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Case Report

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Eisenmenger's syndrome in context of a complete atrioventricular canal defect

Abstract

Eisenmenger's syndrome is defined as obstructive pulmonary vascular disease that develops as a consequence of a large pre-existing left-to-right shunt causing pulmonary artery pressures to increase and approach systemic levels, such that the direction of blood flow then becomes bi-directional or right- to-left. We report the case of a 10years old child with complete CAV defect that was admitted at our hospital with haemoptysis as the first clinical manifestation of Eisenmenger's syndrome. Moreover, we report his good clinical evolution and the improvement of his functional status experimented under oral treatment with bosentan.

Keywords: eisenmenger's syndrome, right-to-left shunt, pulmonary hypertension, complete atrioventricular canal defect, bosentan

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Abbreviations: BPM, beats per minute; b.i.d, bis in die; CAV, atrioventricular canal; PH, pulmonary hypertension

Introduction

Eisenmenger's syndrome refers to any untreated congenital cardiac defect with intracardiac left-to-right communication that leads to PH, reversal of flow and cyanosis. Lesions in Eisenmenger's syndrome are characterized by high pulmonary pressure and/or high pulmonary flow state. Development of the syndrome represents a point at which PH is irreversible. We report a case corresponding to a young patient admitted to our hospital, who was diagnosed withEisenmenger's Syndrome with complete CAV defect and secondary aneurysmatic pulmonary artery. He received treatment with high flow oxygen, diuretic and bosentan, achieving a progressive improvement of functional status. We report this case in order to remark that there are some drugs, such as sildenafil or bosentan, whose use could reduce the high mortality rate of these patients. Moreover, these agents may change the natural progression of the disease, improving patient prognosis.[1,2]

Exclusive breastfeeding is considered the best diet for all newborns and infants. Exclusive nursing requires that the mother should be able to breast feed on demand by the child at any location. Hence it is inevitable that every nursing woman will need to breastfeed in public. Statistics and reviews have shown that the acceptance of public nursing is variable, even when it is protected by laws and policies. Numerous cultural and religious factors are thought to be responsible for this variation around the world. Presence or absence of protective legislation is another factor that may have an impact on public breastfeeding in each country. The negative attitude against breastfeeding in public is often considered responsible for the low breastfeeding rates in different parts of the world.

Case presentation

A 10-year-old man was admitted to our hospital with haemoptysis of 150ml and breathing difficulty. Physical examination showed no fever, non invasive pressure of 110/80mmHg and heart rate of 120 BPM. He also had cyanosis with acropachy (Figure 1), without stridor or pulmonary congestion, rhythmic heartbeat with increased second heart sound and systolic murmur IV/VI and hepatomegaly of 2cm. The ECG showed sinus tachycardia with a heart rate of 120 BPM, right bundle branch block and left anterior hemiblock. He had hyperviscosity syndrome, elevated levels of liver enzymes and hypoxemia with hypocapnia. Enlargement of both pulmonary hilum were demonstrated on chest x-ray. Patient related that his functional situation had been deteriorated during the last two months, but he had never consulted before. He and his family environment belonged to a very isolated ethnic group and had very limited socioeconomic resources.

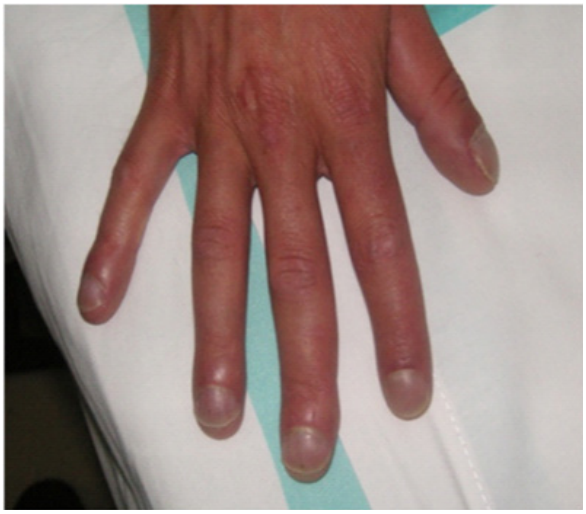

Figure 1 Cyanosis and Acropachy.

The echocardiography showed a disorder in the crux cordis which consists on a complete CAV defect with incompetence of both atrioventricular valves (Figure 2), severe PH and aneurysmatic main pulmonary artery (Figure 3). With the diagnosis of Eisenmenger's Syndrome with complete CAV defect and secondary aneurysmatic pulmonary artery, treatment with high flow oxygen and low doses of diuretic was initiated. Afterwards, the administration of oral bosentan was started at the dose of 62.5mg twice daily and the patient achieved a progressive improvement of functional status. The dosage was increased to 125mg twice daily after 4weeks with perfect tolerance. Nowadays he keeps a functional class II/IV.

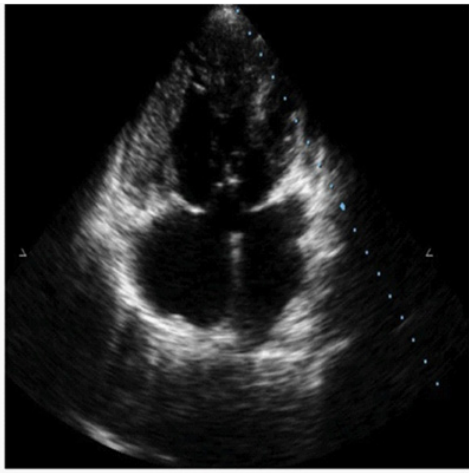

Figure 2 Complete Atrioventricular canal defect.

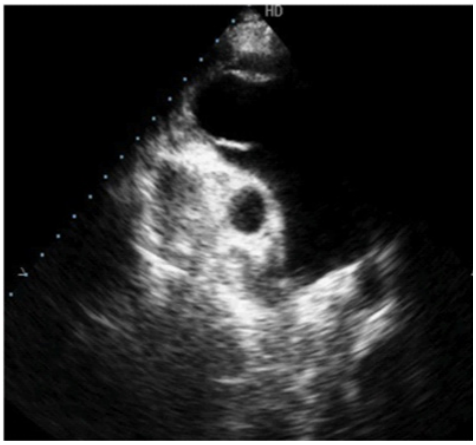

Figure 3 Aneurysmatic main pulmonary artery.

Discussion

Nowadays, the Eisenmenger's syndrome is an uncommon pathology that could be the final phase of cardiopathies with a long-term development left-to-right shunt. Usual abnormalities found in this syndrome include the reduction in the production of endogenous vasodilators and the increase in the synthesis of vasoconstrictors. For this reason, the use of medications with potent vasodilator and anti-proliferative effects, such as analogs of prostacyclin (epoprostenol, iloprost, treprostinil, beraprost), endothelin receptor antagonists (bosentan, ambrisentan, sitaxsentan), and 5-phosphodiesterase inhibitors (sildenafil) is useful in the treatment of this pathology.[3,4] In the past few years, treatment of PH has undergone an extraordinary evolution, which has led to the current approval by regulatory agencies of some drugs with different routes of administration. Additional drugs are expected in the near future.[4,5] Modern drug therapy leads to a significant improvement in patient's symptomatic status and a slower rate of clinical deterioration. Despite this finding, PH remains a chronic disease without a cure.

The therapy of PH patients cannot be considered as a mere prescription of drugs but is characterized by a complex strategy which includes the evaluation of severity, supportive and general measures, the assessment of vasoreactivity, the estimation of efficacy, and combination of different drugs plus interventions.[3,5] Bosentan is an oral active dual endothelin-A and endothelin-B receptor antagonist and the first molecule of its class that was synthesized. Activation of the endothelin system has been demonstrated in both plasma and lung tissue of PH patients. Although it is not clear if the increases in endothelin-1 plasma levels is a cause or a consequence of PH, these data support prominent roles for the endothelin system in the pathogenesis of PH. Bosentan has been evaluated in PH and have shown improvement in exercise capacity, functional class, hemodynamics, echocardiographic and Doppler variables, and time to clinical worsening. Long-term observational studies have demonstrated the durability of the effect of bosentan in adult idiopathic PH patients over time. Increases in hepatic aminotransferases occurred in approximately 10% of the subjects but were found to be dose dependent and reversible after dose reduction or discontinuation. For these reasons, liver function test should be performed monthly in patients receiving bosentan. Reductions on hemoglobin levels and impaired spermatogenesis have also been observed.[5]

Other endothelin receptor antagonists are sitaxsentan and ambrisentan. Sitaxsentan is a selective orally active endothelin-A receptor antagonist. It has demonstrated improvements in exercise capacity and hemodynamics. Monthly checking of liver function tests is required. Sitaxsentan interacts with warfarin, and co-administration requires dose reductions of warfarin to avoid increases of INR. Ambrisentan is a non-sulfonamide, propanoic acid class, endothelin receptor antagonists that is selective for the endothelin-A receptor. This drug has demonstrated efficacy on symptoms, exercise capacity, hemodynamics, and time to clinical worsening. Patients treated with ambrisentan require monthly liver function test assessment. An increased incidence of peripheral edema has been reported with ambrisentan use.[3,5]

Alternative treatment regimen includes drugs such as: Calcium channel blockers, prostanoids and Phosphodiesterase type-5 inhibitors.[2–5] Smooth muscle cell hypertrophy, hyperplasia, and vasoconstriction have long been known to contribute to the pathogenesis of idiopathic PH and this has led to the use of calcium channel blockers. The drugs that have been predominantly used in reported studies are nifedipine, diltiazem, and amlodipine. The daily doses of these drugs that have shown efficacy in idiopathic PH are relatively high. It is advisable to start with a low dose and increase cautiously and progressively to the maximum tolerated dose. The potential side effects of these drugs are systemic hypotension, lower limb peripheral edema, syncope and right ventricle failure [4,5]

Prostacyclin is produced predominantly by endothelial cells and induces potent vasodilatation of all vascular beds. Dysregulation of the prostacyclin metabolic pathways has been shown in patients with PH. The clinical use of prostacyclin in patients with PH has been extended by the synthesis of stable analogues. Epoprostenol needs to be administered continuously by means of an infusion pump and a permanent tunneled catheter. Epoprostenol improves symptoms, exercise capacity, and hemodynamics in both clinical conditions, and is the only treatment shown to improve survival in idiopathic PH, as well as long-term persistence of efficacy. Side effects include flushing, headache, diarrhea and leg pain. Serious adverse events related to the delivery system include pump malfunction, local site infection, catheter obstruction, and sepsis. Iloprost is a chemically stable prostacyclin analogue available for intravenous, oral, and aerosol administration. Inhaled therapy for PH has the theoretical advantage of being selective for the pulmonary circulation. Inhaled iloprost has showed an increase in exercise capacity and improvement in symptoms. Overall, inhaled iloprost was well tolerated, with flushing and jaw pain being the most frequent side effects. The effects of oral iloprost have not been assessed in PH. Treprostinil is a tricyclic benzidine analogue of epoprostenol. It can be administrated both

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intravenous or subcutaneously. It showed improvements in exercise capacity, hemodynamics, and symptoms. The potential side effects include local site pain, flushing and headache. Beraprost is the first chemically stable and orally active prostacyclin analogue. This drug has shown an improvement in exercise capacity that unfortunately persists only up to 3–6months. The most frequent adverse events were headache, flushing, jaw pain and diarrhea.[5]

The pulmonary vasculature contains substantial amounts of Phosphodiesterase type-5. Phosphodiesterase type-5 inhibitors cause significant pulmonary vasodilation and include sildenafil and tadalafil. Sildenafil: is an orally active, potent, and selective inhibitor of Phosphodiesterase type-5. This agent has favourable results on exercise capacity, symptoms, and hemodynamics. Most side effects of sildenafil were mild to moderate and mainly related to vasodilation (headache, flushing, and epistaxis).Tadalafil is a selective Phosphodiesterase type-5 inhibitor that has shown favourable results on exercise capacity, symptoms, hemodynamics, and time to clinical worsening. The side effect profile was similar to that of sildenafil.[2,5] In summary, there are several kind of drugs used in the treatment of PH with a different profile of side effects. Nevertheless, the results are similar among these drugs, improving basically exercise capacity, hemodynamics, and symptoms. The only treatment capable of improving survival is Epoprostenol, with the inconvenience that it needs to be administered intravenously.[5]

In conclusion, the treatment with drugs like bosentan can improve the prognosis and quality of life of those cases with advanced functional class, as the case reported. Despite the progress on the treatment of PH, the functional limitation and the survival of these patients remain unsatisfactory. For these reasons, additional therapeutic strategies targeted to diverse pathobiological changes are being explored in order to improve symptoms and prognosis further.

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Conflicts of interest

Author declares there are no conflicts of interest.

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