

Central Cyanosis and Clubbing in an 18-Year-Old Postpartum Woman Presenting with a Stroke

RAMI N. KHOUZAM, MD; FRANK T. SCHWENDER, MD; FAIZ U. REHMAN, MD;
RICHARD C. DAVIS JR, MD, PHD

ABSTRACT: An 18-year-old woman without previously documented medical history delivered a healthy 32-week-old preterm infant. Severe bleeding occurred during week 1 postpartum secondary to ruptured vaginal condylomas. The consequent anemia was accompanied by complaints of exercise intolerance that resolved with blood transfusion. Six weeks later, the patient was brought to the emergency department of the regional medical center, where she was found to be unresponsive, with a left-sided hemiparesis and with hypoxemia that failed to correct with assisted ventilation and 100% oxygen. A cardiology consultation was obtained, which identified the patient as having central cyanosis and heretofore unappreciated marked clubbing of fingers and toes. This suggested a diagnosis of right-to-left shunting, likely at the cardiac level, together with pre-

sumptive embolic stroke, which was documented by magnetic resonance imaging and magnetic resonance angiography as a left pontine infarct. Transthoracic and transesophageal echocardiography identified anomalous drainage of the inferior vena cava into the left atrium, which was confirmed by a three-dimensional computed tomographic angiogram. Corrective surgery in the form of atrial septostomy and redirection of the inferior vena cava to the right atrium was performed. The patient was subsequently discharged and is in stable condition 3 months later without effort intolerance and with normal arterial oxygen saturation on room air. **KEY INDEXING TERMS:** Cyanosis; Clubbing; Anomalous drainage of inferior vena cava; Embolic stroke. [Am J Med Sci 2005;329(3):153-156.]

The differential diagnosis of central cyanosis with a right-to-left shunt at the cardiac level includes the presence of anatomic shunts of systemic venous blood into the arterial circulation, as in certain types of congenital heart disease. Clubbing can be associated with a variety of disorders, including cyanotic congenital heart disease. It is an obvious sign detected at the bedside, but is often overlooked, in spite of its clinical importance. A paradoxical embolus manifested as a stroke can also be a manifestation of a right-to-left shunt.

Herein we present a case of central cyanosis and clubbing in an 18-year-old postpartum woman who presented with a stroke. Evaluation led to the diagnosis of anomalous drainage of the inferior vena cava to the left atrium, which is an extremely rare

cause of cyanotic congenital heart disease, with only a few cases reported in the literature.

Case Report

An 18-year-old woman with no prior medical history and without effort intolerance or reported episodes of cyanosis during her prenatal evaluations presented with preterm delivery of a healthy 32-week-old infant. Following an uncomplicated vaginal delivery, severe postpartum bleeding secondary to ruptured vaginal condylomas occurred a week later, leading to a drop of the patient's hematocrit from 49% to 32%. Symptoms of exercise intolerance, severe fatigue, and shortness of breath, which accompanied the appearance of anemia, improved with a blood transfusion. At 6 weeks postpartum, the patient presented to the emergency department at the regional medical center in Memphis after being found comatose at home. Her family reported she had abruptly developed left arm weakness and slurred speech. Vital signs in the emergency department revealed a regular heart rate of 81 beats/min, blood pressure of 108/54 mm Hg, a respiratory rate of 10 breaths/min, and oxygen saturation of 65% on room air. The patient's hypoxemia did not improve after intubation and ventilation with 100% supplemental oxygen. A cardiology consultation was obtained, which revealed a single second heart sound without gallops or murmurs, and there was no jugular venous distention. Lungs were clear. Third-degree clubbing with drumstick appearance to the fingernails and toenails was noted. Neurologic examination revealed a left-sided flaccid hemiparesis affecting the patient's left arm more than her left lower extremity. She was obtunded, but could be aroused by

From the Division of Cardiovascular Diseases, University of Tennessee Health Science Center, Memphis, Tennessee.

Submitted July 26, 2004; accepted September 27, 2004.

Correspondence: Rami Kouzam, MD, University of Tennessee Health Science Center, Division of Cardiovascular Diseases, 920 Madison Avenue, Suite 300, Memphis, TN 38163 (E-mail: khouzamrami@yahoo.com).

Anomalous IVC Drainage

tactile and noxious stimuli. There was difficulty with conjugate gaze to the right, mainly with adduction. Laboratory tests revealed hemoglobin 9.8 g/dL, hematocrit 32.1%, and mean corpuscular volume of 76.9 fL. The results of arterial blood gas analysis were as follows: pH 7.41, PCO₂ 36 mm Hg, PO₂ 41 mm Hg, and hemoglobin saturation 65% on room air. Albumin level was 2.6 g/dL. The rest of the laboratory evaluation findings, including electrolytes, were within normal limits. Electrocardiogram demonstrated nonspecific T-inversion in the inferolateral leads and a regular sinus rhythm without arrhythmia. Right and left ventricular hypertrophy were absent and there was no evidence of acute myocardial infarction. A magnetic resonance imaging/magnetic resonance angiography scan of the brain showed a left pontine infarct. Based on a failure of the patient's arterial oxygen saturation to improve on 100% inspired oxygen and the presence of cyanosis, clubbing, and a single second heart sound, a diagnosis of probable right-to-left shunt at the cardiac level was made.

A transthoracic echocardiogram with agitated saline from the right femoral vein suggested an anomalous drainage of the inferior vena cava to the left atrium without evidence of communication between the atria (Figure 1). The same study from an upper extremity peripheral vein led to the appearance of bubbles in the right atrium and right ventricle (Figure 2). A transesophageal echocardiogram confirmed these findings. A pulmonary artery catheter introduced through the right femoral vein under fluoroscopic guidance reached the left atrium and left ventricle sequentially. A three-dimensional computed tomographic angiogram, with contrast injection in the right femoral vein (Figure 3), confirmed the diagnosis of anomalous drainage of the inferior vena cava to the left atrium. The patient underwent corrective surgery in the form of atrial septostomy and baffle redirection of the inferior vena cava to the right atrium. She is in stable condition 3 months after discharge, with no effort intolerance, no dyspnea on exertion, and minimal neurologic deficit for which she continues to improve on physical therapy. She has a normal arterial oxygen saturation of 94% on room air.

Discussion

Anomalous drainage of the inferior vena cava to the left atrium is extremely rare. Only a few cases have been reported in the literature.¹⁻⁸ Absence or paucity

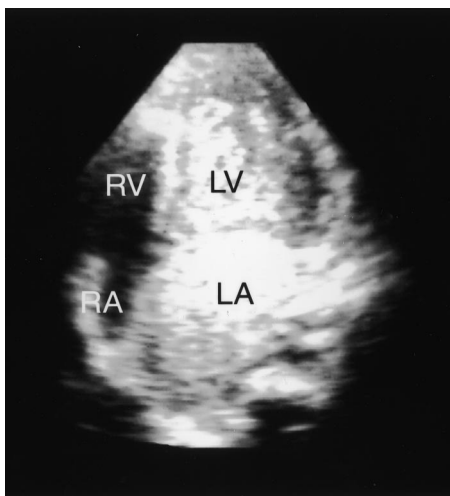


Figure 1. A transthoracic echocardiogram, apical four-chamber view, with injecting agitated saline through the right femoral vein, showing appearance of the bubbles in the left atrium and left ventricle. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

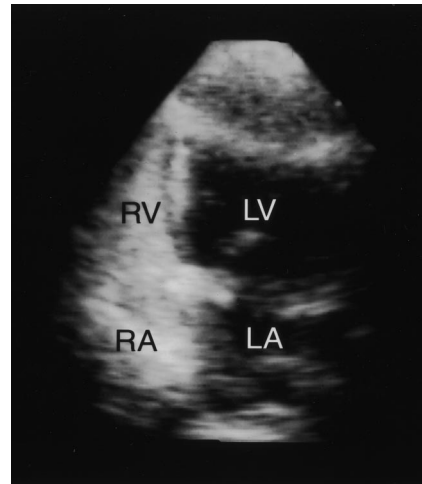


Figure 2. A transthoracic echocardiogram, apical four-chamber view, with injecting agitated saline through an upper extremity peripheral vein, showing appearance of the bubbles in the right atrium and right ventricle. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

of symptoms in patients with conspicuous cyanosis or clubbing is an important feature of the history and physical examination. Symptoms include effort intolerance, dyspnea, and light-headedness that develop on occasion but as a rule do so only late in life and only to a mild degree. Nevertheless, in view of the fact that a right-to-left shunt exists over many decades, it is not unexpected that brain abscess and paradoxical embolus have been reported.⁹

Signs associated with this congenital anomaly include cyanosis, clubbing, and a single second heart sound. *Cyanosis* refers to a bluish discoloration of the skin and mucous membranes resulting from an increased quantity of reduced hemoglobin in the small blood vessels of those regions. It is usually most marked in the lips, nail beds, ears, and malar eminences. Central cyanosis can be detected reliably when arterial oxygen saturation (SaO₂) has fallen to 85%. In dark-skinned persons, it may not be detected until it has declined to 75%, at which point examination of the mucous membranes in the oral cavity and the conjunctivae rather than examination of the skin is more helpful in its detection.¹⁰

Cyanosis can be subdivided into central and peripheral types. In the central type, SaO₂ is reduced or an abnormal hemoglobin derivative is present, and both the mucous membranes and skin are affected. Peripheral cyanosis is due to a slowing of blood flow and greater extraction of oxygen from normally saturated arterial blood presenting with cyanosis of fingers and toes while sparing the mucous membranes of the oral cavity or those beneath the tongue. The differential diagnosis of central cyanosis with a right-to-left shunt at the cardiac level

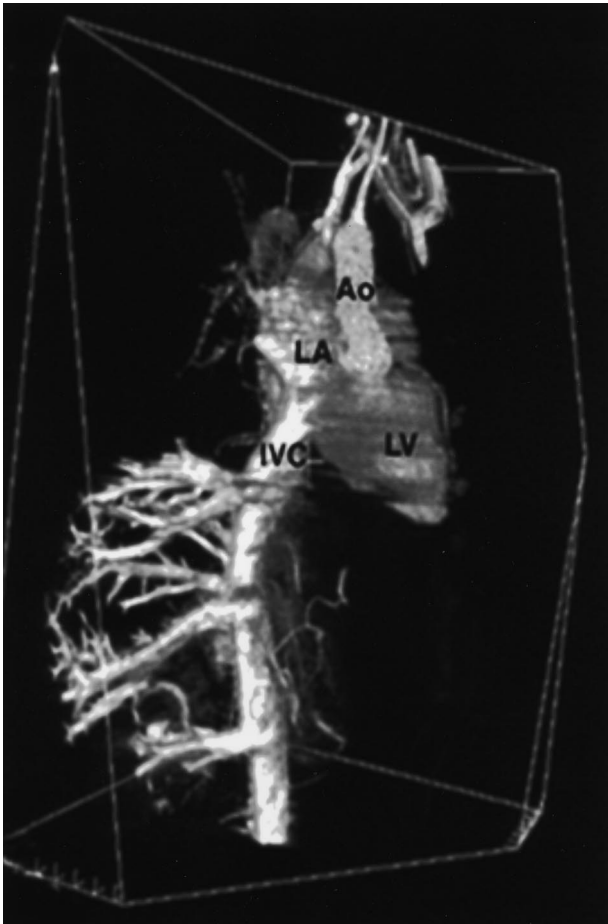


Figure 3. Three-dimensional computed tomography angiogram with coronal reformation, volume-rendered image, through injection of the right femoral vein, showing an anomalous drainage of the inferior vena cava to the left atrium. Ao, aorta; IVC, inferior vena cava; LA, left atrium; LV, left ventricle.

includes the presence of anatomic shunts of systemic venous blood into the arterial circulation, as may occur with certain types of congenital heart disease, pulmonary arteriovenous fistulas, and multiple small intrapulmonary shunts.¹⁰

Clubbing was not previously detected during prenatal evaluation in our patient but could be an important clue. Its exact mechanism is not fully understood but is thought to be due to megakaryocytes that bypass pulmonary capillaries, where they normally break up into platelets. In the systemic circulation, these platelet precursors preferentially lodge in the tips of the digits because of the prevailing pattern of blood flow. Once impacted, these cells release vascular endothelial growth factor, platelet-derived growth factor, hypoxia-inducible factor-1 α , and hypoxia-inducible factor-2 α ,¹¹ which increase endothelial permeability and activate fibroblasts and other connective tissue cells to promote tissue growth.¹² Vascular endothelial growth factor and

platelet-derived growth factor are released after platelet impaction, and their expression is enhanced by hypoxia created by capillary occlusion.¹¹ Clubbing may be hereditary, idiopathic, or acquired and associated with a variety of disorders, including cyanotic congenital heart disease and infective endocarditis.¹⁰

It has been postulated that drainage of the inferior vena cava to the left atrium is due to a persistence of the right valve of the sinus venosus. This rare congenital disorder should be considered in the differential diagnosis of patients presenting with cyanosis, clubbing, and a single second heart sound, without evidence of cardiac murmur or right ventricular hypertrophy.¹ When the inferior vena cava connects directly to the left atrium, an enlarged azygos vein may arise from the anomalous inferior vena cava and communicate with the right atrium. Communications between venae cavae and left atrium seldom occur as isolated congenital anomalies,⁹ as was the case in our patient. Such connections result in right-to-left shunts with directional flow of unoxygenated blood into the left atrial chamber and a subsequent decrease in systemic arterial oxygen saturation and cyanosis, without causing pressure overload of the right ventricle.² Noninvasive two-dimensional contrast echocardiography with color flow imaging establishes many if not most anomalies of vena caval connection and drainage.¹³ Surgical correction of this cyanotic cardiovascular anomaly is indicated for prevention of paradoxical embolus, pronounced effort intolerance, and low peripheral oxygen saturation.¹⁴

Acknowledgment

We would like to thank Dr. Karl T. Weber, Neuton Stern Professor of Cardiovascular Medicine for his thorough revision, valuable suggestions, and critique of this manuscript. We also would like to thank Dr. Christian Gilbert, Professor of Pediatric Cardiovascular Surgery at University of Tennessee Health Science Center (UTHSC), who performed the surgery, and Dr. Richard Felker, Professor of Radiology at UTHSC, for his participation with CT imaging.

References

1. **Genoni M, Jenni R, Vogt PR, et al.** Drainage of the inferior vena cava to the left atrium. *Ann Thorac Surg* 1999;67:543–5.
2. **Perloff JK.** Congenital anomalies of the vena caval connection. In: Perloff JK, editor. *The clinical recognition of congenital heart disease*. 4th ed. Philadelphia (PA): WB Saunders; 1994. p. 703–13.
3. **Gardner DL, Cole L.** Long survival with inferior vena cava draining into left atrium. *Br Heart J* 1955;17:93–7.
4. **Meyers DG, Latson LA, McManus BM, et al.** Anomalous drainage of the inferior vena cava into a left atrial connection: a case report involving a 41-year-old man. *Cathet Cardiovasc Diagn* 1989;16:239–44.

Anomalous IVC Drainage

5. **Singh A, Doyle EF, Danilowicz D, et al.** Masked abnormal drainage of the inferior vena cava into the left atrium. *Am J Cardiol* 1976;38:261–4.
6. **Burri H, Vuille C, Sierra J, et al.** Drainage of the inferior vena cava to the left atrium. *Echocardiography* 2003;20:185–9.
7. **Chantepie A, Marchand M, Dupre la Tour R, et al.** [Inferior vena caval return to the left atrium with intact interauricular septum: apropos of 2 cases surgically treated with success.] *Arch Mal Coeur Vaiss* 1986;79:684–91.
8. **Cabrera A, Arriola J, Llorente A.** Anomalous connection of inferior vena cava to the left atrium. *Int J Cardiol* 1994;46:79–81.
9. **Shapiro EP, Al-Sadir J, Campbell NP, et al.** Drainage of right superior vena cava into both atria: review of the literature and description of a case presenting with polycythemia and paradoxical embolization. *Circulation* 1981;63:712–7.
10. **Braunwald E.** Hypoxia and cyanosis. In: Braunwald E, Fauci AS, Isselbacher KJ, et al, editors. *Harrison's principles of internal medicine*. 15th ed. Vol. 1. New York (NY): McGraw-Hill; 2001. p. 214–7.
11. **Atkinson S, Fox SB.** Vascular endothelial growth factor (VEGF)-A and platelet-derived growth factor (PDGF) play a central role in the pathogenesis of digital clubbing. *J Pathol* 2004;203:721–8.
12. **Murray JF.** History and physical examination. In: Murray JF, Nadel JA, editors. *Textbook of respiratory medicine*. 3rd ed. Vol. 2. Philadelphia (PA): WB Saunders; 2000. p. 585–606.
13. **Foale R, Bourdillon PD, Somerville J, et al.** Anomalous systemic venous return: recognition by two-dimensional echocardiography. *Eur Heart J* 1983;4:186–95.
14. **Arsenian MA, Anderson RA.** Anomalous venous connection of the superior vena cava to the left atrium. *Am J Cardiol* 1988;62:989–90.