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Case Study

Targeting the Tumor Before Birth: Transplacental Everolimus Therapy for Fetal Cardiac Rhabdomyoma Associated with Suspected Tuberous Sclerosis – A Case Report

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Fetal cardiac tumors are rare but clinically significant findings during antenatal evaluation. Among these, cardiac rhabdomyoma represents the most common primary cardiac tumor detected in the fetal and neonatal period. Although histologically benign, these tumors are of considerable clinical importance because of their strong association with tuberous sclerosis complex , a genetic disorder characterized by hamartomatous growths involving multiple organs including the brain, heart, skin, kidneys, and lungs. In many cases, fetal cardiac rhabdomyoma serves as the earliest detectable manifestation of tuberous sclerosis, often preceding the development of neurological and dermatological features. Advances in prenatal ultrasonography and fetal echocardiography have significantly improved the early detection of intracardiac tumors, allowing timely evaluation and counseling. While many rhabdomyomas undergo spontaneous regression after birth, large or strategically located tumors may result in complications such as arrhythmias, ventricular outflow tract obstruction, cardiac dysfunction, or hydrops fetalis, potentially threatening fetal survival.Careful antenatal monitoring and multidisciplinary management are essential in such pregnancies. Recent therapeutic advances have introduced the use of mammalian target of rapamycin inhibitors, such as everolimus, which target the molecular pathway involved in tuberous sclerosis. Emerging evidence suggests that transplacental administration of everolimus may lead to regression of fetal cardiac rhabdomyomas, offering a promising prenatal therapeutic option in selected cases. We report a case of fetal cardiac rhabdomyoma detected antenatally in a 43-year-old primigravida with an intracytoplasmic sperm injection (ICSI) conception, in whom transplacental everolimus therapy was administered with subsequent reduction in tumor size, highlighting the role Powered by Editorial Manager® and ProduXion Manager® from Aries Systems Corporation of targeted prenatal therapy and multidisciplinary management.

Keywords: Tuberous Sclerosis; Fetal Cardiac Rhabdomyoma; Targeted Therapy; mTOR inhibitors; Transplacental Everolimus Therapy.

INTRODUCTION

Fetal cardiac tumors are rare but clinically significant findings during antenatal evaluation. Among these, cardiac rhabdomyoma represents the most common primary cardiac tumor detected in the fetal and neonatal period. Although histologically benign, these tumors are of considerable clinical importance

because of their strong association with tuberous sclerosis complex (TSC), a genetic disorder characterized by hamartomatous growths involving multiple organs including the brain, heart, skin, kidneys, and lungs. In many cases, fetal cardiac rhabdomyoma serves as the earliest detectable manifestation of tuberous sclerosis, often preceding the development of neurological and dermatological features. Advances in prenatal ultrasonography and fetal echocardiography have significantly improved the early detection of intracardiac tumors, allowing timely evaluation and counseling. While many rhabdomyomas undergo spontaneous regression after birth, large or strategically located tumors may result in complications such as arrhythmias, ventricular outflow tract obstruction, cardiac dysfunction, or hydrops fetalis, potentially threatening fetal survival. Therefore, careful antenatal monitoring and multidisciplinary management are essential in such pregnancies. Recent therapeutic advances have introduced the use of mammalian target of rapamycin (mTOR) inhibitors, such as everolimus, which target the molecular pathway involved in tuberous sclerosis. Emerging evidence suggests that transplacental administration of everolimus may lead to regression of fetal cardiac rhabdomyomas, offering a promising prenatal therapeutic option in selected cases. We report a case of fetal cardiac rhabdomyoma detected antenatally in a 43-year-old primigravida with an intracytoplasmic sperm injection (ICSI) conception, in whom transplacental everolimus therapy was administered with subsequent reduction in tumor size, highlighting the role of targeted prenatal therapy and multidisciplinary management.

CASE REPORT

A 43-year-old primigravida with an intracytoplasmic sperm injection (ICSI) conception after eight years of marriage was diagnosed antenatally with fetal cardiac rhabdomyoma during routine obstetric ultrasonography. A detailed fetal echocardiography was performed, which confirmed the presence of intracardiac masses suggestive of rhabdomyoma. Given the well-known association between fetal cardiac rhabdomyoma and tuberous sclerosis complex (TSC), a pediatric genetic consultation was obtained, and the parents were counseled regarding the possible diagnosis and the need for postnatal evaluation. At 35 weeks of gestation, the patient was admitted for transplacental everolimus therapy in view of the suspected diagnosis of tuberous sclerosis and the presence of fetal cardiac rhabdomyoma. During therapy, close maternal and fetal monitoring was undertaken. Serial fetal echocardiography was performed to assess tumor progression. Following initiation of everolimus therapy, a reduction in the size of the cardiac tumor was noted on follow-up fetal echocardiography, suggesting a favorable response to treatment. The patient subsequently presented at 37 weeks and 1 day of gestation, when an emergency lower segment caesarean section (LSCS) was performed. After delivery, the neonate underwent further evaluation. A pediatric neurosurgery consultation was sought to assess for associated neurological manifestations of tuberous sclerosis. Neurosonography was performed, which demonstrated findings suggestive of intracranial lesions consistent with subependymal nodules, raising suspicion for tuberous sclerosis complex. The neonate was advised ongoing follow-up with pediatric cardiology, neurology, and genetics teams for further evaluation and long-term surveillance.

DISCUSSION

Cardiac rhabdomyoma is the most common primary cardiac tumor in fetuses and neonates. Although cardiac tumors are rare overall, rhabdomyomas account for nearly 60–70% of cardiac tumors detected during fetal life. The condition has a well-established association with tuberous sclerosis complex (TSC), an autosomal dominant neurocutaneous disorder characterized by the development of hamartomatous lesions in multiple organs including the brain, heart, skin, kidneys, and lungs. Mutations in the TSC1 and TSC2 genes, which encode hamartin and tuberin respectively, lead to dysregulation of the mTOR signaling pathway, resulting in abnormal cellular proliferation and hamartoma formation. [12] Prenatal detection of cardiac rhabdomyoma has increased significantly with the widespread use of high-resolution obstetric ultrasonography and fetal echocardiography. These tumors are typically visualized as well-defined, homogeneous, hyperechoic masses within the ventricular myocardium or interventricular septum. Multiple lesions are frequently observed and strongly raise

suspicion for tuberous sclerosis. [3] The presence of multiple cardiac rhabdomyomas during fetal life is considered one of the earliest detectable manifestations of TSC and often precedes the appearance of other systemic features. Several studies have demonstrated a strong association between fetal cardiac rhabdomyoma and tuberous sclerosis. Approximately 50–80% of fetuses diagnosed with cardiac rhabdomyoma are eventually diagnosed with TSC, particularly when multiple tumors are present. [4] Conversely, cardiac rhabdomyomas are detected in a substantial proportion of patients with tuberous sclerosis during infancy. Therefore, identification of these tumors during prenatal imaging should prompt detailed evaluation and counseling regarding the possibility of tuberous sclerosis. In addition to cardiac evaluation, further investigations such as fetal magnetic resonance imaging (MRI) may help identify associated neurological abnormalities, including cortical tubers and subependymal nodules, which are characteristic of TSC. Early detection of these lesions is clinically important because neurological manifestations, particularly epilepsy and developmental delay, represent the major determinants of long-term prognosis in affected individuals. [5] Although histologically benign, cardiac rhabdomyomas may produce clinically significant complications depending on their size and location. Potential complications include arrhythmias, obstruction of ventricular outflow tracts, cardiac failure, and rarely hydrops fetalis. [6] However, a unique feature of rhabdomyomas is their tendency for spontaneous regression after birth, which occurs in the majority of cases due to apoptosis of tumor cells. [7] as a result, many infants can be managed conservatively with close monitoring rather than immediate surgical intervention. Management during pregnancy primarily focuses on serial fetal echocardiographic surveillance to monitor tumor size, cardiac function, and the presence of arrhythmias or obstruction. Delivery planning should be individualized based on fetal condition and the potential risk of neonatal cardiac compromise. [8] In most cases, delivery at a tertiary care center with neonatal cardiology support is recommended. Postnatal evaluation is essential for confirming the diagnosis and assessing for other manifestations of tuberous sclerosis. Dermatological examination, neuroimaging, ophthalmologic assessment, and genetic testing may be required for comprehensive evaluation. Early identification of TSC allows timely initiation of surveillance and management strategies, particularly for neurological complications such as epilepsy. [9] Recent advances in targeted therapy have also improved management options in selected cases. mTOR inhibitors such as everolimus and sirolimus have shown promising results in reducing the size of cardiac rhabdomyomas and controlling other manifestations of tuberous sclerosis. [10] These therapies are particularly useful in cases with significant hemodynamic compromise or refractory arrhythmias. The present case highlights the importance of recognizing fetal cardiac rhabdomyoma as an important prenatal marker of tuberous sclerosis[11]. Early diagnosis facilitates parental counseling, multidisciplinary perinatal management, and appropriate postnatal follow-up[12]. Continuous surveillance is essential, as the long-term outcome largely depends on the neurological manifestations associated with tuberous sclerosis rather than the cardiac tumor itself.

CONCLUSION

Fetal cardiac rhabdomyoma is an important prenatal marker of tuberous sclerosis complex, and early detection allows timely counseling and multidisciplinary management. This case demonstrates that transplacental everolimus therapy may lead to in-utero reduction in tumor size, offering a promising therapeutic option in selected cases. Careful maternal–fetal monitoring and long-term postnatal follow-up are essential to detect and manage associated manifestations of tuberous sclerosis.

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