Platypnea-orthodeoxia syndrome related to right hemidiaphragmatic elevation and a 'stretched' patent foramen ovale

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SUMMARY

Patent foramen ovale (PFO), although frequently observed in adults, rarely causes adverse clinical consequences. The most serious among them, are cryptogenic strokes and less commonly significant hypoxia resulting from right-to-left shunt (RLS). Platypnea-orthodeoxia syndrome referring to abnormal oxygenation in the upright position has been correlated with reopening of foramen ovale and acute right-to-left intracardiac shunt. We report a case of platypnea-orthodeoxia syndrome secondary to the development of RLS through a 'stretched' PFO, in a patient admitted to the intensive care unit with severe respiratory failure requiring mechanical ventilation. The RLS was associated with right hemidiaphragmatic elevation, without an increased interatrial pressure gradient. The patient was successfully weaned from the ventilator after the percutaneous closure of PFO through a catheter-deployed double-umbrella device, presenting a full recovery.

BACKGROUND

Patent foramen ovale (PFO), an anatomical remnant of embryological development, is common in the general population, with an overall prevalence of 10–35%, leading occasionally to adverse clinical consequences.^{1 2}

Clinical symptoms arise when paradoxical emboli occur to the systemic circulation, or when a right-to-left anatomic shunt develops under certain circumstances, leading to varying degrees of hypoxaemia.^{3 4} A right-to-left shunt (RLS) is usually associated with elevated pressures in the right atrium and/or pulmonary vasculature. Right-to-left shunt may be transient as during 'Valsalva' manoeuvres, but may persist in acute right heart syndromes, as it happens in acute pulmonary embolism and right ventricular infarction. Rarely, an RLS may occur without the presence of elevated right-sided pressures or pulmonary hypertension.^{5 6} In these cases, anatomical changes that favour the streaming of blood from vena cava through foramen ovale (FO) are probably implicated. Postural changes may exacerbate the clinical signs and symptoms of the RLS, such as dyspnoea and arterial desaturation, giving rise to platypnea-orthodeoxia syndrome.

We report a rare case of platypnea-orthodeoxia syndrome due to RLS through a 'stretched' PFO, in the presence of right hemidiaphragmatic elevation. After the successful percutaneous PFO closure, the patient was successfully weaned from the ventilator presenting a complete resolution of hypoxaemia.

CASE PRESENTATION

A 72-year-old female patient was transferred to the emergency department due to progressive dyspnoea, where she was found to be severely hypoxic. Three weeks earlier, she underwent an urgent laparotomy due to perforation of the appendix and peritonitis. She was non-smoker, and from her medical history she reported mild arterial hypertension treated with an angiotensin receptor blocker, a transient ischaemic attack in the past 5 years, mild depression under a selective serotonin reuptake inhibitor (sertraline) and a hydatid liver cyst excision 25 years ago.

INVESTIGATIONS

Her arterial blood gases at the emergency department were as follows: pH 7.42, pCO₂ 28 mm Hg, pO₂ 49 mm Hg and HCO₃ 19 mmol/l, on room air. Lung auscultation showed diminished breath sounds over the lower part of the right hemithorax. Laboratory testing was unremarkable for the presence of an active infection, while d-dimers were within the normal range. She presented only a slight improvement in her oxygenation, while breathing 100% oxygen via a facemask. Chest x-ray showed a significant right hemidiaphragmatic elevation with no other remarkable findings from the lung parenchyma. Diaphragmatic elevation was not present on her chest x-ray 1 month earlier, before the abdominal operation, while it was identified postoperatively, on the routine chest x-ray, upon hospital discharge.

DIFFERENTIAL DIAGNOSIS

A few hours later she presented abrupt worsening with cardiorespiratory collapse. Due to the clinical suspicion of massive pulmonary embolism she received thrombolysis.

A transthoracic echocardiography (TTE) revealed left ventricular internal dimensions and global contractility in normal range, right ventricular dilatation with hypokinesis of its free wall and moderate elevation of the right ventricular systolic pressure (RVSP 45 mm Hg).

TREATMENT

She was subsequently intubated and transferred to the intensive care unit. Over the following 3 days she was gradually improved. Spiral chest CT scan was inconclusive for pulmonary embolism, as it was also the triplex ultrasound of the lower extremities for deep venous thrombosis. However, she continued to receive anticoagulation treatment for possible pulmonary embolism, as it could not be excluded. A full coagulation work-up did not identify a hypercoagulable state.

To cite: Sakagianni K, Evrenoglou D, Mytas D, et al. *BMJ Case Reports* Published online: 10 December 2012
doi:10.1136/bcr-2012-007735

Due to the persisting right hemidiaphragmatic elevation she underwent a bronchoscopic evaluation, which did not reveal an endobronchial lesion. After her extubation, she presented a rapid worsening with refractory hypoxaemia, platypnea and orthodeoxia, with hypoxaemia and breathlessness being more pronounced in the upright position, and also during coughing. A transient oxygenation improvement was initially remarked by the use of non-invasive ventilation (bi-level positive airway pressure), but as she presented no further clinical improvement she was reintubated. A full-body CT scan was undertaken with no pathological findings except for the right hemidiaphragmatic elevation and the atelectasis of the unilateral lower lung lobe, which, however, could not explain the severe hypoxaemia of the patient.

A transoesophageal echocardiography with agitated saline contrast study was performed which revealed a 'stretched' patent FO and a severe RLS (figure 1). TTE performed at the same time, showed a mild increase of the RVSP, estimated to be between 35 and 40 mm Hg. A Swan-Ganz catheter was subsequently introduced, which showed the following measurements: right atrial pressure (RAP) 14 mm Hg, pulmonary artery pressure (PAP) 36/19 mm Hg, mean PAP 24 mm Hg, pulmonary capillary wedge pressure 15 mm Hg. Mixed venous blood oxygen saturation (SvO_2) varied between 61% and 68%. Cardiac output using the thermodilution method was 4.5 l/min, and cardiac index was 2.5 l/min/m². Systemic vascular resistance was 1012 dyne-sec/cm⁵ and pulmonary vascular resistance was 160 dyne-sec/cm⁵. Several weaning trials having failed, we decided to proceed to the closure of the FO. As the patient was still intubated and under mechanical ventilation, the least

invasive procedure was chosen and percutaneous closure was performed in a specialised centre of invasive cardiology.

OUTCOME AND FOLLOW-UP

Closure of the atrial septum defect (ASD) was performed under intracardiac echocardiographic (ICE) guidance, which clearly detected a 'stretched' PFO. An ultrasound ICE catheter (AcuNav—Biosense Webster Corp, Diamond Bar, California, USA) was advanced through an 8F, 25 cm sheath from the right femoral vein to the mid-right atrium under fluoroscopy. In order to assess the interatrial shunt, 10 ml of agitated normal saline was injected via a second 10F sheath inserted in the right femoral vein. Manifestation of contrast bubbles in the left atrium confirmed the shunt. Following, a multipurpose catheter was utilised, under ICE guidance, in order to insert a wire across the defect and allocate it into the left pulmonary vein. The defect was sized with a 24 mm Amplatzer sizing balloon (AGA Medical Corp, Plymouth, Minnesota, USA). Occluder's diameter was selected based on the measurement of the stop-flow diameter, which was recorded to be 20 mm. Subsequently, a 9F Amplatzer (AGA Medical Corp) guiding catheter was advanced via the right femoral vein through the 10F sheath. During device deployment, continuous imaging was used for close observation of the device's alignment, relation with neighbouring structures (particularly atrioventricular valves) and septum capture. Closure of the defect was successfully completed, with a 22 mm ASD occluder (AGA Medical Corp) according to standard protocols.^{7 8}

After the successful PFO closure the patient presented a remarkable improvement and was finally weaned from the ventilator. No bleeding complications or other adverse sequelae were

Figure 1 Transoesophageal echocardiographic study with agitated saline contrast and colour Doppler imaging reveals a patent foramen ovale (A, thin arrow), multiple microbubbles from right atrium (RA) to left atrium (LA) (B) and a severe right-to-left shunt (C and D, thick arrows).

observed during or after the procedure. Arterial oxygen saturation (SaO_2) after extubation was 97% on FiO_2 0.35. A week later, after complete recovery and mobilisation, she no longer needed supplemental oxygen. By breathing room air she maintained an SaO_2 of 96%. However, her chest x-ray continued to present a significant right hemidiaphragmatic elevation, which could not be completely resolved. A transoesophageal echocardiography contrast study that was performed 1 month later confirmed the correct placement of the device and showed no residual shunt through the atrial septum (figure 2). The patient underwent a regular clinical and echocardiographic examination. Three years later the patient remains asymptomatic with arterial blood gases in the normal range. TTE shows correct functioning of the device with no leaks. Serial chest x-rays during the follow-up period of the 3 years reveal a gradual return of the right hemidiaphragm to its normal position.

DISCUSSION

Platypnea-orthodeoxia syndrome is encountered rarely and has been correlated with several clinical entities. Reopening of FO and acute right-to-left intracardiac shunt is an important cause of this syndrome. It is characterised by breathlessness and arterial deoxygenation induced by the upright position and relieved by the supine position.⁹ Several reports of this syndrome are associated with right pneumonectomy.¹⁰ The presumed mechanism is mediastinal deviation towards the right side, which alters the anatomical relation between the caval orifices and atrial septum.

There are rare reports in the literature of acute right-to-left interatrial shunt causing severe hypoxaemia in the setting of right hemidiaphragmatic elevation. To our knowledge so far,

there are five single case reports and a case series of three patients presenting with refractory hypoxaemia related to right hemidiaphragmatic dysfunction and FO reopening.^{11–16} The exact pathophysiological mechanism is not clear, but it resembles that observed after right pneumonectomy. It is speculated that diaphragm displacement leads to a shift in the anatomical relation of inferior vena cava and interatrial septum, allowing blood flow to be directed through the septal defect.¹¹

The agitated saline contrast study performed during TEE examination and Valsalva manoeuvre is the gold standard test for the detection of PFOs.^{2 4 17} Passage of microbubbles from the right to the left atrium within three cardiac cycles usually identifies a PFO. Mild shunting corresponds to the passage of less than five bubbles, moderate shunting to 5–25 bubbles and marked shunting when more than 25 bubbles are detected in the left atrium. Coughing or Valsalva manoeuvres improve the sensitivity of the study as they transiently increase RAP and the likelihood of detecting RLS by echocardiography.^{4 17} In intubated patients under mechanical ventilation, application of end-expiratory occlusion may substitute Valsalva manoeuvre. This technique was also performed in our patient with remarkable results.

There is growing evidence in the literature that percutaneous transcatheter closure of PFOs is associated with improved outcomes, as it concerns stroke recurrence.¹⁸ Compared with the surgical closure, the percutaneous closure is associated with fewer complications.¹⁹ Currently, there are no clearly-defined guidelines with reference to PFO management due to the lack of randomised controlled trials comparing the different treatment options.³ There is even less evidence concerning the optimal management of patients with severe hypoxaemia from

Figure 2 Transoesophageal echocardiography performed after percutaneous transcatheter patent foramen ovale closure, confirmed through various echocardiographic views the correct placement of the device, showing no residual shunt through the atrial septum.

RLS due to reopening of an FO.^{9, 20} Recent studies suggest that percutaneous closure is an effective treatment in hypoxemic shunts with functional improvement of the patients and resolution of acute respiratory failure.⁵ The results of shunt closure are questionable when these are associated with chronic respiratory failure, as hypoxaemia often persists despite shunt closure.²⁰

We presume that the recent laparotomy, in which our patient was submitted, was associated with the unilateral diaphragmatic paralysis, as it occurred after the operation and we could not identify any other etiological factor. The diaphragms on the pre-operative chest x-ray were symmetric and the patient had no prior symptoms of respiratory distress. Acute pulmonary embolism was highly suspected though not confirmed by the spiral CT scan that was, however, performed after thrombolysis administration. Yet, both echocardiography and right heart catheterisation did not confirm significantly elevated pressures in the pulmonary circulation.

Mechanical ventilation and application of end-expiratory positive airway pressure (PEEP) normally increase right-to-left shunting with worsening of hypoxaemia. On the contrary, our patient presented a gradual oxygenation improvement, while mechanically ventilated with PEEP application and also during non-invasive bi-level ventilation. It has been suggested that the elevated diaphragm was probably 'pushed down' by the positive pressures leading to an anatomical position not favouring streaming of blood through the 'stretched' PFO, and thus reducing RLS.¹⁶

The diagnosis of RLS through a PFO as a cause of hypoxaemia is often challenging. It should be suspected in the setting of refractory hypoxaemia that does not respond to 100% oxygen supply, and the diagnostic work-up has excluded the presence of vascular or parenchymal lung disease. In these situations, a contrast TEE should be performed in order to diagnose an RLS through a PFO. The decision to intervene depends mainly on the severity of symptoms and the reversibility of the clinical entity that led to the reopening of the FO and the RLS.^{6, 9} Anatomical variations, such as right hemidiaphragmatic dysfunction, should be considered as possible etiological factors of clinically significant RLS and hypoxaemia and should prompt the appropriate diagnostic and therapeutic procedures.

Learning points

- ▶ Patent foramen ovale (PFO) is common in the general population, with an overall prevalence of 10–35%, leading occasionally to adverse clinical consequences.
- ▶ Acute right-to-left shunt (RLS) through foramen ovale reopening is usually associated with elevated pressures in the right atrium and/or pulmonary vasculature, but also in the presence of normal right-sided pressures and may lead to platypnea-orthodeoxia syndrome.
- ▶ The diagnosis should be suspected in the face of refractory hypoxaemia that does not respond to 100% oxygen supply, without significant vascular or parenchymal lung disease.
- ▶ Anatomical changes, such as right hemidiaphragmatic elevation should be considered as possible etiological factors of clinically significant RLS though PFO.
- ▶ Percutaneous transcatheter closure of atrial septal defects represents an effective treatment in hypoxemic shunts with functional improvement of the patients and resolution of acute respiratory failure.

Competing interests None.

Patient consent Obtained.

REFERENCES

- 1 Hagen PT, Scholz DG, Edwards WD. Incidence and size of patent foramen ovale during the first 10 decades of life. *Mayo Clin Proc* 1984;59:17–20.
- 2 Fisher DC, Fisher EA, Budd JH, et al. The incidence of patent foramen ovale in 1,000 consecutive patients. A contrast transesophageal study. *Chest* 1995;107:1504–9.
- 3 Hara H, Virmani R, Ladich E, et al. Patent foramen ovale: current pathology, pathophysiology, and clinical status. *J Am Coll Cardiol* 2005;46:1768–76.
- 4 Hausmann D, Mugge A, Becht I, et al. Diagnosis of patent foramen ovale by transesophageal echocardiography and association with cerebral and peripheral embolic events. *Am J Cardiol* 1992;70:668–72.
- 5 Godart F, Rey C, Prat A, et al. Atrial right-to-left shunting causing severe hypoxemia despite normal right-sided pressures. *Eur Heart J* 2000;21:483–9.
- 6 Toffart AC, Bouvaist H, Feral V, et al. Hypoxemia-orthodeoxia related to patent foramen ovale without pulmonary hypertension. *Heart Lung* 2008;37:385–9.
- 7 Suárez De Lezo J, Medina A, Pan M, et al. Transcatheter occlusion of complex atrial septal defects. *Catheter Cardiovasc Interv* 2000;51:33–41.
- 8 Zanchetta M. On-line intracardiac echocardiography alone for Amplatzer Septal Occluder selection and device deployment in adult patients with atrial septal defect. *Int J Cardiol* 2004;95:61–8.
- 9 Chen GP, Goldberg SL, Gill EA. Patent foramen ovale and the platypnea-orthodeoxia syndrome. *Cardiol Clin* 2005;23:85–9.
- 10 Bhattacharya K, Birla R, Northridge D, et al. Platypnea-orthodeoxia syndrome: a rare complication after right pneumonectomy. *Ann Thorac Surg* 2009;88:2018–19.
- 11 Murray KD, Kalanges LK, Weiland JE, et al. Platypnea-orthodeoxia: an unusual indication for surgical closure of a patent foramen ovale. *J Card Surg* 1991;6:62–7.
- 12 Cordero PJ, Morales P, Mora V, et al. Transient right-to-left shunting through a patent foramen ovale secondary to unilateral diaphragmatic paralysis. *Thorax* 1994;49:933–4.
- 13 Ghamande S, Ramsey R, Rhodes JF, et al. Right hemidiaphragmatic elevation with a right-to-left interatrial shunt through a patent foramen ovale. *Chest* 2001;120:2094–6.
- 14 Maholic R, Lasorda D. Successful percutaneous closure of a patent foramen ovale causing hypoxia in the setting of an elevated hemidiaphragm due to Guillain-Barre syndrome. *J Invasive Cardiol*. 2006;18:434–5.
- 15 Perkins LA, Costa SM, Boethel CD, et al. Hypoxemia secondary to right-to-left interatrial shunt through a patent foramen ovale in a patient with an elevated right hemidiaphragm. *Respir Care* 2008;53:462–5.
- 16 Darchis JS, Ennezat PV, Charbonnel C, et al. Hemidiaphragmatic paralysis: an underestimated etiology of right-to-left shunt through patent foramen ovale? *Eur J Echocardiography* 2007;8:259–64.
- 17 Marriott K, Manins V, Forshaw A, et al. Detection of right-to-left atrial communication using agitated saline contrast imaging: experience with 1162 patients and recommendations for echocardiography. *J Am Soc Echocardiogr* Published Online First: 15 Oct 2012. doi:10.1016/j.echo.2012.09.007
- 18 Maredu RK, Shah MS, Mesa JE, et al. Percutaneous closure of patent foramen ovale: a case series and literature review. *Clin Med Res* 2007;5:218–26.
- 19 Cifarelli A, Musto C, Parma A, et al. Long-term outcome of transcatheter patent foramen ovale closure in patients with paradoxical embolism. *Int J Cardiol* 2010;141:304–10.
- 20 El Tahlawi M, Jop B, Bonello B, et al. Should we close hypoxaemic patent foramen ovale and interatrial shunts on a systemic basis? *Arch Cardiovasc Dis* 2009;102:755–9.

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