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Review article

Cardiac tumours in infancy

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ABSTRACT

Cardiac tumours in infancy are rare and are mostly benign with rhabdomyomas, fibromas and teratomas accounting for the majority. The presentation depends on size and location of the mass as they tend to cause cavity obstruction or arrhythmias. Most rhabdomyomas tend to regress spontaneously but fibromas and teratomas generally require surgical intervention for severe haemodynamic or arrhythmic complications. Other relatively rare cardiac tumours too are discussed along with an Indian perspective.

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Cardiac tumours, rare as they are in the paediatric age group, with a prevalence of 0.0017–0.28%,¹ rarer still are they in infancy, with only anecdotal case reports. Infact the incidence in foetal life is higher at around 0.14%.² An increase in the incidence of primary cardiac tumours – 0.06% (1980–84); 0.22% (1985–89) and 0.32% (1990–95)³ is probably surrogate to increased diagnostic and imaging capabilities. Mostly benign, rhabdomyomas, fibromas and teratomas, account for majority of the primary tumours of the heart in infancy.¹

Presentation depends on the size and location of the mass,⁴ rather than their histologic type, as they have proclivity to produce inflow or outflow tract obstruction and arrhythmias. They may cause infant respiratory distress, congestive heart failure, low cardiac output and sudden death.⁵ Besides the constitutional signs and symptoms, right sided tumours may additionally present with syncope, pericardial effusion, vena cava syndrome, pulmonary embolism and cyanosis,⁶ and left sided tumours may embolize leading to seizures, transient

ischaemic attacks and cerebro-vascular and peripheral vascular accidents.⁴ Not infrequently an asymptomatic cardiac murmur may be the presentation.⁷

Cardiac tumours may be associated with sporadic ailments like hypoplastic left heart^{2,8} Tetralogy of Fallot² and endocardial fibroelastosis.² Whether they are cause, effect or an association is difficult to speculate.⁹ Even extra cardiac anomalies such as cleft palate,¹⁰ polycystic kidney and club foot¹¹ have also been reported. An as yet unreported association of imperforate anus with a cardiac rhabdomyoma has been made by S. K. Kaushik et al. later in this issue.¹² Echocardiography,¹³ either transthoracic or transoesophageal, CT and MRI Scans¹⁴ are the gold standard diagnostic modalities and cardiac catheterization is rarely, if ever, required.¹ Infact MR first pass perfusion may identify malignant masses from benign ones.¹⁵ Intra operative, or sometimes pre operative, biopsy may be required for histological assessment.¹³ Holter monitoring is recommended to identify arrhythmias.⁵

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Though waitful watching is the norm for majority of tumours, especially rhabdomyomas, surgical resection, if indicated for refractory arrhythmias or 'malignant' haemodynamic behaviour, is safe and usually definitive.^{13,16} Operative mortality of 5%¹⁶–17.5%¹⁷ with freedom from tumour related reoperation after 10 years of $91 \pm 8.7\%$, NYHA class I status in 85% and sinus rhythm in 100%¹⁸ have been reported. However, follow up serial echocardiography is recommended to look for post operative LV aneurysm or LV dysfunction.¹⁶

Rhabdomyomas are the commonest primary cardiac tumour accounting for more than 60% of cases in infancy and childhood³ and are infant hamartomas.⁶ Multiple tumours are highly associated (60–80%) with tuberous sclerosis (TS)^{19,20} and vice versa, 47% of TS patients have cardiac tumours.²¹ The genetic basis of TS is heterogenous. Two disease genes: TSC-1,^{6,22} at Chromosome 9q34 and TSC-2²³ at Chromosome 16p13 have been implicated. The TSC-1 gene encodes hamartin and TSC-2 Tuberin - proteins involved in tumour suppression.⁶ Rarely Trisomy 21,²⁴ 13 & 18 have been documented with a single ventricular rhabdomyoma.²⁵ In these cases detailed family history profiling and genetic counselling should be offered.²⁶

Arrhythmias may occur in 16–47%¹ and rarely rhabdomyomas, if located in the atrio-ventricular junction, may act like accessory pathways, as the tumour cells are structurally similar to the Purkinje cells, and may lead to pre excitation syndromes²⁷ and as the tumour regresses, so do the delta waves.²⁸

On echocardiography, they appear as homogenous, well circumscribed, echo bright masses. MRI is often used in rhabdomyomas to evaluate the brain, liver and kidneys for evidence of tuberous sclerosis. On histopathology, they appear as nodules of enlarged, glycogen rich cardiomyocytes with clear cytoplasm, interspersed with 'Spider Cells'.

Acting through Ubiquitin pathway,²⁹ Rhabdomyoma cells lose their mitotic potential after birth with more than 80% of these disappearing during early childhood.³⁰ Surgery is employed only for serious, life threatening symptoms mainly due to obstruction of the cavity outflow/inflow or intractable arrhythmias.³¹ A chance finding of regression of a cardiac rhabdomyoma after receiving everolimus opens new avenue for mTOR (mammalian target of rapamycin) inhibition as a possible novel therapy.³²

Fibromas are second most common cardiac tumours in infancy but rank first in surgical series.³³ Around 3% of patients with Gorlin syndrome have cardiac fibromas and possibly result from germ line mutations in the PTCHI gene, which maps for Chromosome 9q 22.3.^{6,34} Most commonly located in the ventricular septum, they may occasionally be found in the free walls of the ventricle.⁶ They may cause obstruction to blood flow, valvular dysfunction, arrhythmias (VT in >50%),¹⁶ syncope or sudden death in upto 10–30% cases.^{35,36} Mechanisms of arrhythmia include compression of the His Bundle resulting in conduction block, possible creation of re-entry pathways producing VT and regions of asynchronous refractoriness within the tumour mass producing electrical instability, bradyarrhythmias and ventricular fibrillation.^{5,16,35,36} Gadolinium enhanced MRA and first pass perfusion imaging demonstrate a hypoperfused tumour core that is readily distinguishable from the surrounding perfused myocardium.⁶

Cardiac fibroma regression is unreported⁷ and surgery should be offered early because of its tendency to grow fast and cause severe haemodynamic complications.³⁷ Though complete surgical resection with chamber reconstruction using pericardium or eptfe patch for atrium and dynamic cardiomyoplasty, using electrically stimulated Latissimus Dorsi muscle, for ventricular reconstruction, have been reported for adult population,³⁸ these techniques have not yet found much application in infant population. However, excellent mid term results have been reported even with partial resection¹⁶ and Beghetti et al³⁹ have employed bidirectional cavo-pulmonary connection to off load the RV in a setting of subtotal resection of RV fibroma. Lee et al⁴⁰ have used palliative BT shunt to relieve cyanosis as a bridge to surgical resection with good results. Other innovative hybrid procedures for obstructive neonatal left ventricular tumours too have been reported.⁴¹ ICD implantation may be mandated for persistent arrhythmias due to non-resectable tumours.⁴² Failing all, cardiac transplantation may be a final option.

Teratomas are usually located in the pericardial cavity.⁴³ The main clinical findings relate to either pericardial effusion or to the mass effect of the tumour, if intra cardiac.⁴⁴ Macroscopically they have a typical cystic and multi-lobulated appearance and histologically they contain multiple immature elements including epithelium, neurological tissue, thyroid, pancreas, smooth and skeletal muscle, cartilage and bone. Although generally considered benign, tumour recurrence and malignant differentiation have been reported and hence surgical resection is recommended.

Haemangiomas may rarely present in neonates,⁴⁵ especially in association with multiple haemangiomas in the skin⁴⁶ and may have an association with erythropoietin treatment.⁴⁷ They are benign and undergo spontaneous regression, but may rarely have an unfavourable prognosis due to high output cardiac failure, haemorrhage from ruptured vessels, thrombocytopenia, ventricular tachycardia and cardiac tamponade.⁴⁶ Complete surgical excision has excellent prognosis but when not feasible, alternative modalities like radiotherapy⁴⁸ and steroids⁴⁹ may be tried.

Myxomas are exceedingly rare in infancy³³ but familial ones may be reported in younger patients⁵⁰ and are best treated surgically with complete excision and have a good prognosis.

Histiocytoid cardiomyopathy also known as oncocytic cardiomyopathy, Purkinje cell tumour, focal lipid cardiomyopathy and idiopathic infantile cardiomyopathy⁵¹ are rare arrhythmogenic disorders and are essentially hamartomatous proliferation of cardiac cells with oncocytic features.⁶ The most common clinical presentation is with arrhythmias such as paroxysmal atrial tachycardia, atrial fibrillation, ventricular fibrillation, ventricular tachycardia and junctional tachycardia⁵² and may even lead to sudden unexpected death in infancy.⁵³ Five percent cases may be familial.⁶ Similar oncocytic cells may be found in trachea, adrenal, thyroid, anterior pituitary and salivary glands.^{54,55} Associated cardiac ailments like ASD, VSD, hypoplastic left heart syndrome and extra cardiac anomalies of eye, skin and CNS may be found in 30% cases.^{53,54} Typically they are subendocardially located, yellow-tan nodules or plaques and have pathognomonic nests of foamy appearing myocytes resembling macrophages on

Table 1 – Cardiac tumours in infancy (< 1 Year) – Indian perspective.

Author (personal communication)	Period	Pathology (n)	Comments
Surgical series			
• Dr. Balram Airan (AIIMS, Delhi)	10 years	2 Rhabdomyomas 2 Fibromas	All were operated for obstructive symptoms
• Dr. Krishna Iyer (EHIRC, Delhi)	20 years	3 Rhabdomyomas 1 Bronchogenic Cyst in Septum	Operated for obstructive symptoms
• Dr. Devi Shetty (Narayan Hrudayalaya, Bangalore)	5 years	Nil	Youngest child operated was 4 years old
• Dr. Rajesh Sharma (EHIRC, Delhi)	10 years	Nil	—
• Dr. Suresh Rao (AIMS, Kochi & KD Ambani Hospital, Mumbai)	15 years	3 Rhabdomyomas Operated – Nil	- Multiple in septum & LV free wall - LV outflow/inflow obstruction - Medical follow up
Medical series			
• Dr. Bharat Dalvi (Glenmark Cardiac Centre, Mumbai)	5 years	12 Rhabdomyomas	- All had tuberous sclerosis - LV > RV > atrium - 50% multiple - 7 Showed regression - 3 Prenatal diagnosis
• Dr. Krishna Kumar (AIMS, Kochi)	1 year	3 Rhabdomyomas 1 LV Myxoma	- All rhabdomyomas regressed - LV myxoma operated for obstruction
• Dr. Snehal Kulkarni (KD Ambani Hospital, Mumbai)	3 years	1 Rhabdomyoma	- LV & RV (multiple) - Presented with ventricular ectopics - Spontaneous regression
AIIMS – All India Institute of Medical Sciences, EHIRC–Escorts Heart Institute and Research Centre, AIMS–Amrita Institute of Medical Sciences, KD–Kokilaben Dhirubhai Ambani Hospital, LV–Left ventricle, RV–Right ventricle.			

histopathological examination. Electrophysiological mapping and surgical excision, direct vision cryo-ablation or catheter ablation may be indicated in patients with refractory arrhythmias.^{6,52,56}

Inflammatory myofibroblastic tumours: Recently Burke et al⁵⁷ have reported 10 cases of these tumours, which appear as inflammatory, reactive-appearing proliferations to low grade sarcomas originating from the endocardium. They are most likely non-neoplastic, however, have embolic potential and may lead to sudden death from coronary occlusion.

Rarely papillary fibroelastoma,⁵⁸ hamartoma,⁵⁹ lymphoma⁶⁰ and intrapericardial pheochromocytoma⁶¹ too have been reported, with surgical resection and radiotherapy offering limited success. Synchronous histologically distinct cardiac tumours too are known to occur.⁶²

Malignant cardiac tumours in childhood are extremely rare and may take form of angiosarcoma, rhabdomyosarcoma or fibrosarcoma and have consistently poor prognosis due to extensive local infiltration, intracavitary obstruction and death.^{63,64}

Indian perspective

On exhaustive search of literature with due diligence, not a single published series from any Indian centre could be found. Professional Associations too do not have any Registry or database to fall back upon. However, an effort was made to get an Indian perspective by direct contact and some informal information could be obtained (Ref Table 1). Most leading luminaries have only anecdotal encounters and the profile and presentation of cardiac tumours conform to published data, with multiple rhabdomyomas being most frequent and obstruction of cavity the prime indication for surgery.

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