CASE STUDY

Positional hyperventilation-induced hypoxaemia in pectus excavatum

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ABSTRACT: The presented case is of a young male (aged 19 yrs) with a pectus excavatum who showed significant exercise intolerance, despite normal pulmonary function at rest, including carbon monoxide diffusing capacity. Clinical exercise testing led to a strong suspicion of a right-to-left shunt due to an abnormally wide alveolo–arterial oxygen gradient (26.4 kPa) at peak oxygen uptake, with severe arterial hypoxaemia (arterial oxygen tension 12.54 kPa).

A right-to-left shunt was confirmed by transoesophageal echocardiography demonstrating a permeable foramen ovale, despite normal right heart pressures. The right-to-left venous flow was mainly dependent on the upright body position and the deep inspiration. Indeed, *i.v.* dobutamine infusion to selectively affect cardiac output and hyperventilation induced by tidal volume expansion at constant breathing rate in the supine position did not result in arterial oxygen desaturation or shunting. Closure of the foramen ovale through atrial umbrella placement dramatically improved clinical and physiological abnormalities.

This observation demonstrates that a hyperventilatory manoeuvre in the upright position is able to detect a permeable foramen ovale favouring flow in the inferior vena cava in the direction of the abnormal pre-existing atrial channel in a patient with a pectus excavatum.

KEYWORDS: Clinical exercise testing, foramen ovale, hyperventilation, hypoxaemia, pectus excavatum, shunt

The current case study reports an unusual physiological phenomenon of hypoxaemia due to hyperventilation. This was due to a rare occurrence of permeable foramen ovale related to positional changes in a young male with pectus excavatum in the absence of elevated right atrial pressure. Cardiovascular shunts resulting from reopening of a permeable foramen ovale are usually associated with increases in right atrial pressures. Positional shunts in relation to particular anatomical abnormalities can, however, develop leading to the transient observation of shunting only upon assumption of various body positions. In this study, a specific case is presented in which a series of manoeuvres confirmed that hyperventilation at rest induced severe hypoxaemia, which could be explained by realignment of the inferior vena cava flow with the foramen ovale.

CASE REPORT

A 19-yr-old Caucasian male, in whom a marked pectus excavatum evolving since childhood had not been operated upon, presented with exertional dyspnoea upon moderate exercise. He suffered rheumatoid purpura when aged 9 yrs without secondary effects, and was a current nonsmoker and worked as a plasterer. Clinical examination was normal except for the thoracic deformity. The electrocardiogram showed a regular sinus rhythm with a left axis of +80°, and no repolarisation or conduction abnormality with a heart rate of 70 beats·min⁻¹ and a normal arterial blood pressure of 130/70 mmHg. Serum chemistry was normal. Chest radiography showed the thoracic deformity with a vertebral–sternal distance of 4.6 cm, while lung fields were clear. Resting spirometry was normal (table 1). Transthoracic echocardiogram at rest showed normal left ventricular diastolic and systolic functions with no evidence of valvular defects. Computed tomography of the thorax showed median and inferior anterior thoracic wall deformity with an index of pectus excavatum severity of 3.87 (ratio of transverse thoracic diameter to the minimal vertebral to sternal length [1]). The pleura and lung parenchyma were normal and the heart was displaced to the left (fig. 1).

| TABLE 1	Resting pulmonary function data before correction of a right-to-left shunt in a patient with a pectus excavatum

October 2002	Observed	% predicted
FEV_1 L	4.79	102
VC L	5.37	95
TLC L	8.04	105
RV L	2.69	155
ERV L	127	71
FRC L	3.96	115
$D_{L,CO}/V_A$ mL·min^{-1}·mmHg^{-1}·L^{-1}	4.19	84

FEV_1: forced expiratory volume in one second; VC: vital capacity; TLC: total lung capacity; RV: residual volume; ERV: expiratory reserve volume; FRC: functional residual capacity; $D_{L,CO}$: diffusing capacity of the lung for carbon monoxide; V_A: alveolar volume.

A graded cycle-ergometer cardiopulmonary exercise testing (CPET) showed an abnormally low peak oxygen uptake ($V'O_{2,peak}$) with marked hyperventilation, but no ventilatory limitation as peak ventilation remained at 56% of the predicted maximal ventilation. Peak heart rate was 82% of the maximal predicted heart rate. Exercise resulted in a marked decrease in blood gases from rest (arterial oxygen tension (P_{a,O_2}) 9.57 kPa; arterial oxygen saturation (S_{a,O_2}) 94.5%; alveolar–arterial oxygen tension difference (P_{A-a,O_2}) 5.45 kPa) to peak exercise (P_{a,O_2}: 5.08 kPa; S_{a,O_2}: 76.2%; P_{A-a,O_2}: 10.64 kPa). The dead space to tidal volume ratio (V_D/V'_T), and the arterio–alveolar CO_2 gradient remained elevated at $V'O_{2,peak}$ (table 2).

In view of these exercise-induced pulmonary gas exchange abnormalities, the hypothesis of a right-to-left shunt was proposed. This was further confirmed by a transoesophageal echocardiogram performed under resting sitting conditions showing a largely permeable foramen ovale with no associated intracardiac communication or aortic anomaly and revealing normal right atrial pressures.
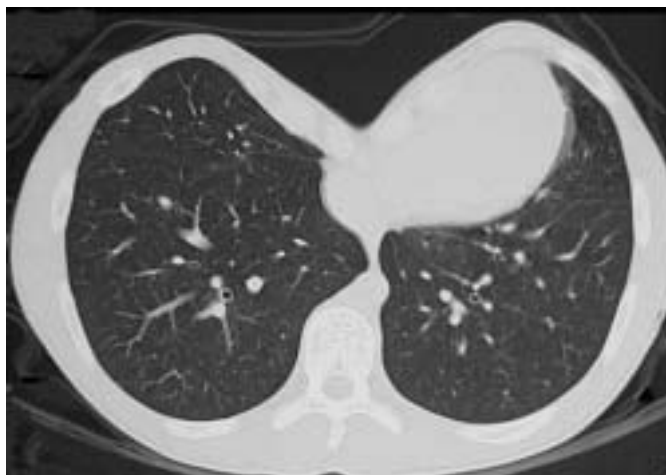
FIGURE 1. High-resolution thoracic scan at the lower lobes level (provided courtesy of P.M. Rémy-Jardin).

TABLE 2	Rest and maximal cycling exercise values in a patient with a pectus excavatum and a permeable foramen ovale from October 2002

	Rest	Maximum	Expected maximal values
Work W	0	130	210
$V'O_2$ mL·min^{-1}	296	1691	2619
$V'O_2$/kg mL·kg^{-1}·min^{-1}	4.9	28.2	44
RER	0.92	1.17	$\geqslant$1.15
$V'E$ L·min^{-1}	13.6	83.1	190
$V'T$ mL	669	2491	46% FVC
BF	20	33	<40
$V'E/V'O_2$	46	49	NA
$V'E/V'CO_2$	50	42	NA
$V_D/V'T$	0.43	0.34	<0.15
HR bpm	74	166	201
$V'O_2$/HR mL·kg^{-1}·beat^{-1}	0.07	0.17	0.22
pH	7.46	7.40	NA
P_{a,O_2} mmHg	72.5	38.2	>90
P_{a,CO_2} mmHg	30.8	32	NA
S_{a,O_2} %	94.5	76.2	>96
P_{A-a,O_2} mmHg	41	80	<20
$P_{(a-ET)CO_2}$ mmHg	5	6	
Serum lactate mmol·L^{-1}	0.7	4.6	NA

$V'O_2$: oxygen uptake; RER: respiratory exchange ratio; $V'E$: minute ventilation; $V'T$: tidal volume; BF: breathing frequency; $V'CO_2$: carbon dioxide production; V_D: dead space volume; HR: heart rate; P_{a,O_2}: arterial oxygen tension; P_{a,CO_2}: carbon dioxide arterial tension; S_{a,O_2}: arterial oxygen saturation; P_{A-a,O_2}: alveolar-arterial oxygen tension difference; $P_{(a-ET)CO_2}$: arterial minus end-tidal CO_2 difference; NA: not applicable. 1 mmHg=0.133 kPa.

In order to assess the mechanism by which the shunt developed, S_{a,O_2} was monitored during various clinical interventions selectively affecting ventilation or circulation to examine more specifically whether an exercise-induced increase in cardiac output contributed to the observed right-to-left shunt. First, increasing doses of dobutamine were administered intravenously with the patient lying in a semirecumbent position (45°) to affect cardiac output, but not ventilation. This resulted in an increase in heart rate up to 160 beats·min^{-1}, but without evidence of hyperventilation or of any arterial oxygen desaturation.

In contrast, when hyperventilation was induced in the upright position by voluntarily increasing $V'T$ while breathing rate was maintained at 16–18 breaths·min^{-1}, an immediate marked decrease in S_{a,O_2} was observed, which was reversed upon decreasing $V'T$ to resting values (fig. 2). The manoeuvres were repeated while the patient assumed various body positions. Maximal desaturation, and presumably shunting, was observed in the upright position, but this was absent while lying flat, in left or right lateral dorsal decubitus, or in the ventral position.

The persistent foramen ovale was then verified through right heart catheterisation, which confirmed normal right heart pressures and revealed a 12-mm foramen ovale diameter, later
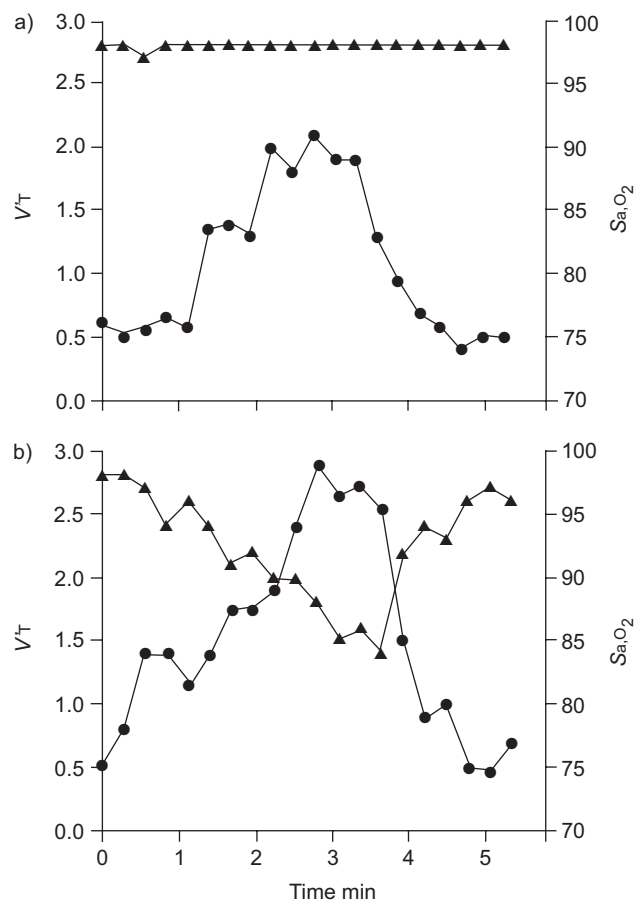
FIGURE 2. Variations of the transcutaneous arterial saturation (S_{a,O_2}; ▲) and tidal volume (V_T; ●) during a resting sustained voluntary hyperventilation in the supine (a) and upright (b) positions. Breathing frequency was maintained at 16–18 breaths·min⁻¹.

| TABLE 3 | Maximal cycle exercise values obtained in a patient with a pectus excavatum before, and 3 and 6 months after transcutaneous closure of a permeable foramen ovale |

Maximal exercise	October 2002	June 2003	October 2003
Work W	130	165	180
V'_{O_2} mL·min⁻¹	1691	2297	2307
V'_E L·min⁻¹	83.1	70.3	72.3
V'_E/V'_{O_2}	49	30	31
V'_E/V'_{CO_2}	42	30	29
V_D/V'_T	0.34	0.16	0.16
P_{a,O_2} mmHg	38.2	77.3	86.6
P_{A-a,O_2}	80	35	30.7

V'_{O_2}: oxygen uptake; V'_E: minute ventilation; V'_{CO_2}: carbon dioxide production; V_D: dead space volume; V'_T: tidal volume; P_{a,CO_2}: carbon dioxide arterial tension; P_{A-a,O_2}: alveolar-arterial oxygen tension difference. 1 mmHg=0.133 kPa.

9.2–27.3% [2, 3, respectively] of the population. An acquired intracardiac right-to-left shunt *via* a persistent foramen ovale usually results from an elevated pulmonary pressure leading to an inversion of the normal atrial pressure gradient. In the present case, it cannot be excluded that any increase in pulmonary pressure may occur due to the evolving hypoxia and secondary pulmonary vasoconstriction resulting in some pulmonary hypertension. Clearly, this may not cause the shunt but may add to it. Nonetheless, right-to-left shunts with normal atrial pressures have been described [4, 5], and are characterised by their positional nature, as in the rare "platypnoea-orthodeoxia" syndrome. Two theories have been proposed to explain these right-to-left shunts with normal right atrial pressures [6, 7]. First, transitory elevations in right atrial pressure may occur during coughing or in Valsalva manoeuvres leading to a transient pressure gradient and shunting. Examples of these are seen in: 1) elderly subjects; 2) patients with a right atrial myxoma or right-sided infarction; 3) or in the presence of positive end-expiratory pressure ventilation. Secondly, cardiac, thoracic or abdominal structural anomalies, such as those seen in acute or chronic constrictive pericarditis [8], pneumonectomy, right hemi-diaphragm paralysis [9, 10] or cirrhosis of the liver [11], may exist, which redirect the preferential flow from the inferior vena cava towards the interatrial septum and foramen ovale allowing shunting to occur. Therefore, this hypothesis implies two associated conditions. First, there is a persistent foramen ovale and, secondly, the flow from the inferior vena cava is directed onto the atrial septum at the level of the foramen ovale. In the present case, the most likely explanation is that the thoracic deformity of the pectus excavatum alters the anatomical integrity of the mediastinum, such that there is an anterior and leftward rotation of the heart leading to a deviation of the inferior cava flow towards the permeable foramen ovale.

In the present case, the CPET played an essential role in the diagnosis of persistent foramen ovale, since its functional repercussions were largely underestimated by the resting clinical investigation. There are some reports of exercise testing in pectus excavatum [12–23]. Results commonly show a

closed through positioning of a 35-mm Amplatz® umbrella (AGA Medical Corporation, Golden Valley, MN, USA). Finally, graded exercise tests were repeated 3 and 6 months after closure of the shunt which showed an improvement in exercise tolerance pulmonary gas exchange parameters and $V'_{O_2,peak}$ (table 3). In addition, hyperventilation manoeuvres were repeated in various positions and did not induce oxygen desaturation.

DISCUSSION

To the best of the current authors' knowledge, this is the first description of an immediate severe paradoxical hypoxaemia induced by voluntary hyperventilation. This observation in a patient with pectus excavatum may be explained by the hyperventilation-induced alignment of the inferior vena cava flow with the foramen ovale leading to a right-to-left shunt with normal right heart pressures.

The foramen ovale is an embryonic relic that allows the foetal circulation to flow from the right atrium to the left atrium, thereby bypassing the pulmonary vessels. The structure normally closes shortly after birth as left and right atrial pressures rise and fall, respectively. However, an incomplete closure termed "persistent foramen ovale" may also be seen in

reduced $V'O_2,max$ which may [12, 13, 15–17] or may not [14, 18–21] be related to the resulting alterations in the exercise-induced ventricular filling and exercise cardiac output to physical deconditioning [22] or to the extent of thoracic deformity [12, 14]. Although mitral valve prolapse has been frequently noted with pectus excavatum, to date there is no echocardiographic or heart catheterisation evidence to support the contribution of an impaired exercise cardiac output in the exercise intolerance of these patients [23, 24].

Similarly, there are little data on the exercise blood gases to substantiate a potential role of an impaired gas exchange to the exercise intolerance [12, 22]. In the present case, a right-to-left shunt was suspected because of the important alveolo–arterial oxygen gradient at rest and more specifically the exaggerated widening seen upon maximal exercise, which largely exceeds the expected values. A hyperventilation-induced hypoxaemia is an unusual phenomenon, since even in patients with chronic circulatory or respiratory disorders, hyperventilation always leads to an elevation in alveolar oxygen partial pressure and, depending on the normality of the ventilation–perfusion exchanges, a lesser or greater increase in P_a,O_2. There have been some reports of hypoxaemia resulting from a reflex hypoventilation following hyperventilation manoeuvres, but no report of hypoxaemia concomitant to hyperventilation [25–27]. In the present case, the degree of hypoxaemia may be related to the amplitude of diaphragmatic movements associated with the imposed $V'T$ expansion. This is well illustrated by the absence of arterial desaturation when hyperventilation was performed in the lying position. During inspiration in this position, contraction of the diaphragm pushes the abdominal contents downwards and backwards increasing the longitudinal and transverse diameters of the thorax. In contrast, in the upright position, the increase in $V'T$ expansion during hyperventilation exaggerates the stretching of the deviated inter-auricular septum, thereby favouring aligment of the inferior cava and the potentially permeable foramen ovale.

The right-to-left shunt was immediately corrected by placement of an intracardiac umbrella. This correction resulted in a marked improvement in exercise tolerance as seen from the increase in $V'O_2,peak$, the reduction in peak minute ventilation and $V_D/V'T$, and the dramatic improvement of the alveolar–arterial O_2 gradient (table 3). Further improvement in the peak exercise P_a,O_2 and alveolar–arterial O_2 gradient upon the CPET performed 6 months after closure of the foramen ovale may be taken to suggest that local atrial fibrosis solidified umbrella placement to eliminate the persistence of a small residual right-to-left shunt upon immediate placement of the umbrella.

The present case demonstrates that a hyperventilation manoeuvre in the situation of a pre-existing thoracic deformity may reveal the presence of a patent foramen ovale, which might be due to the channelling of the inferior vena cava flow towards the intra-atrial communication, thereby revealing an arterial desaturation, the degree of which is modified by the amplitude of the movement of the diaphragm.

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