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, have 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. We aimed to evaluate clinical presentation, outcome of patients diagnosed as CRs, association with TSC, present our results with everolimus treatment.

Methods: Medical data of children diagnosed as CRs between 2013-2017 were retrospectively reviewed.

Results: 30 patients (median age 7 months (1 day-16 years 8 months), 13 male, 17 female) were diagnosed as CR. 13 patients (43%) were diagnosed prenatally. 21 patients (%70) had multiple CRs, 9 patients (30%) had solitary CR by echocardiography. During the follow-up, 21 patients (70%) had TSC and epilepsy. Rhabdomyomas were complicated by arrhythmias (7 patients, 23%), left (4 patients, 13%) and right (1 patient, 3%) ventricular inflow obstruction, left (5 patients, 17%) and right (1 patient, 3%) ventricular outflow tract obstruction. 4 patients had ventricular tachycardia, one patient required implantable cardiac defibrillator, 1 patient had supraventricular tachycardia. 7/30 patients (23%), median age 18 days (7 days-12 years) were given everolimus (optimal dose, 0.25 mg, twice per day, 2 days per week). Indications for everolimus were inoperable outflow tract obstruction in 4 patients, inflow obstruction in 3 patients. Everolimus were effective (reduced tumor size by at least 50%, decreased tumor numbers) in 6/7 patients (86%). Surgery was performed in 3 patients (10%). Follow period was median 14 months.

Conclusions: In our series, multiple CRs were more closely associated (95%) with TSC than previously reported in literature (75%). Although CRs are benign in nature, 18/30 (60%) of our patients had complications. Patients with multiple CRs must be under careful follow-up for development of TSC, renal angiomyomas, subependymal astrocytomas. To our knowledge, this is the largest series reported so far with everolimus in treatment of CRs. Rapid tumor regression was observed in 86% of patients even in one month which were unlikely from a spontaneous regression. Everolimus and other mTOR inhibitors may be possible novel therapies for patients with hemodynamically significant CRs.