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Case Study

# Challenge in Cardiac Rhabdomyoma in Pediatric Age Group

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## Abstract

Primary cardiac tumors in pediatric age group are rare it could be divided into benign or malignant neoplasms. this paper presents two cases of cardiac rhabdomyomas which consider the commonest pediatric tumors to high light the different scenarios in presentations [1].

***Keywords:*** *Rhabdomyoma; Tuberous Sclerosis; Benign Tumor; Hamartoma; Everolimus*

## Abbreviations

CMR: Cardiac Magnetic Resonance Image; CT: Computed Tomography; ECG: Electro-Cardo-Gram

## Introduction

Cardiac tumors could arise from all cardiac layers in addition to the lining pericardium with predominance of benign tumor. Rhabdomyomas consider the most common of the cardiac benign tumors. Metastatic tumors are more frequent than primary form. The prevalence of primary cardiac tumors in pediatric is 0.0017 to 0.28 in autopsy series. The incidence of cardiac tumor during fetal life nearly 0.14%. Around of 10% of pediatric cardiac tumors are malignant. Sarcomas considered the commonest primary cardiac malignant tumor in pediatric. The 2ry cardiac malignant tumors are 10 - 20 times more prevalent than primary ones [2].

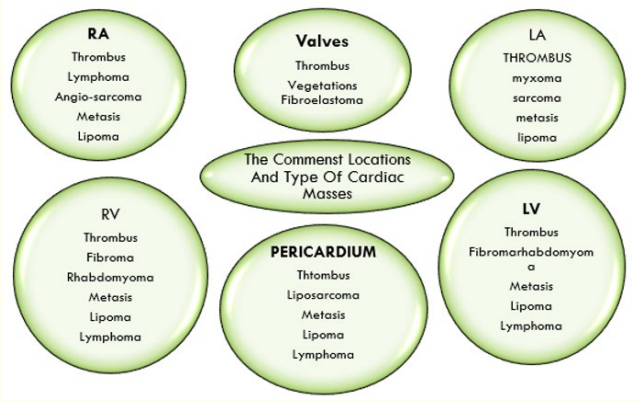



***Figure 1:*** *Smart art shows the commonest locations and types of cardiac masses adapted from Tyebally., et al. [3].*

Presenting symptoms are challenging. once the malignant tumor diagnosed the diagnosis considered poor due to metastatic nature of the tumor. Interestingly, due to the enhancement and increased use of noninvasive imaging modalities, an increase in the incidence of pediatric cardiac tumors has been reported in the last decades.

Presentation could be in prenatal or postnatal life. the clinical picture at presentation depends on size and site of the tumor [4].

Fetal cardiac tumors are expected to grow antenatally due to progressive nature of the pregnancy. In the fetus it usually reported during routine anti-natal examination as intracardiac mass, as early as 20 weeks of gestation although it could be missed during early scanning, the majority detected later on during pregnancy course. It manifests as cardiac rhythms disturbance, congestive heart failure, fetal hydrops and rarely stillbirth [5].

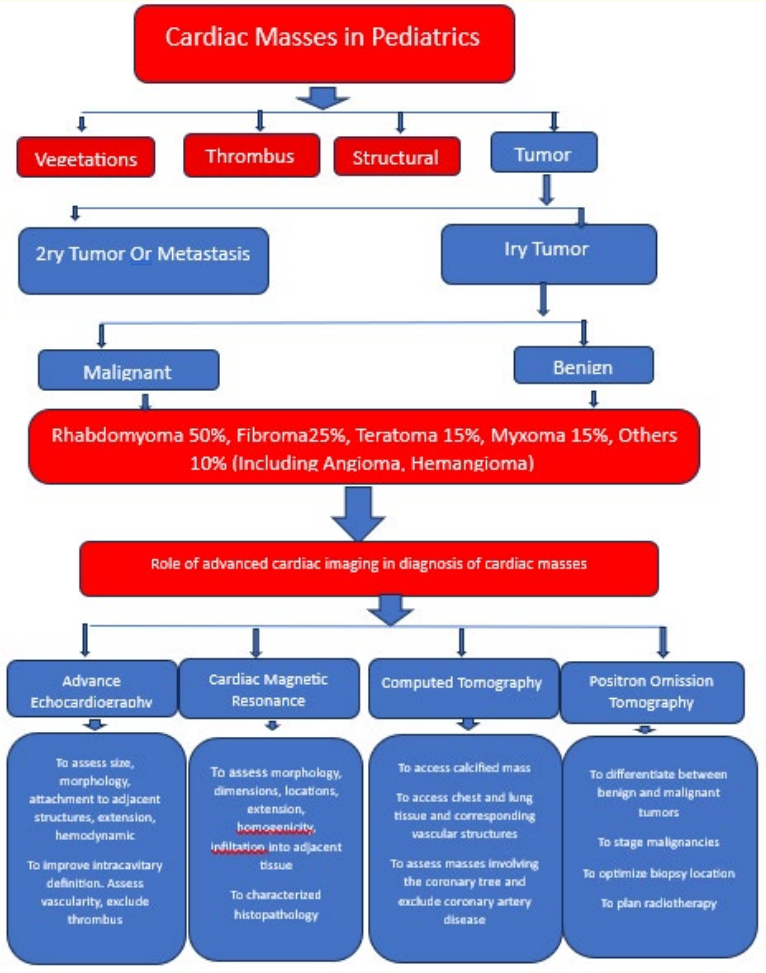



***Figure 2:*** *Illustrated diagram 1 shows cardiac masses in pediatrics and advanced diagnostic tools adapted from Tyebally., et al. [3].*

| Tumour | Histopathology | Role of Biopsy | Role of Surgery |
|---|---|---|---|
| Myxoma | Spindle or stellate cells, pseudo-vascular structure, myxoid matrix, hemorrhage, Dystrophic calcification can be present | Not usually needed | Complete resection to prevent embolic complications |
| Lipoma | Mature adipocytes, occasionally with entrapped myocytes at the periphery | Not usually needed | Considered only in sever complicated cases |
| Fibroma | Fibroblasts and collagen bundles, some elastic fibers, calcification is a common finding | Not usually needed | Considered for severally complicated cases |
| Teratoma | Contain multiple immature elements including epithelium, neuroglial tissue, thyroid, pancreas, smooth and skeletal muscle, cartilage and bone. | Not usually needed | Complete surgical excision, because |
| Rhabdomyoma | Spider cell (vacuolated enlarged cardiac myocyte with clear cytoplasm due to abundant glycogen | Not usually needed | Usually not needed due to regression course but could be in complicated cases |
| Papillary Fibroelastoma | Endocardium-coated fronds with an avascular collagenous core containing mucopolysaccharide and elastin | Not usually needed | Recommended for left side lesion due to risk of embolic complications |
| Angio-Sarcoma | Highly vascularized, myocardial infiltration, pleomorphism, necrosis, and mitosis | Usually required if possible | Complete surgical resection or debulking |
| Leio-Myo-Sarcoma | Compact bundles of spindled cells with blunt nuclei, regions of necrosis, and mitotic figures with epithelioid regions are often present | Usually required if possible | Complete surgical resection or debulking |
| Rhabdo-Myo-Sarcoma | Embryonal type with rhabdom oblasts containing abundant glycogen and expressing desmin, myoglobin, and myogen | Usually required if possible | Complete surgical resection or debulking |
| Osteo-Sarcoma | Histologically heterogeneous, most composed of spindle cell lesions or malignant fibrous histiocytoma, with microscopic foci of osteosarcoma and chondrosarcoma in the spindle regions | Usually required if possible | Complete surgical resection or debulking |
| Undifferentiated Sarcoma | Consist of undifferentiated plump spindle cells with frequent mitotic activity and (often) nuclear pleomorphism | Usually required if possible | No role of surgery |
| Primary Cardiac Lymphoma | Diffuse large B-cell lymphoma is the most common subtype, although Burkitt lymphoma, low-grade B-cell lymphoma, and T-cell lymphoma have also been described | required | Complete surgical resection or debulking |
| Mesothelioma | Epithelioid (plump, rounded), sarcomatoid (spindled), or a combination of either | Pericardial biopsy or pericardial fluid analysis | Complete surgical resection or debulking |
| Metastasis | Largely dependent on primary tumor | Typically required at site of 1ry tumor | Surgical debulking in complicated cases |

**Table:** Histopathology, role of biopsy, and role of surgery in the management of benign and malignant cardiac tumors.

Illustrated diagram 1 shows cardiac masses in pediatrics and advanced diagnostic tools adapted from Tyebally., *et al*. [3].

## Rhabdomyoma

The most common primary cardiac tumor in infants and children. It represents 60% off 1ry cardiac tumors. It usually presents in the ventricles but rarely present in the atriums. If present within the atrioventricular junction, it may act like an accessory pathway with its resultant pre-excitation effect on cardiac electrophysiology. Fetal diagnosis occurs usually during routine neonatal screening at 20-week gestation as multiple or solitary intracardiac masses or accidentally during fetal arrythmia [6].

Symptoms after birth usually related to obstruction of inflow or outflow and manifest clinically as murmur abnormal pulse, cyanosis or rhythm disturbances, which is rare symptoms occurs only in 16 to 47% of cases with cardiac rhabdomyoma. Atrial and ventricular arrythmia my occur although wolf parkinsonian white is common in patient with associated tuberous sclerosis (1.5%) compared to the general population (0.15%). The tumor could act as accessory fiber. As the tumor regress these abnormal rhythms disturbance will disappear spontaneously [7].

In macroscopic examination it appears solid rounded mass brighter than surrounding myocardial structures predominantly located in the ventricular wall with less presence in atrial wall, usually multiple with around 50% intracavitary extension, echocardiography study is usually diagnostic and appear as an intramural cardiac mass with cavitary extension. Microscopically each tumor shows pathognomonic spider cells with centrally placed cytoplasm containing the nucleus and myofibrils radiating to the cell wall. Rhabdomyomas not considered as a true tumor rather than hamartomas occurring solely in straited muscle fiber of the heart. Rhabdomyomas exhibit immunoreactivity with the muscle markers desman, actin, myoglobin, vimentin, and also with hamartin and tuberin. Immunohistochemical studies showed that the spider cells exhibit immunoreactivity with ubiquitin. The ubiquitin pathway is associated with the degradation of myofilaments, progression of cytoplasmic vacuolization with the formation of spider cells, enlargement of glycogen vacuoles, apoptosis, myxoid degeneration and regression of the rhabdomyomas. The above cascade explains the process of its degeneration [8].

Outcome antenatally usually favorable, once fetus complete his somatic growth the hamartomas lose their mitotic growth and start apoptosis. Most of tumors stop growth although rally growth continues till 3trd trimester which complicated rarely with stillbirth as a consequence of intrauterine arrythmia or blood flow obstruction [9].

Following birth regression of the tumor is the role rather than exception as the rhabdomyoma cells loss their ability to divide this regression usually reach 80% by the end of childhood and for that treatment is usually conservative with close observation with echocardiography and ECG monitoring [7].

There are reports describe the successful treatment of rhabdomyomas with everolimus which associated with rapid tumor regression which observed during follow up by echocardiography. Surgical intervention should be rendered to complicated cases with sever inflow, outflow obstruction or malignant arrythmia not responding to medical management [7,11].

There is usual association between multiple rhabdomyomas and tuberous sclerosis incidence of association from 60 to 80% although association between solitary one is not clear.

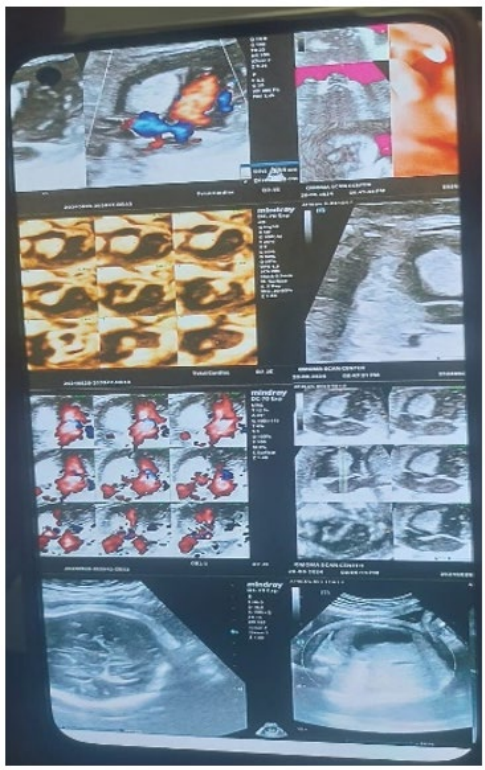
Solitary form of rhabdomyoma may associated with smaller missed ones so examination must be done carefully to avoid missing smaller ones. Multiple cardiac rhabdomyomas in fetal life may herald the diagnosis of tuberous sclerosis before the other features of the disease, such as character tic skin signs and or seizures which appears during infancy. While in patient with tuberous sclerosis the incidence from 43 - 72% of cases. The presence of rhabdomyoma in these cases confirm the diagnosis. Although the diagnosis must not consider tuberous sclerosis without its strict criteria and presence of rhabdomyoma raise only the suspicion of its presence not confirm the diagnosis in such group of patients genetic counseling coupled with proper imaging study in diagnosis.

Fetal and neonatal cardiac rhabdomyomas are frequently diagnosed by echocardiography. Echocardiography appears as multiple or solitary brighter than surrounding structures intramural mass which may extend in the ventricular cavity. Computed tomography and cardiac magnetic resonance can be used in the diagnosis. On contrast-enhanced cardiac CT, these lesions appear as hypodense myocardial areas. But rarely used to limit exposure to radiation. On cardiac MRI appear isointense to normal on T1-weighted images, but hyperintense on T2-weighted images. These lesions typically demonstrate no or minimal post gadolinium contrast-delayed enhancement family pedigree must be taken [6].

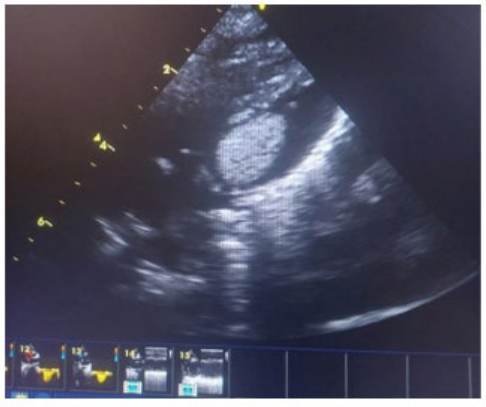
## Case Study

### Case 1

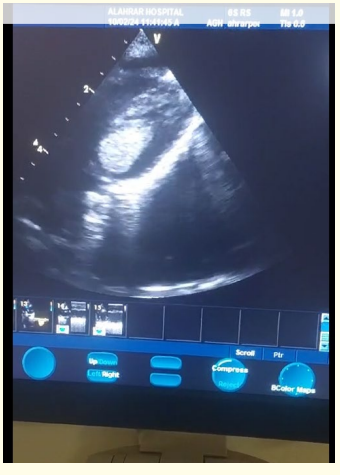
Neonate male patient 7 days old diagnosed as intrauterine cardiac mass during routine follow up of the mother during pregnancy Fetal echo requested, shows mass in the left ventricle suspected as a case of rhabdomyoma. There is smooth intrauterine course, baby delivered by CS with smooth post neonate course, on breast milk feeding, there is positive consanguinity, baby has one older sister delivered by *in vitro* fertilization, sister is healthy, in examination stable vitally, non-syndromic no abnormal features, normal anthropometric measurement systemic examination show no abnormal finding. ECG done regular sinus rhythm 120-min, Blood pressure 70-45 mmhg, Echo examination show structurally normal heart, Smal PFO and well-defined large mass, solid attached to interventricular septum with no inflow or outflow obstruction, cardiac MRI support the diagnosis, brain MRI is normal, patient diagnosed as solitary large rhabdomyoma not associated with manifestations or investigation suggesting tuberous sclerosis for conservative management.



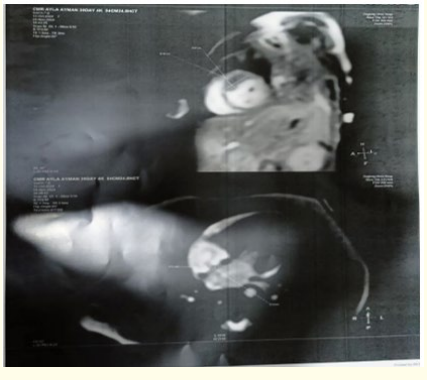
***Picture 1:*** *Fetal echo done at 35 week of gestation shows single left ventricular mass measuring 16 x 12 mm with partial obstruction of left ventricular out flow.*



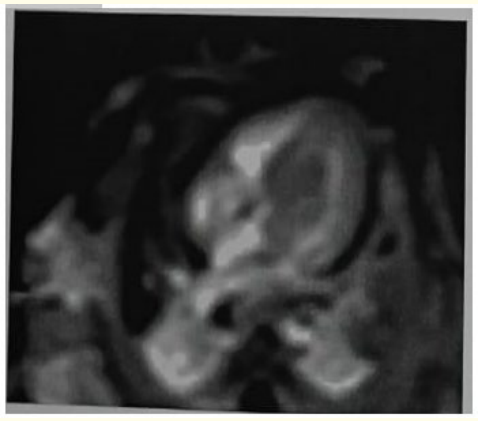
***Picture 2:*** *Post natal echo baby at 7 days old show large solitary mass attached to interventricular septum with no left ventricle obstruction.*



***Video 1:*** *Echo study of apical 4 chamber view at day 7 of birth shows large solitary mass attached to interventricular septum with no left ventricle obstruction.*

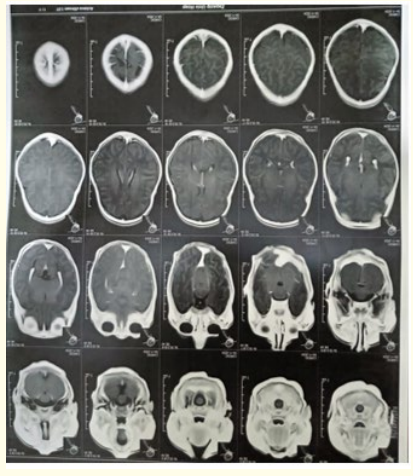


***Picture 3***



***Picture 3***

***Picture 3 and 4:*** *Cardiac MRI fairly defined left ventricular cardiac mass seen intra myocardial involving anteroseptal wall of basal ventricular, exhibit iso intense signal on T1 and T2, no signal loss SPIR, minimal post GD enhancement measuring 15 x10 mm, small PFO.*



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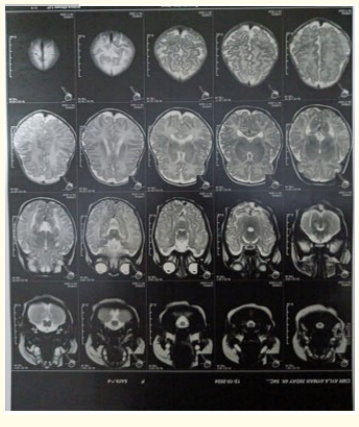

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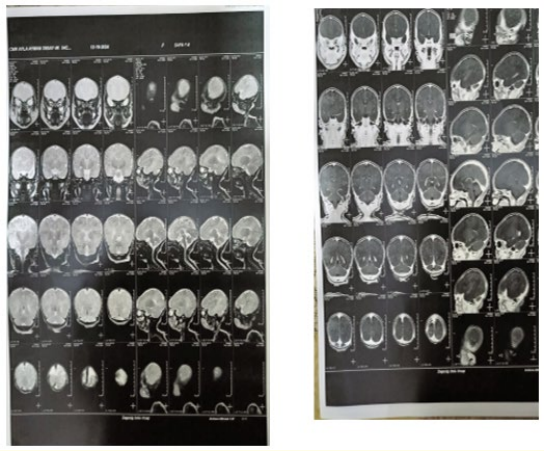


***Picture 6***

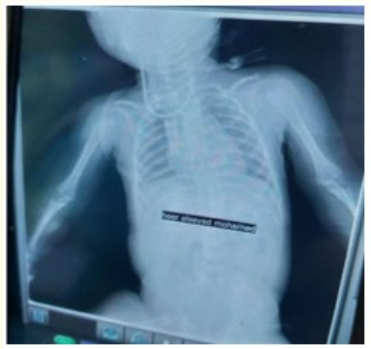
***Picture 5-8:*** *Brain MRI shows normal brain structure.*

## Case 2

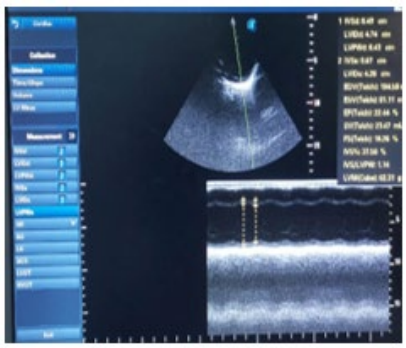
9-month-old female baby, known case of tuberous sclerosis brought to our ER with intractable convulsions, baby resuscitated and anticonvulsant given, electrolytes and basic investigations. Withdrawn, chest x-ray requested. Initial evaluation shows high grade fever, tachypnea, tachycardia, bilateral course crepitations, initially the case diagnosed as a case of tuberous sclerosis complicated with respiratory tract infection. Patient transferred to ICU. In ICU meticulous examination of the case show that the baby shows high grade fever 39c, HR 90/ min, RR 40, subcostal and intercoastal retraction and decrease air entry in Rt side with bilateral coarse crepitation, delayed milestones only head support, hypopigmented macular spots in his back and on the back of her RT leg. The baby after stabilization frequently convulsing. So the baby ventilated and heavily sedated in addition to double anti-convulsant medications, initial investigation shows microcytic hypochromic anemia and with leukocytosis and neutrophilia, chest x-ray gives picture of peri-bronchial infiltration and Rt lung aspiration. History revise with the mother she said baby diagnosed in the fifth month after intractable convulsions admitted in hospital, CT requested which confirm the diagnosis in addition to appearance of hypopigmented white macular spot and delayed milestones, which attract the attention to the diagnosis. The physician prescribes vigabatrin to control fits. The family history revised with the mother. The mother is gravida 3 para 2 her first baby died at $7^{th}$ month of gestation. Heart screening not done. In subsequent days baby shows sinus bradycardia, which explained initially due to aggressive anti convulsion therapy and deep sedation, as the saturation was 100% on 30% $O_2$ support, on assisted pressure support ventilation, normal capillary refill time, and within average blood pressure for age. Cardiac consultation requested.

ECG shows sinus bradycardia HR is 90-70/minutes decrease to 60/m sometimes during sleep. Normal electrolytes and acid base status. Bed side echocardiography shows multiple hyper illuminated echogenic masses related to septum, papillary muscle, and free left ventricular wall with no outflow or inflow obstruction. For which rhabdomyomas highly suspected. cardiac MRI and Holter study requested following stabilization of the case.

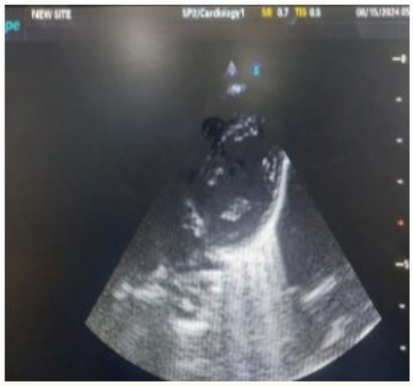
The patient died in the next day as there is sever intractable convulsions, complicated with pneumothorax bilaterally for which bilateral chest tube inserted unfortunately the baby died from cardiopulmonary arrest.



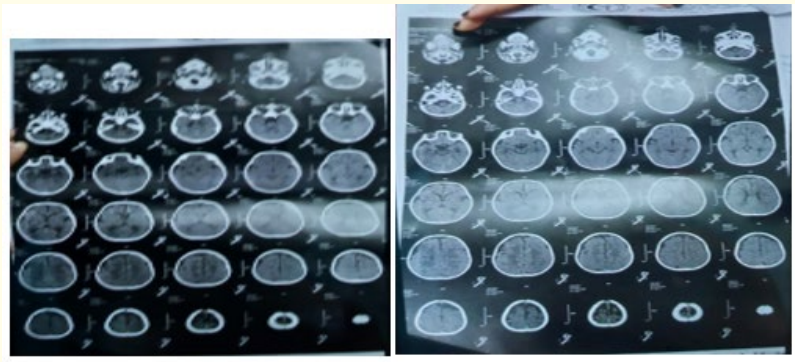
***Picture 9:*** *Chest x-ray done during ventilation of the baby shows aspiration pneumonia.*



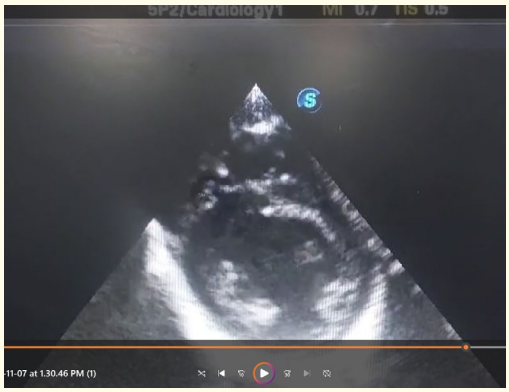
***Picture 10:*** *Echo study shows normal cardiac function.*



***Picture 11:*** *Echo study apical 4 chamber view shows multiple bright echogenic masses related to the interventricular septum, apex, free left ventricular wall and papillary muscle.*



***Picture 12 and 13:*** *Shows (CT brain shows multiple bilateral hypodense subendymal nodules along both lateral ventricles as well as bilateral frontal subcortical hypodense lesions picture suggestive tuberous sclerosis).*



***Video 2:*** *Echo study short axis parasternal view shows multiple bright masses related to papillary muscle.*

## Discussion

Cardiac neoplasms are referred to primarily by their biological classification, as defined by the WHO. Hamartomata's lesions, although not technically neoplastic, will be considered under the benign neoplasms category. As reported by Joseph., *et al*. [11] there is no family history in both conditions although there is previous still birth in case 2 at 7 months of intrauterine life and 1ry and 2ry infertility in case one and both have history of consigns marriage. Discovered prenatally, as in 1st case during routine neonatal screening, or accidentally discovered during routine screening of tuberous sclerosis patient presented with intractable convulsions as reported by Potarch., *et al.* [2].

In both cases tumor arise only from ventricle whether from the septum, free wall or papillary muscles. May present as solitary lesion like case one or multiple lesions like 2nd case, and multiple lesions usually associated with tuberous sclerosis like case 2 while single solitary mass usually not associated with tuberous sclerosis like 1st case as mentioned by Ren., *et al*. [4].

Echo cardiography considered the golden role in diagnosis confirmed by cardiac MRI in 1st case and by the presence of tuberous sclerosis in 2nd case.

The fate of the case accidentally discovered worse than the case discovered during fetal life as precautions and management can done wisely in the case discovered in the fetal period. The 1st case diagnosed with fetal echo has large solitary mass partially obstructing the left ventricular outflow although in post neonatal echo this obstruction not detected so it may signify reduction in size postnatally of the more accurate postnatal study than that intrauterine one [3].

Diagnostic triad of seizures, mental retardation, and cutaneous change must be taken in consideration to screen cases for cardiac rhabdomyoma not to be missed like our 2nd case. There is heart rhythm disturbances reported in 2nd case but unfortunately patient die before completion of investigation to detect the etiology of rhythm disturbance. The same like Lee., *et al*. [12].

In our case echocardiography is the gold stander in diagnosis although MRI was only confirmatory. Decision taken in the surviving case is carful follow up observationally as there is no rhythm disturbance or outflow obstruction of blood stream, although the case has solitary mass and tuberous sclerosis less likely but MRI confirming the diagnosis and case clinically observed no to miss tuberous sclerosis detection. This the role by many authors as Tzani., *et al*. [6].

Therefore, the clinical presentation of affected patients is highly variable, ranging from asymptomatic to heart failure owing to obstruction and/or arrhythmia or intractable convulsion if associated with tuberous sclerosis the same as reported by Krieken., *et al*. [7].

## Conclusion

The clinical presentation of children with cardiac tumors varies due to tumor location, size, number, and the nature of the tumor. Its nonspecific manifestations often result in an incorrect or missed diagnosis and delayed time to optimal treatment, causing major complications or death. Therefore, prenatal testing is extremely important for timely diagnosis and treatment of primary cardiac tumors in children [13].

## Conflict of Interest

Declare if any financial interest or any conflict of interest exists.

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