CARDIAC RHABDOMYOMAS, ASSOCIATION WITH TUBEROUS SCLEROSIS COMPLEX AND EVEROLIMUS TREATMENT: SINGLE CENTER EXPERIENCE

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INTRODUCTION

Cardiac rhabdomyoma (CR) is the most common pediatric heart tumor, has a natural history of spontaneous regression. Surgery is only necessary when hemodynamically significant obstruction is present. Rhabdomyomas are closely associated with tuberous sclerosis complex (TSC), an autosomal dominant neurocutaneous disorder where TSC mutation results in abnormal cellular proliferation and differentiation. Recent reports on everolimus (mammalian target of rapamycin (mTOR) inhibitor), have shown favorable results for treatment of CRs

AIM

The aim of this study is to evaluate clinical presentation, outcome of patients diagnosed as CRs, their association with TSC, and to present our results with everolimus treatment .

PATIENTS and METHODS

Medical data of children diagnosed as CRs between 2013-2017, in our center were retrospectively reviewed. 30 patients were diagnosed as CR, median age at diagnosis was 7 months (1 day-16 years 8 months), 13 patients (43%) were diagnosed prenatally, 12 (40%) were diagnosed in the neonatal period. 21 patients (70%) had multiple CRs and 9 (30%) had solitary CR. 20/21 patients (95%) with multiple CRs and 3/9 patients (33%) with solitary CR had TSC and epilepsy during the follow-up. Abdominal ultrasonography was performed in 18 patients, 4 had renal angiomyolipoma. Flow diagram of the follow-up is given in Figure 1.

RESULTS

Rhabdomyomas were complicated by arrhythmias in 7 patients (23%). Left and right ventricular inflow obstruction were present in 4 (17%) and 1 patient (3%), respectively. Left and right ventricular outflow tract obstruction were present in 5 patients (7%) and 1 patient (3%), respectively (Table 1). 7/30 patients were given everolimus treatment (optimal dose, 0.25 mg, twice a day, 2 days per week). Indications for everolimus were inoperable outflow tract obstruction in 4, inflow obstruction in 3 patients. Everolimus was effective (reduced tumor size by 50%, decreased tumor numbers) in 6/7 patients (86%). Surgery was performed in 3/30 patients (10%) with hemodynamically significant outflow tract obstruction. 4/7 patients had ventricular tachycardia, one required implantable cardiac defibrillator in the postoperative period, 1/7 patient had supraventricular tachycardia. Ecochardiographic improvement of a patient is given in Figure 2.

Figure 1. Flow diagram of patients with cardiac rhabdomyoma associated with tuberosclerosis

Table 1. Cardiac complications of the patients with TSC and cardiac rhabdomyoma

	n	(%)
Arrhythmias	7	23
Left ventricular inflow obstruction	5	17
Right ventricular inflow obstruction	1	3
LVOT obstruction	5	17
RVOT obstruction	1	3

Figure 2. Pre and post- treatment echocardiographic images of a patient with CR

CONCLUSION

- ❖ Rapid tumor regression was observed in 86% of patients treated with everolimus which were unlikely to have a spontaneous regression.
- ❖ Everolimus and other mTOR inhibitors may be possible alternatives or adjuvant therapies for patients with CRs.