

# Multiple cardiac anomalies in an elderly man with Klinefelter's syndrome

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## ABSTRACT

We report a case of an elderly man with Klinefelter's syndrome and multiple cardiac defects, including partial anomalous pulmonary venous connection, atrial septal defect and pulmonary arterial hypertension. To the best of our knowledge, partial anomalous pulmonary venous connection in association with Klinefelter's syndrome has never been described in the literature. This anomalous pulmonary connection was a serendipitous discovery following the malpositioning of a peripherally inserted central catheter.

**Keywords:** Klinefelter's syndrome, partial anomalous pulmonary venous connection

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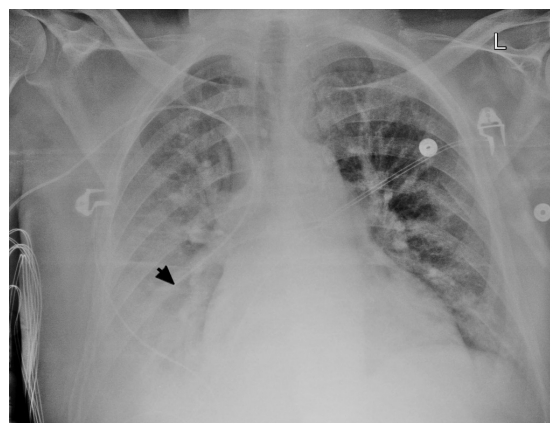
## INTRODUCTION

Cardiac anomalies are frequently encountered in autosomal trisomies but are relatively rare in sex chromosome trisomies. Klinefelter's syndrome or 47 XXY syndrome represents one of the most common sex chromosome trisomies. Klinefelter's syndrome has been associated with cardiac anomalies such as mitral valve prolapse, atrial septal defect (ASD), ventricular septal defect, tetralogy of Fallot, patent ductus arteriosus and hypertrophic obstructive cardiomyopathy.<sup>(1,2)</sup>

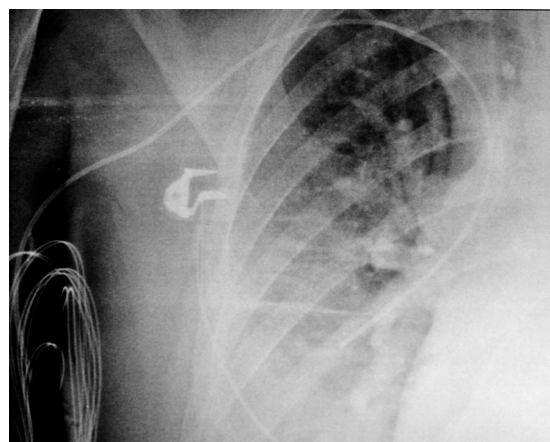
Peripherally inserted central catheters (PICC) are becoming increasingly common in patients requiring long-term venous access for the intravenous administration of antibiotics, fluids, blood products or hyperalimentation. A PICC is generally inserted into the cephalic or basilic vein in the upper arm above the elbow, and advanced until it reaches the junction between the superior vena cava (SVC) and right atrium. The incidence of complications, including the malpositioning and migration of a PICC, is rare.

## CASE REPORT

A 67-year-old male nursing home resident with a past medical history of borderline mental retardation and diabetes mellitus was admitted with progressive dyspnoea over the last several months. His past cardiac



**Fig. 1** Anteroposterior chest radiograph shows the tip of the peripherally inserted central catheter projecting over the mid-right lung/right infrahilar region (black arrowhead).



**Fig. 2** Magnified view of Fig. 1 shows the right lung with the course of the peripherally inserted central catheter.

history included moderate aortic stenosis and moderate to severe tricuspid regurgitation. On examination, the patient was somnolent, tachypnoeic, tachycardic and normotensive. His face showed significant prognathism, upward slanting palpebral fissures, ocular hypertelorism and a depressed nasal bridge. The patient's habitus was eunuchoid, with narrow chest and shoulders as well as long, thin tapering extremities and a bilaterally exaggerated cubitus valgus. Auscultation of the precordium was significant for a grade III blowing crescendo-decrescendo murmur that was heard in the right second intercostal space with radiation to the carotids. Auscultation of the posterior lung fields

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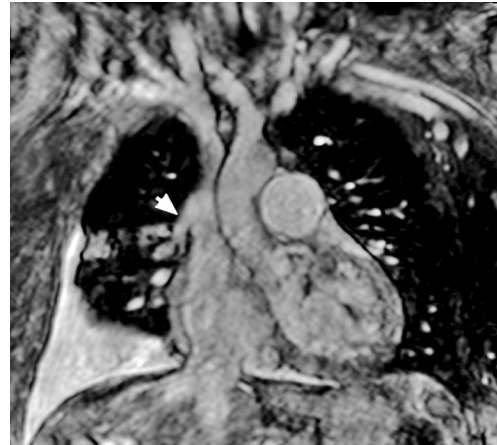
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**Fig. 3** Contrast-enhanced axial T1-W cardiac MR image at the level of bifurcation of the pulmonary artery shows the right pulmonary vein draining into the superior vena cava (white arrowhead).



**Fig. 4** Contrast-enhanced coronal T1-W cardiac MR image shows the pulmonary vein from the right upper lobe draining into the proximal superior vena cava (white arrowhead). A large right-sided pleural effusion is also evident.

revealed the absence of lung sounds over the right lower lung field. In addition, elevation of jugular venous pulsations up to the mandible and pitting oedema bilaterally up to the knees were present.

An arterial blood gas performed on admission revealed hypercapnic respiratory acidosis. A chest radiograph revealed a large right pleural effusion. Noninvasive positive pressure ventilation was initiated, which markedly improved the patient's symptoms over the next few hours. Subsequent thoracentesis confirmed the presence of a culture-negative, transudative pleural effusion.

A transthoracic echocardiogram (TTE) was performed to evaluate whether the patient's valvular disease was the possible aetiology of his symptoms. The TTE showed biatrial enlargement with a dilated right ventricle and mild right-sided systolic dysfunction. The presence of moderately severe calcific aortic stenosis (estimated valve area 0.9 cm<sup>2</sup> and peak/mean gradients 68/38 mmHg) and 3+ tricuspid regurgitation was noted. The estimated right ventricular systolic pressure was 68 mmHg, which was consistent with moderately severe pulmonary hypertension. There was evidence of severe circumferential mitral annular calcification with 1+ mitral regurgitation but not stenosis. Interestingly, a shunt at the level of the interatrial septum was present, with early appearance of saline contrast on the left side of the heart. The systolic function and the size of the left ventricle were normal. A transesophageal echocardiogram was performed, which confirmed the presence of ASD with bidirectional shunting. Examination of the mitral apparatus revealed mitral subvalvular calcification of the chordae in addition to calcification of the anterior and posterior mitral leaflets.

The patient was noted to be febrile (38.8°C), tachycardic, tachypnoeic and hypotensive (systolic blood pressure 78 mmHg) on Day 5. He was fluid resuscitated and started on empiric broad-spectrum antibiotics (vancomycin and piperacillin-tazobactam). Blood cultures drawn prior to the initiation of antibiotics demonstrated the presence of methicillin-resistant *Staphylococcus aureus*. After the clearance of blood cultures, a PICC was placed for the administration of medium-term intravenous antibiotics. Chest radiograph revealed the tip of the PICC projecting over the mid-right lung/right infrahilar region (Figs. 1 & 2).

Cardiac magnetic resonance (MR) imaging was performed to explore the possibility of anomalous venous channels draining into the SVC. The cardiac MR image revealed a partial anomalous pulmonary venous connection (PAPVC) draining the posterior segment of the right upper lobe into the proximal SVC (Figs. 3 & 4). The presence of an interatrial shunt was again confirmed. The left and right ventricular outputs were found to be abnormally high (10.7 litres/min and 11.7 litres/min, respectively). Based on the estimated ventricular volumes, the ratio of right ventricular flow to left ventricular flow was calculated to be 1.1.

A right heart catheterisation was performed to characterise the nature of the pulmonary hypertension and to evaluate the possibility of administering vasoreactive therapy. The right heart haemodynamics were as follows: mean right atrial pressure 10 mmHg, right ventricular pressure 54/10 mmHg, pulmonary artery pressure 60/24 mmHg (mean 33 mmHg), pulmonary capillary wedge pressure 9 mmHg, cardiac output (Fick) 13.9 litres/min and cardiac index (Fick) 5.9 litres/min/m<sup>2</sup>. After receiving inhaled nitric oxide, the patient's mean pulmonary artery

pressure decreased to 22 mmHg, while the pulmonary capillary wedge pressure remained the same, suggesting an element of pulmonary arterial vasoreactivity.

Workup for high output cardiac failure was initiated. As the patient was noted to be anaemic (haemoglobin 9.0 g/dL) and thrombocytopenic (platelet count 90,000/ $\mu$ L), a bone marrow biopsy was performed. The bone marrow aspirate and core biopsy revealed a reactive cellular marrow with trilineage haematopoiesis. Routine chromosomal analysis on the aspirate showed that several metaphasic cells were disomic for chromosome X. No structural rearrangement of any chromosome within the limits of resolution was noted. The likelihood of the constitutional nature of the chromosomal anomaly (47, XXY) was confirmed by a peripheral blood lymphocyte chromosome analysis, which revealed a mosaic variant pattern (47, XXY/46, XY). Further workup for the patient's high output heart failure revealed a serum thiamine level of 10 (normal range 70–140) ng/mL; therefore, the high output state was presumed to be secondary to wet beriberi. The patient was placed on therapeutic doses of thiamine.

## DISCUSSION

This case presents an elderly man with Klinefelter's syndrome and coexistent structural heart disease, including PAPVC, ASD and severe pulmonary hypertension. To the best of our knowledge, PAPVC has not been described in association with Klinefelter's syndrome. We describe a serendipitous discovery of a PAPVC, found subsequent to the malpositioning of a PICC. The discovery of a PAPVC in the context of a malpositioned jugular venous catheter has been previously described,<sup>(3,4)</sup> but not the migration of PICC into a pulmonary vein via a PAPVC.

Cardiac anomalies are frequently encountered in autosomal trisomies but are relatively rare in sex chromosome trisomies. Some cardiac defects described in association with Klinefelter's syndrome include mitral valve prolapse, ASD, ventricular septal defect, tetralogy of Fallot, patent ductus arteriosus and hypertrophic

obstructive cardiomyopathy.<sup>(1,2)</sup> Our patient's cardiac anomalies included biatrial and right ventricular dilatation, calcific aortic stenosis, severe mitral annular calcification, pulmonary arterial hypertension, PAPVC and ASD. It is unclear whether the multivalvular calcification was an age-related degenerative process or a predisposition secondary to an abnormal genotype.

PAPVC accounts for 0.5% of all congenital cardiac defects,<sup>(5)</sup> with drainage of the right upper lobe into the SVC representing the most common variant. This condition is generally asymptomatic and usually discovered as an incidental finding on chest imaging. The majority of patients with PAPVC have a good long-term prognosis if the total anomalous flow is less than 50% of the total pulmonary venous flow.<sup>(6)</sup> PAPVC has been identified as a significant risk factor for pulmonary hypertension in patients with ASD and intact atrial septa.<sup>(7,8)</sup> It is believed that the combination of increased blood flow through the pulmonary circuit along with reflex pulmonary vascular changes is responsible for causing pulmonary hypertension.

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