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Multiple intracardiac benign tumors treated with low-dose everolimus

CASE REPORT

INTRODUCTION

Cases of primary intracardiac benign tumors are rare in infants and children. This rate is reported at 0.027% to 0.08% according to pediatric autopsies (1). Cardiac tumors are mostly benign, and the most common type is rhabdomyoma (61.5%); however, mortality and morbidity depend on their size and location in the heart (2). In this case report, we report a neonatal case treated with low-dose everolimus.

CASE REPORT

The patient, weighing 3,700 g at term, noted to have a murmur on the third postnatal day, was referred to the pediatric cardiology clinic. There were no unusual features in her personal and family histories. A 2/3 degree systolic murmur was noted on auscultation during her physical examination. No other pathological symptoms were found. Transthoracic echocardiography revealed multiple intracardiac masses in the left ventricular outflow tract associated with the aortic valve, at the right ventricular apex and in the left ventricular posterior wall with diameters of 6×7 mm, 6.7×7.8 mm and 4.5×3.4 mm, respectively (Fig. 1).

In the left ventricular outflow tract, a pressure gradient of maximum systolic pressure of 42 mm Hg and mean of 24 mm Hg were detected by echocardiography. Rhabdomyoma was considered primary in the echocardiographic evaluation because of the echogenicity and the multiple tumors. As the patient was scanned for tuberous sclerosis, a well-circumscribed tumor (suspected to be a retinal hamartoma) was observed on the lower temporal branch of the retinal artery. Abdominal ultrasound assessment was normal. Everolimus treatment was decided after evaluation by neonatal, cardiology and pediatric oncology departments (0.65 mg/m^2/day). Everolimus blood level was determined to be between 3–8 µg/L in control examination. The patient was discharged 22 days after hospitalization to continue the treatment at home. Echocardiographies were performed at 1, 2, and 3 months of follow-up, and there was no tumor seen, and the left ventricular outflow tract was opened at the end of the third month of treatment (Fig. 2). Everolimus was

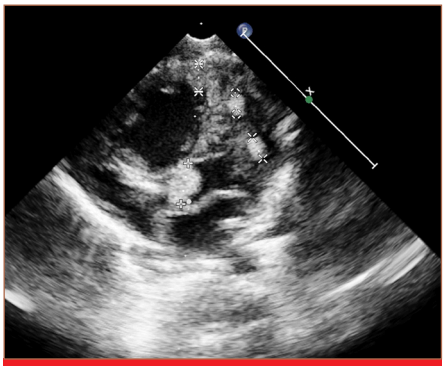

Figure 1. Echocardiographic image before treatment

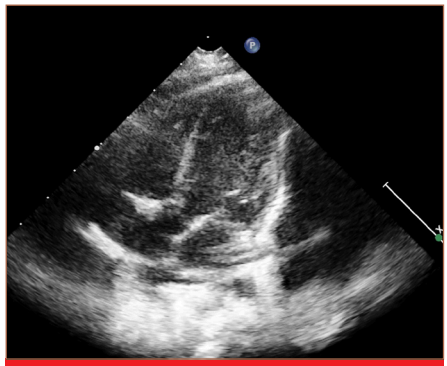

Figure 1. Echocardiographic image before treatment

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stopped in the 17th week of treatment. There was no drug dependency complication in the follow-up.

DISCUSSION

Intracardiac tumors may be asymptomatic or may present with serious clinical findings such as outflow obstruction, heart failure, pulmonary hypertension, cardiac tamponade, and arrhythmia. It is reported that 50%–80% of rhabdomyoma can regress spontaneously (3).

The efficacy of everolimus in the treatment of rhabdomyoma associated with tuberous sclerosis has been shown in various studies (4, 5). Everolimus acts through the inhibition of mTOR (mammalian target of rapamycin) receptors, which play a role in the pathophysiology of tumoral formations seen in patients with tuberous sclerosis. Although several dosage regimens have been used, a dramatic response in patients after a short time with low-dose therapy has been reported in recent years (5).

The recommended dose of everolimus therapy is 4.5 mg/m^2/day for managing cerebral subependymal giant cell astrocytomas (SEGA) in children with tuberous sclerosis.

A serum level of 5–15 ng/mL has been shown to be effective in reducing the tumor size of SEGAs (6). Demir et al. (7) is a pioneer in using everolimus to treat neonatal patients with cardiac rhabdomyoma. Initially, they used a high dose regimen of 0.25 mg every 6 hours (equivalent to 5 mg/m^2/day), which resulted in a high serum level of 83 ng/mL. The dosage was subsequently reduced to 0.25 mg every 12 hours for 2 days a week. After 75 days of treatment, the tumor decreased in size without any complications.

The first to do so, Goyer et al. (8) reported 2 premature neonatal cases treated with low-dose everolimus (0.65 mg/m^2/day), and their cardiac tumors regressed smoothly. Chang et al. (4) treated 3 newborns suffering from rhabdomyoma with low-dose everolimus therapy. They demonstrated that the tumor size decreased in 2 months, and the serum levels between 3 and 7 ng/mL are effective in causing tumor regression in neonatal patients with rhabdomyoma (4). In our case, significant regression in tumor measurements and even complete resolution were observed with low-dose everolimus treatment.

Studies have reported multiple side effects of everolimus such as immunosuppression, an increase in the frequency of infection, and stunted growth (5). However, we did not find any side effects in our patient during the treatment.

Informed consent: Informed consent was signed and given by the patient's parent.

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