Medical Expertise

"Development of the European Network in Orphan Cardiovascular Diseases"
„Rozszerzenie Europejskiej Sieci Współpracy ds Sierocych Chorób Kardiologicznych"

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CASE SUMMARY

The authors presented a case of patient with trisomy 21, Eisenmenger's syndrome due to intraventricular septal defect AVCD type associated with myocardial hypertrophy of both ventricles, particularly intraventricular septum, as in hypertrophic cardiomyopathy. The patient presented moderate form of mental retardation, left-sided hypoacusis, and serious speech disorder. In physical examination central cyanosis, systolic heart murmur 3/6 in the Erb's point, and increased accentuation of the pulmonary component of the second heart sound were observed. Anamnesis revealed unusual tiredness and decreased exercise tolerance. Standard ECG showed extreme dextrogram, sings of right atrium and right ventricular hypertrophy, without arrhythmias and conduction disorders in Holter monitoring. Laboratory tests revealed poliglobulia with polycythemia RBC – 6,13 mln, Ht – 62,6%, Hb – 20,3g/l), highly elevated NT-proBNP (1186 pg/ml), proteinuria, (100 mg/dl), elevated total cholesterol level (292 mg/dl) and TGC (420 mg/dl) and uric acid (9,1 mg/dl). The distance in 6-minutes walking test was 205 m, breathlessness and fatigue was described as 3rd degree in Borg scale. The test was terminated due to lower limb pain, decreased saturation from 82% to 54%, stable blood pressure (about 100/70 mm Hg) and elevation of pulse from 90 to 108 bpm. In echocardiography a double outlet right ventricle with a inflowing intraventricular septal defect, with bidirectional shunt and significant myocardial hypertrophy, particularly of the intraventricular septum (28 mm) and a tendency to obstruct left ventricular outflow tract were observed. Tricuspid regurgitation was 5 m/sec. In hemodynamic assessment from 1999 and 2000 deterioration of the pulmonary hypertension (in first assessment the pulmonary pressure equaled systemic, in the next it was supra-systemic) and right-left shunt (Qp/Qs from 0,82 to 0,45) were observed. PCWP in 2000 was 35 mmHg. Parents of the patient did not give consent for a proposition of heart and lung transplant. The patient was initially treated with Digoxin, and since 2005 additionally with Nifedypine, and apart from that since 2010 – with Sildenafil and Arginine.

DISCUSSION

Down syndrome is an effect of trisomy of 21st chromosome, most common among aneuploidies, which is observed in 3-4% clinically diagnosed pregnancies (1). Patients with this syndrome apart from various degrees of mental disabilities are prone to congenital heart diseases (particularly AVCD, VSD, ASD, PDA, TOF), gastrointestinal abnormalities, leukemia, Alzheimer's disease, immune system deficiencies, hypothyroidism, diabetes, obstructive sleep apnea, and also problems concerning hearing and sight in comparison to healthy population. Life expectancy in Down's syndrome is about 50 years.

The reported prevalence of Down's syndrome is around 1 in 750 live births, much higher prevalence (about 1 in 100) is reported in children born by mothers >35 y.o. (1).

As far as predisposition to early development of obstructive pulmonary hypertension in total AVCD in patients with trisomy 21 is well known and requires early qualification to surgical treatment (till the end of first six months), hypertrophic cardiomyopathy is in this syndrome vary rare and remains a diagnostic and therapeutic challenge. Therefore this case deserves attention.

EXPERT'S OPINION

Hypertrophic changes of myocardium particularly intraventricular septum present in the echocardiography assessment suggests hypertrophic form of cardiomyopathy. This abnormality rarely coexists with trisomy 21. There is a notable increase of publications presenting non-familiar primary hypertrophic cardiomyopathy in combination with genetic syndromes, with or without associated congenital heart disease (2). Such cases have already been reported, in Poland as well. Podolec et al. presented a case of a 19-year-old patient with Down's syndrome after correction of ASD II, VSD and PDA with HCMP (3).

In presented case there are no indications for implementation of ICD, which are strictly established (4).

Examination data show advanced changes in pulmonary vascular bed. Clinical symptoms reveal that the patient is in class III due to WHO. Achieved in the 6MWT distance of <250 m, with systemic desaturation significantly over >10% (from 82% to 54% ! at the end of the test) have negative prognostic value, even considering the fact, that the result belongs to patient with trisomy 21, who does not cooperate fully in this type of examination. Additionally there is tachycardia (90-100 bpm), and blood pressure value (about 100/70 mmHg) (5). Present in heart catheterization in 2000 PCWP – 35 mm Hg is incredibly high and may be a false measurement. Increasing of this value may be due to hypertrophic changes of the left heart. High NT-proBNP also indicates advanced stage of the disease, right ventricle insufficiency and requires adjustment of current treatment.

In patients with Eisenmenger's syndrome in this class WHO-FC, apart from applied therapy with Sildenafil also Bosentan should be taken into account, which turned out to be efficient in therapy of grown-up pulmonary hypertension patients with Down syndrome (6). Additionally, in case of no improvement, drugs from the group of prostanoids may be taken into account.

Nifedipine in a patient with a tendency to tachycardia and with relatively low blood pressure (about 100/70 mm Hg) does not seem reasonable. The use of Dilzem or Amlodypine may be considered later (due to coexisting hypertrophic changes of left ventricle myocardium

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and a tendency to increasing obstruction of LVOT). However, this drugs require vary cautious monitoring because they may predispose to blood pressure drops, fainting and right ventricle failure. Administration should be preceded by another heart catheterization with hemodynamic assessment after implementation of combined therapy with Sildenafil and Bozentan and vasoreactivity test. Generally in patients with Eisenmenger's syndrome CCB is not recommended.

Administration of Digoxin in patients with hypertrophic CMP and beginning of obstruction of left ventricle tract is not recommended as well.

Diuretics in hypertrophic CMP and Eisenmenger's syndrome and Ht oscillating at about 60% should be used extremely cautiously and mainly considering Spironolactone.

Influenza and pneumococcal vaccination is recommended.

Night oxygen therapy does not seem to change the course of the disease in advanced Eisenmenger's syndrome. It may be recommended in patients with constantly decreased pO2 (about 60 mm Hg) if clinical improvement is observed.

Phlebotomy with isovolemic fluid correction is recommended when Ht is over 65%.

Anticoagulants are recommended in case of thromboembolic changes in pulmonary artery and heart failure (D-dimmer monitoring) and when no haemoptysis is observed.

CONCLUSION

Coincidence of congenital heart shunt associated with Eisenmenger's syndrome and hypertrophic cardiomyopathy in a patient with trisomy 21 remains a vary rare condition. Hovever still not proved but probable is association of this cardiomyopathy with a genetic abnormality.Complex characteristics of changes cause therapeutic difficulties and is associated with poor prognosis.

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