Rev Port Cardiol. 2013;32(2):153–157

Revista Portuguesa de
Cardiologia
Portuguese Journal of Cardiology
www.revportcardiol.org

CASE REPORT

Subvalvular aortic stenosis associated with 8p23 deletion☆

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Received 22 April 2012; accepted 3 May 2012
Available online 16 February 2013

KEYWORDS
Chromosomal abnormality;
Congenital heart disease;
8p23 deletion;
Subvalvular aortic stenosis

Abstract We report the case of a 35-year-old man admitted due to heart failure, who had had moderate cognitive deficit, craniofacial dysmorphism, epilepsy, panic attacks and congenital heart disease (subvalvular aortic stenosis) associated with chronic atrial fibrillation since childhood.

In view of his facial dysmorphism and clinical presentation, karyotype analysis was performed and revealed a *de novo* interstitial deletion in chromosome 8 in the region p23.1–p23.2.

This is a rare chromosomal anomaly (about 50 descriptions in the literature), whose most common manifestations include heart defects, cognitive retardation and behavioral disturbances. In this paper we present the first case with associated subvalvular aortic stenosis and review the literature on this chromosomal abnormality.

PALAVRAS-CHAVE
Anomalia cromossómica;
Cardiopatia congénita;
Deleção 8p23;
Estenose aórtica subvalvular

Estenose aórtica subvalvular associada à deleção 8p23

Resumo Relata-se o caso de um homem, 35 anos, internado por insuficiência cardíaca, que desde a infância apresenta quadro de défice cognitivo moderado, dismorfias faciais, epilepsia, crises de pânico e cardiopatia (estenose aórtica subvalvular) associada a fibrilhação auricular crónica.

Face às dismorfias e espectro clínico realizou cariotipo que revelou a deleção da extremidade distal do braço curto do cromossoma oito (8p23). Esta anomalia cromossómica é rara (cerca de 50 descrições na literatura), e as suas manifestações mais comuns incluem malformações cardíacas, atraso cognitivo e distúrbio comportamental. No presente artigo descreve-se o primeiro caso associado a estenose aórtica subvalvular e revê-se a literatura disponível acerca desta anomalia cromossómica.

☆ Please cite this article as: Aguiar, P. Estenose aórtica subvalvular associada à deleção 8p23. Rev Port Cardiol. 2013. http://dx.doi.org/10.1016/j.repc.2012.05.025.
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Introduction

Congenital heart defects are associated with submicroscopic chromosomal abnormalities in around 17% of cases.[1] Improvements in medical and surgical treatments mean that 85% of patients with congenital heart disease now survive to adulthood.[2]

Deletion of the distal portion of the short arm of chromosome 8 (8p23) is a rare abnormality, whose most common manifestations include heart defects (most frequently atrioventricular septal defects), cognitive retardation and behavioral disturbances.[3] There has been no report to date of association with subvalvular aortic stenosis.

Subvalvular aortic stenosis can be caused by a fibrous membrane in the left ventricular outflow tract, muscular constriction due to thickening of the subvalvular ventricular septum, or both.[4] The literature contains widely varying figures for its association with other cardiovascular malformations, ranging from 13% to 71%; the most common associations are with ventricular septal defect or bicuspid aortic valve.[5]

Case report

We report the case of a 35-year-old man, Caucasian, illiterate, employed in a café, who had had moderate cognitive deficit, craniofacial dysmorphism, epilepsy, panic attacks, subvalvular aortic stenosis and chronic atrial fibrillation since childhood. He had undergone cardiac surgery twice, at the ages of 12 and 24, to implant a mechanical aortic valve prosthesis, to resect a fibromuscular subaortic ring and to correct a cleft mitral valve. He was being medicated with digoxin, furosemide, acenocoumarol, carbamazepine, sodium valproate, risperidone, alprazolam and ethyl loflazepate. He had no other medical or surgical history and did not drink alcohol or smoke.

Family history included his mother who had mild facial dysmorphism (facial paresis, possibly associated with birth trauma) and mild cognitive retardation. There was no history of consanguinity, similar phenotypes, heart disease or premature or sudden death.

Around a week before admission, he began to suffer progressively worsening dyspnea on exertion, orthopnea and paroxysmal nocturnal dyspnea associated with chest pain, cough with mucous expectoration and panic attacks of increasing intensity.

On arrival at the hospital he was agitated and polypneic (respiratory rate 32 cpm), with blood pressure 111/75 mmHg, pulse 103 bpm (arrhythmic) and tympanic temperature of 36.7 °C. Cardiopulmonary auscultation revealed crackling rales in the lower third of both hemithoraxes, generalized wheezing, and a metallic second heart sound, due to the mechanical valve, audible throughout the precordium. No jugular distension or peripheral edema was observed. His face (Figure 1) exhibited dolicocephaly, micrognathia, flattened base of nose, low-set ears and a wide, short neck.

Initial diagnostic assessment revealed partial respiratory insufficiency (Table 1); the electrocardiogram (Figure 2) showed atrial fibrillation with controlled ventricular rate (90 bpm) and nonspecific ventricular repolarization

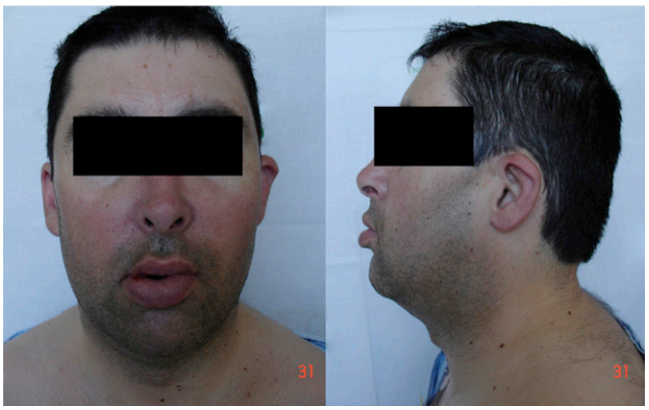

Figure 1 Facial phenotypic abnormalities.

abnormalities, while the posterior–anterior chest X-ray (Figure 3) revealed cardiomegaly and interstitial infiltrate in the lower third of both lung fields, suggestive of edema.

On echocardiography (Figure 4) there was slight left ventricular dilatation, although with good systolic function, left ventricular hypertrophy and right atrial dilatation; no signs of prosthetic valve dysfunction were observed. Pulmonary artery systolic pressure was 35 mmHg, similar to previous exams.

Karyotype analysis revealed an interstitial deletion in chromosome 8 in the region p23.1–p23.2. Cytogenetic analysis of the parents by fluorescent in situ hybridization (FISH) showed normal karyotypes.

Discussion

The 8p23 deletion (of the most distal portion of the short arm of chromosome 8) was first described in 1988 by Fagan et al., who located the factor VII regulator on band 8p23.1.[6] Since then, around 50 cases of this isolated chromosome abnormality have been reported, with no differences in gender or ethnicity. The lack of a specific phenotype, and the possibility of extremely small deletions, mean that its true prevalence is probably underestimated.[8,9]

Most 8p23 deletions are terminal, i.e. they include the end of the chromosome, but in some cases (including the patient presented here) interstitial deletions are found between bands 23.1 and 23.2.3 The quantity of genetic

Table 1 Initial diagnostic assessment.

Hemogram	Normal
INR	2.59
Renal function	Normal
Serum electrolytes	Normal
Transaminases	Normal
Myocardial necrosis	None
BNP	Not measured
C-reactive protein (mg/dl)	0.6
Blood gas analysis	PaO_2: 62 mmHg
	$PaCO_2$: 34 mmHg

BNP: brain natriuretic peptides; INR: international normalized ratio.