives. The significance to emphasize the key to treat the primary disease SLE is because the progression and deterioration of PAH of SLE are both affected by basic condition induced by SLE. Immunosuppressive treatment should be conducted throughout the treatment process of PAH of SLE for stopping and even reversing the PAH.[4] Of course we should also pay attention on other systems involvement by SLE. For this boy, symptomatic and supportive therapies such as making cardiac function better, expressing inflammation of the lung, correcting of decreased PLT count, and others were included.

4. CONCLUSION

In general, PAH of SLE often has a devastating prognosis in pediatrics. The patients should timely approach to hospital, establish proper diagnosis and have a treatment as soon as possible.

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CONFLICTS OF INTEREST DISCLOSURE

The authors have declared no conflicts of interest.

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