Fetal Education Series

March 8th,

Children's Mercy Hospital, Kansas City MO

Fetal Myocardial Tumors

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BEST CHILDREN'S HOSPITALS U.S.News RANKED IN 10 SPECIALTIES

MAGNET RECOGNIZED AMERICAN NURSES CREDENTIALING CENTER

UMKC School of Medicine

Objectives

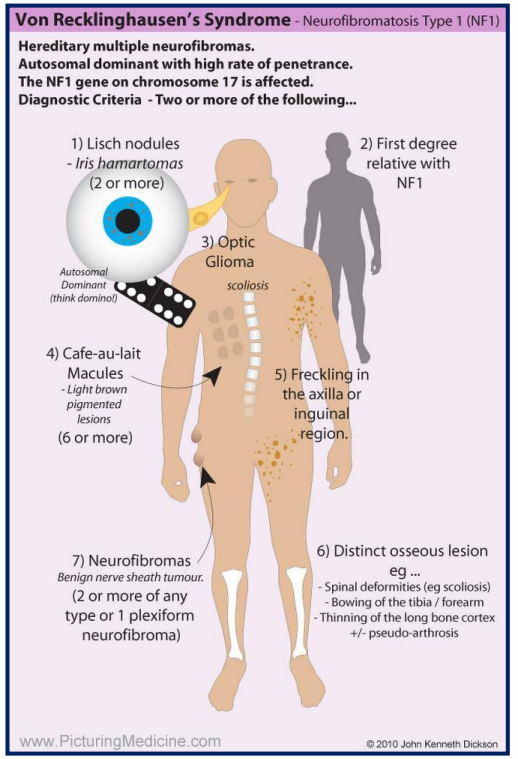
- Review types, frequency, genetics and outcomes of fetal cardiac tumors
- Review imaging characteristic of fetal cardiac tumors
- Review their prenatal physiology and management
- Review their postnatal physiology, clinical presentation and management

Fetal Cardiac Tumors: History

- 1862 **Dr Friedriech Daniel von Recklinghausen**

German Pathologist (1833-1910)

Describes cardiac rhabdomyomas in children



Fetal Cardiac Tumors: History

- 1982 **De Vore et al**
  First in utero diagnosis of a cardiac tumor

Incidence of Fetal Cardiac Tumors

Fetal cardiac tumors are relatively rare, represent 0.02% to 0.13% in fetal series

1995, Holley D et al JACC

1996, Allan L et al JACC

2002, Bader R et al JPeds → ~2%

Presentation

- Detection of a mass in screening US
- Pericardial effusion
- Arrhythmias
- Family history of TS

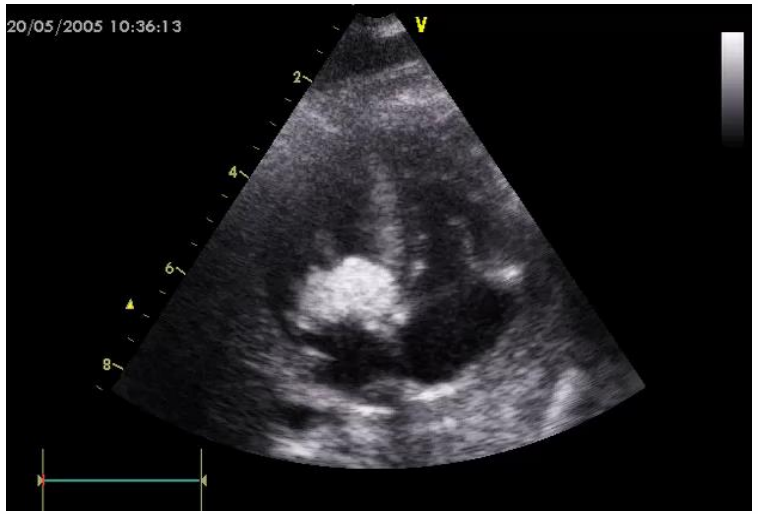
Incidence and Types of Fetal Cardiac Tumors

• Rhabdomyoma	70-80%
• Pericardial Teratoma	10-15%
• Fibroma	10-15%
• Hemangioma	<5%
• Myxomas	<1%
• Lipomas	<1%
• Malignancies	<1%

Presentation

- Detection of a mass in screening US
- Pericardial effusion
- Arrhythmias
- Family history of TS

- *Gestational age at diagnosis ranges from 21 to 38 weeks*
- *Usually they become apparent at the third trimester*
- *Commonly they are benign but have a malignant behavior*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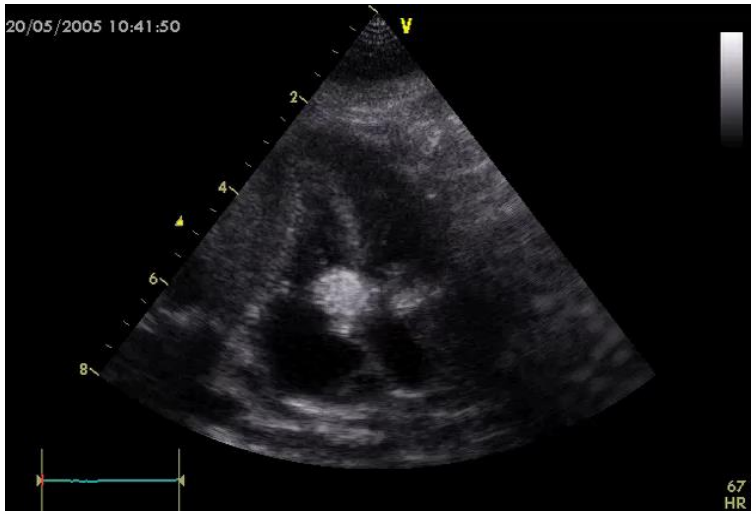
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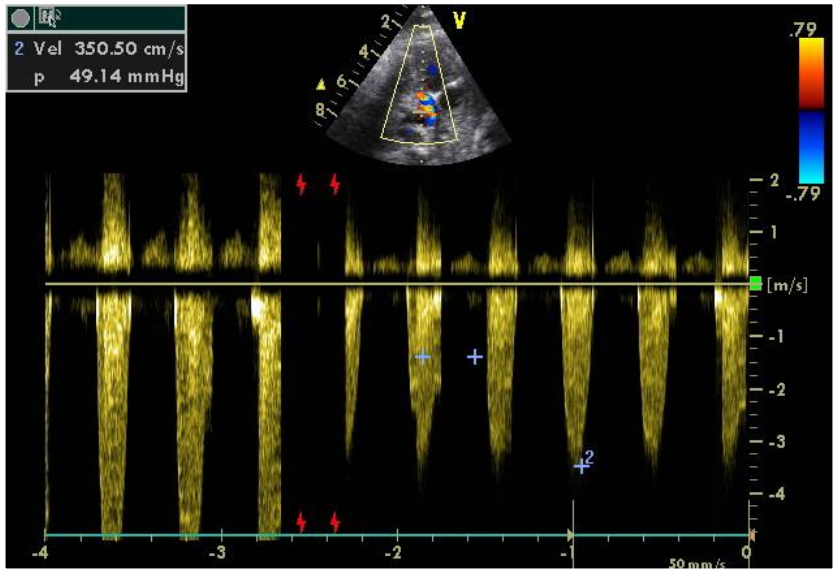
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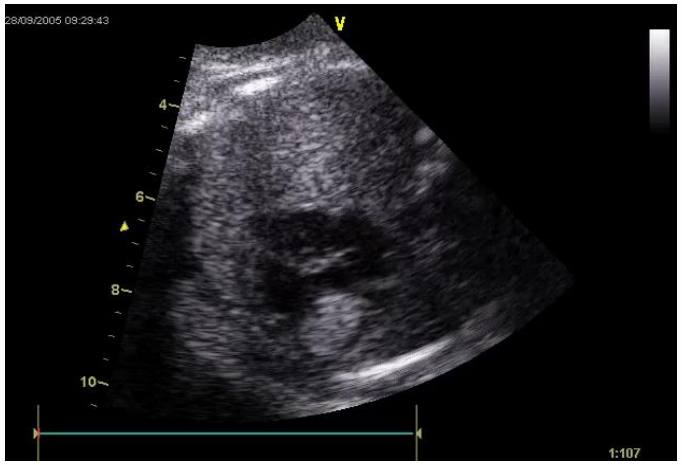
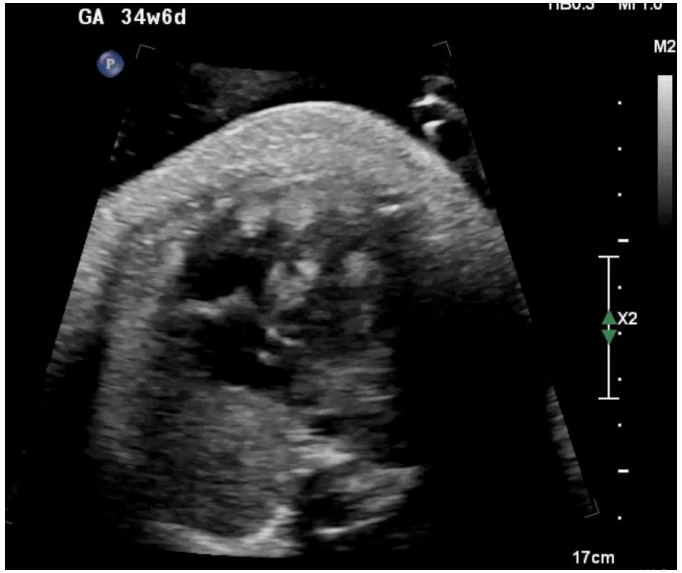
Rhabdomyoma

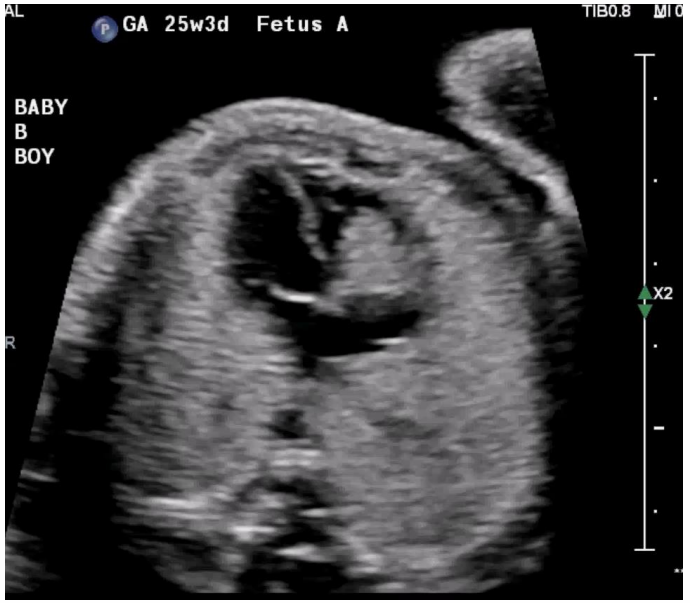
- By far the most common fetal cardiac tumor accounting for 70-80% in fetal cases
- It is a hamartoma (noncancerous tumor made of an abnormal mixture of normal tissues and cells from the area in which it grow) – nonmalignant tumor of striated muscle
- Echocardiographic features
  - May be single or usually there are multiple
  - Intracavitary of intramural (within the free wall, the IVS, papillary muscles, less common within the atria)
  - Homogeneous and echogenic
  - Well circumscribed
  - Usually sessile but can be pedunculated/ mobile

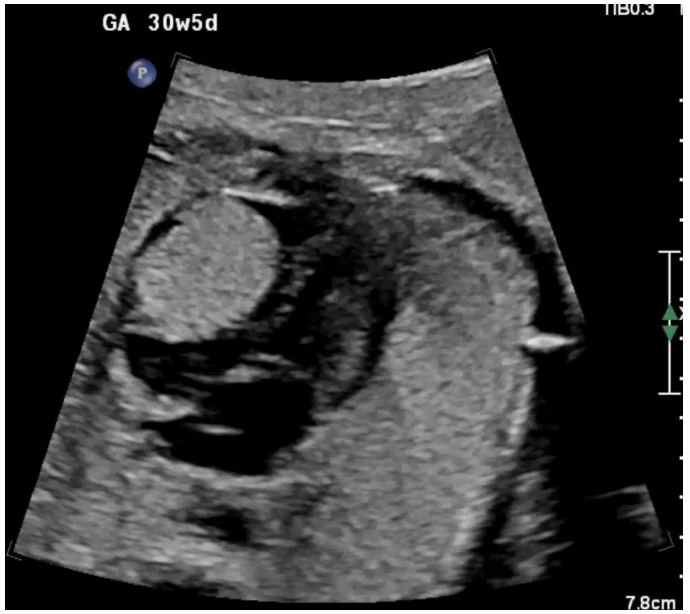




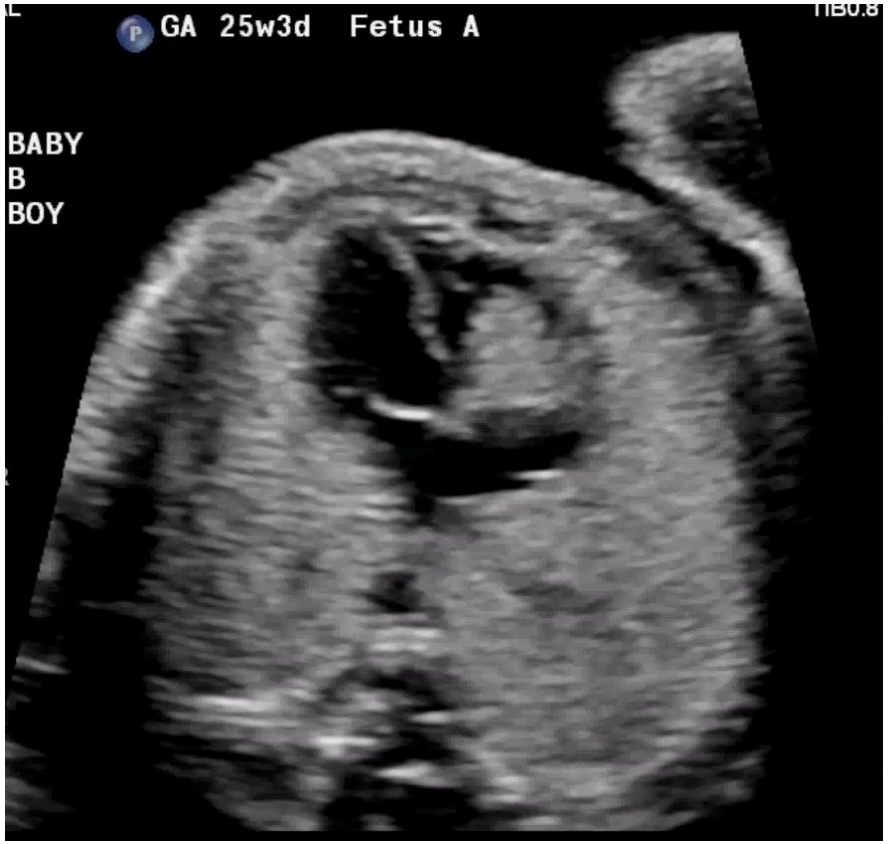
Rhabdomyoma

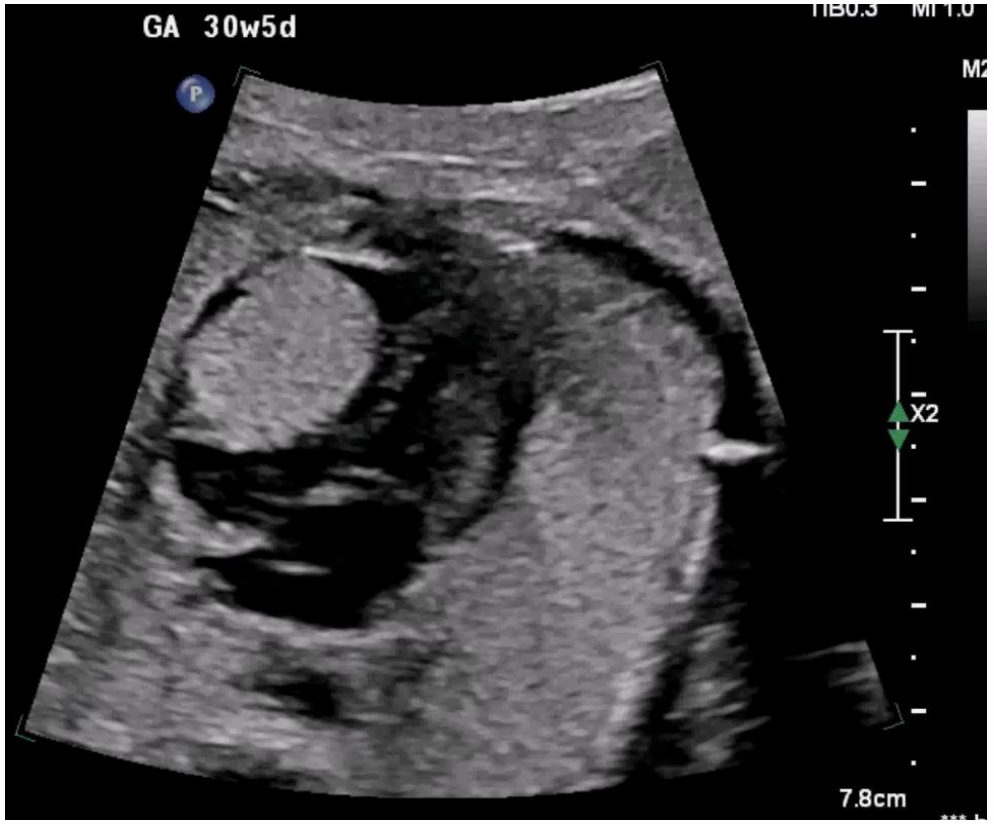
- May grow in size prior to 32 weeks and regress thereafter
- May cause outflow obstruction, although only ~6% of fetal diagnoses reported to have needed surgical intervention
- Up to 5% can be very large, leading to hydrops or fetal demise.
- In 10-20 % of cases they are associated with:
  - Atrioventricular valve regurgitation
  - Arrhythmias and conduction abnormalities
    - Atrial or ventricular ectopy
    - SVT
    - Ventricular tachycardias
    - Repolarization abnormalities
    - Rarely AV block.



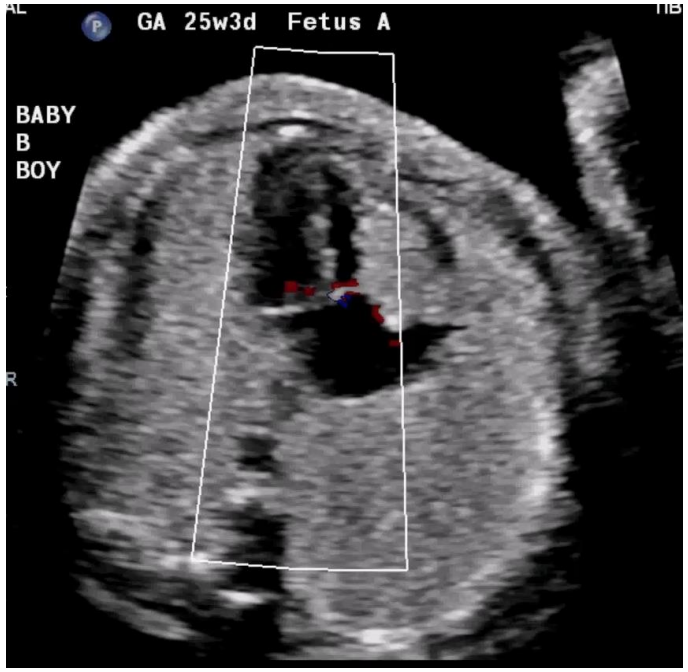


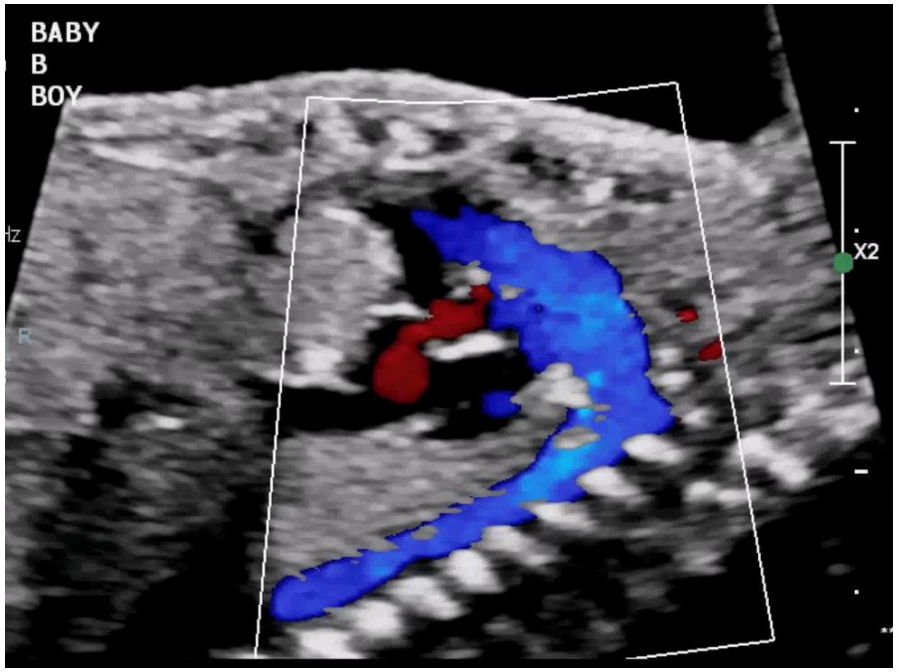
Rhabdomyoma

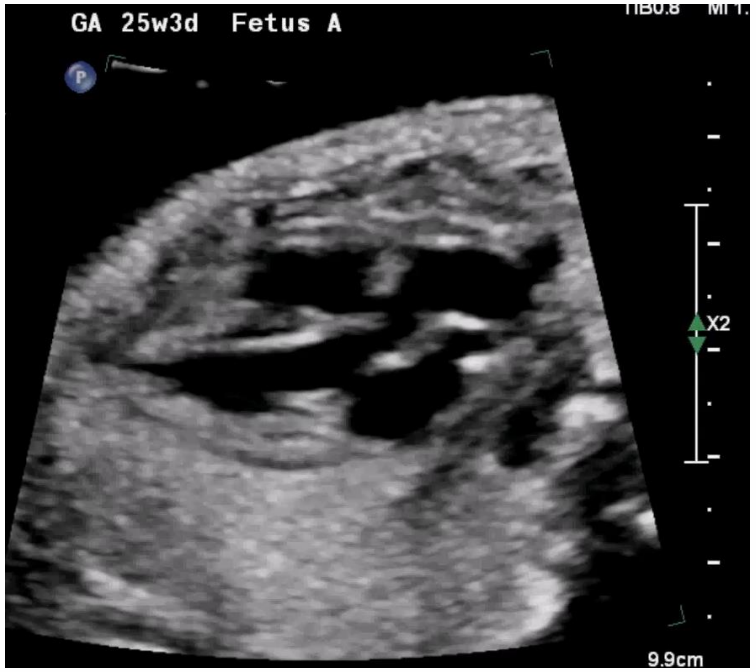




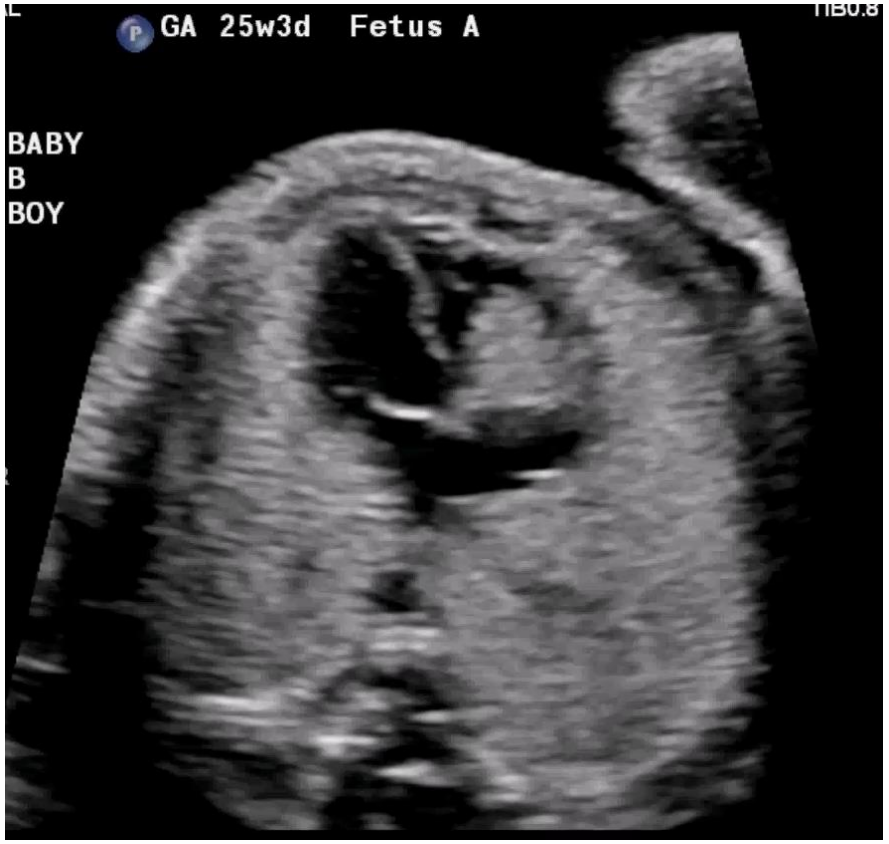
Rhabdomyoma

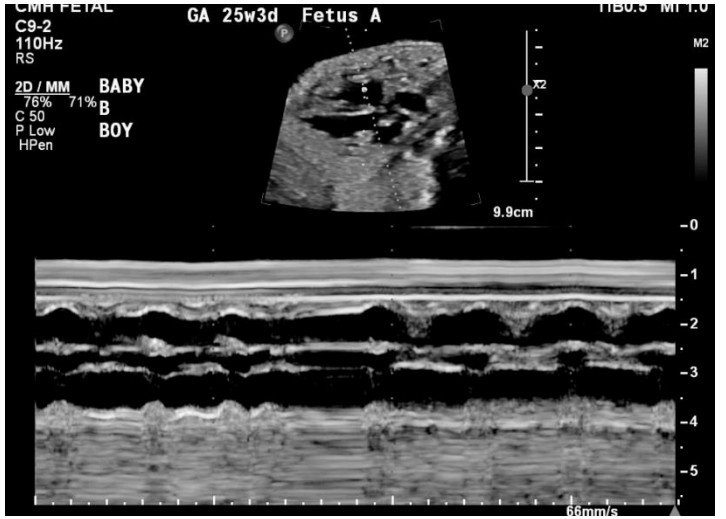


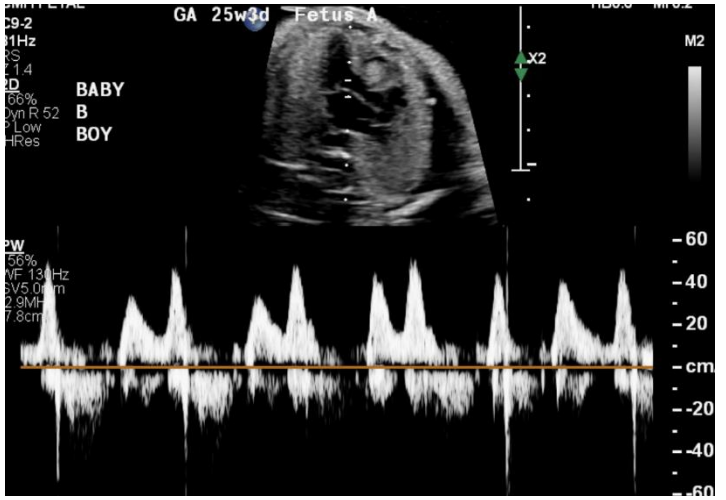




Rhabdomyoma – Twin SVT







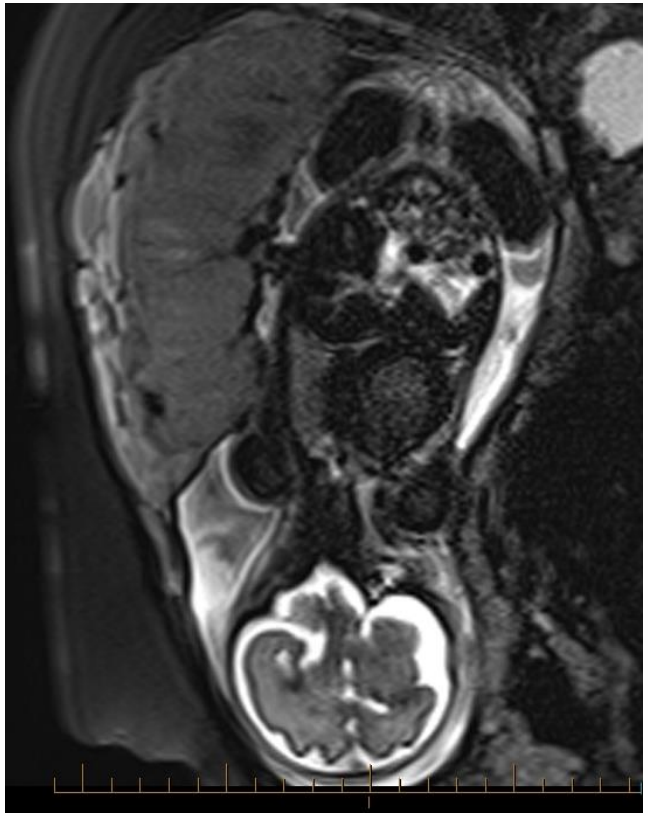
Rhabdomyoma – Anatomical Associations and Genetics

- Sporadic associations with CHD: TOF, HLHS, endocardial fibroelastosis
- Usually associated with Tuberous Sclerosis Complex (TSC) as a consequence of mutations in the tumor suppressor genes
  - TSC1 – encodes the protein hamartin
  - TSC2 – encodes the protein tuberin
- TSC is an autosomal dominantly inherited condition with variable expression, but in up to 2/3 of cases it can be a spontaneous mutation
- Clinical Features
- Skin lesions [hypomelanotic lesions (ash macules), angiofibromas, shagreen patches]
- Renal angiolipomas
- Retinal hamartomas
- CNS lesions (cortical tubers, subendymal nodules, giant cell astrocytomas)

Rhabdomyoma – Tuberous Sclerosis

- Presence of multiple rhabdomyomas is associated with TSC in 95% of cases
- Presence of single lesion associated with TSC in 23-50% of cases

► Fetal MRI in order to locate CNS and renal lesions (yield maybe low)



Rhabdomyoma – Association with TSC

Association Between Cardiac Tumors and Tuberous Sclerosis in the Fetus and Neonate

Wayne Tworetzky, MD, Doff B. McElhinney, MD, Rene Margossian, MD, Anita J. Moon-Grady, MD, Denver Sallee, MD, Elizabeth Goldmuntz, MD, Mary E. van der Velde, MD, Norman H. Silverman, MD, and Lindsay D. Allan, MD

- Multicenter retrospective studyCHOP, Columbia, UCSF, Rainbow Babies, CHBSubjects:
  - All patients diagnosed with cardiac tumors by echo
    - in utero or by <3 months of age

Courtesy Dr Juan Carlos G. Muñiz

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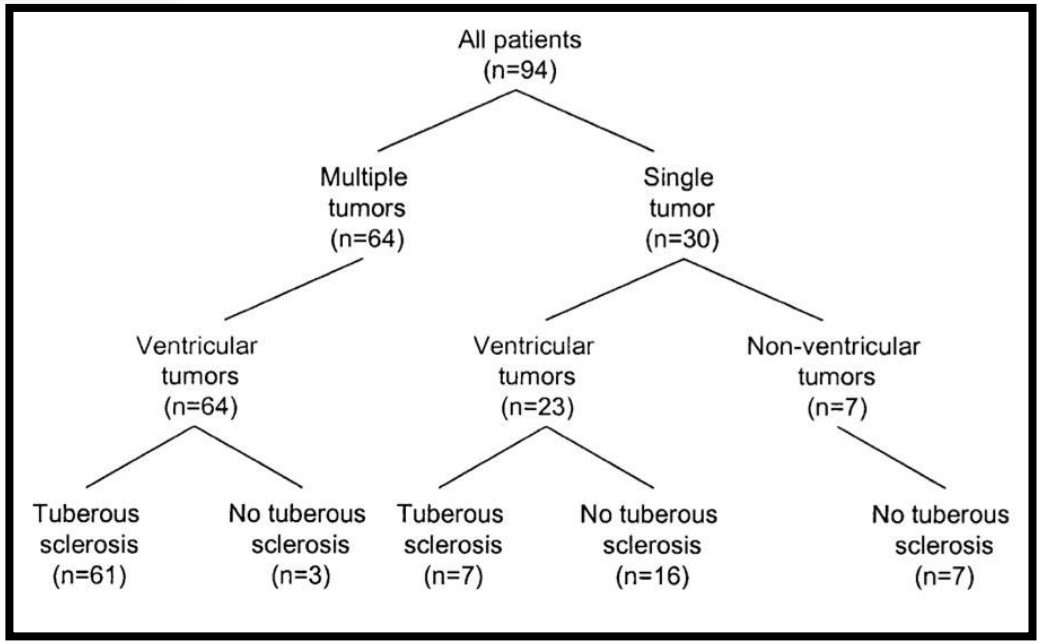
Important Points:
-Most BUT NOT ALL multiple ventricular tumors are associated with TS
-61/64 = 95%

-Even some Single tumors are associated with TS

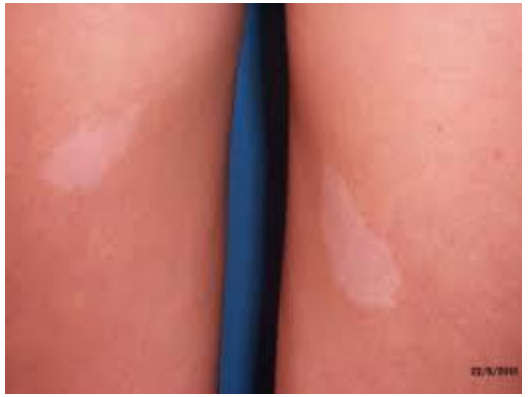


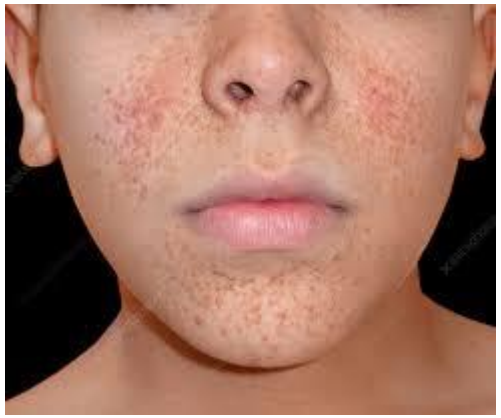
Definition of TS=
1.Familt history
2.Skin findings
3.CNS findings (seizures or imaging)
4.Renal
5.Retinal

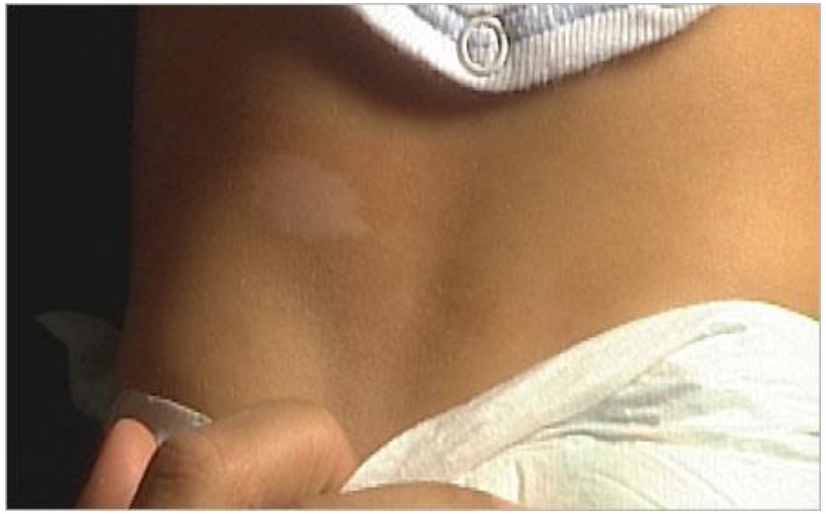
Courtesy Dr Juan Carlos G. Muñiz

(Am J Cardiol 2003;92:487–489)

Rhabdomyoma – TSC features







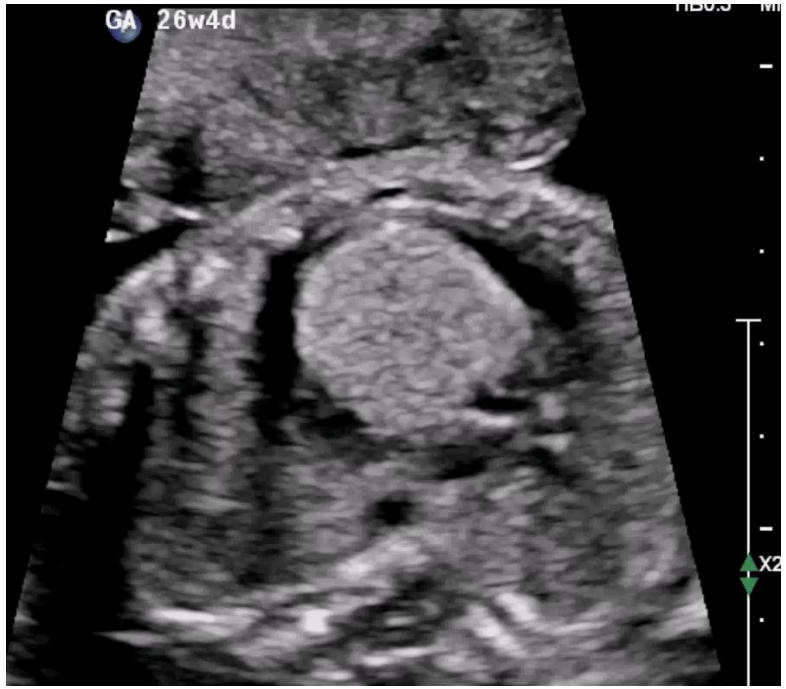
Rhabdomyoma – Prenatal Management

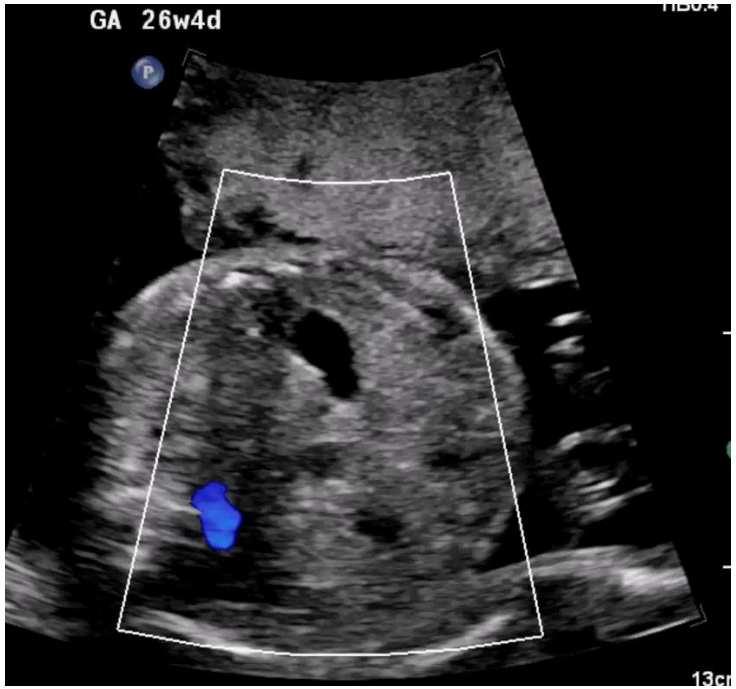
- Prenatally there are limited options for intervention
- Close follow-up since there is a risk for progression
  - Pregnancies at risk for TS need serial evaluations after 22-23 wks through 32 weeks.
- If the patient develops arrhythmia ►antiarrhythmics
- If there is hemodynamic compromise ►early delivery
- Treatment with mTOR inhibitors: sirolimus or everolimus
  - targets upregulated rapamycin pathway in TS

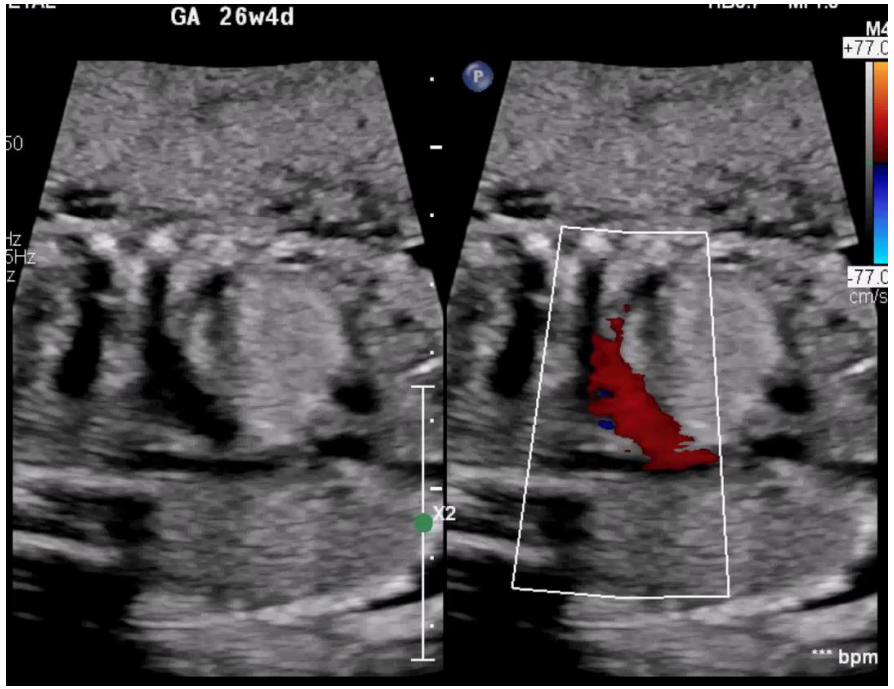
Rhabdomyoma – Prenatal Management

- Treatment with mTOR inhibitors: sirolimus or everolimus
  - Treatment as early as 21 weeks
  - Reduction in tumor size
  - Tumor regression with live birth between 36-39 weeks
  - Achievement of therapeutic levels at ~ 2/3 of cases (33-64%)
  - Tumor might enlarge postnatally (rebound) but responsive to Rx.
- Sirolimus: load orally with 15 mg then 5-8 mg qd (or 2 mg/m2/day, preferably 3-3.5 mg/m2/day) target level ► 10-15 ng/ml
- Everolimus

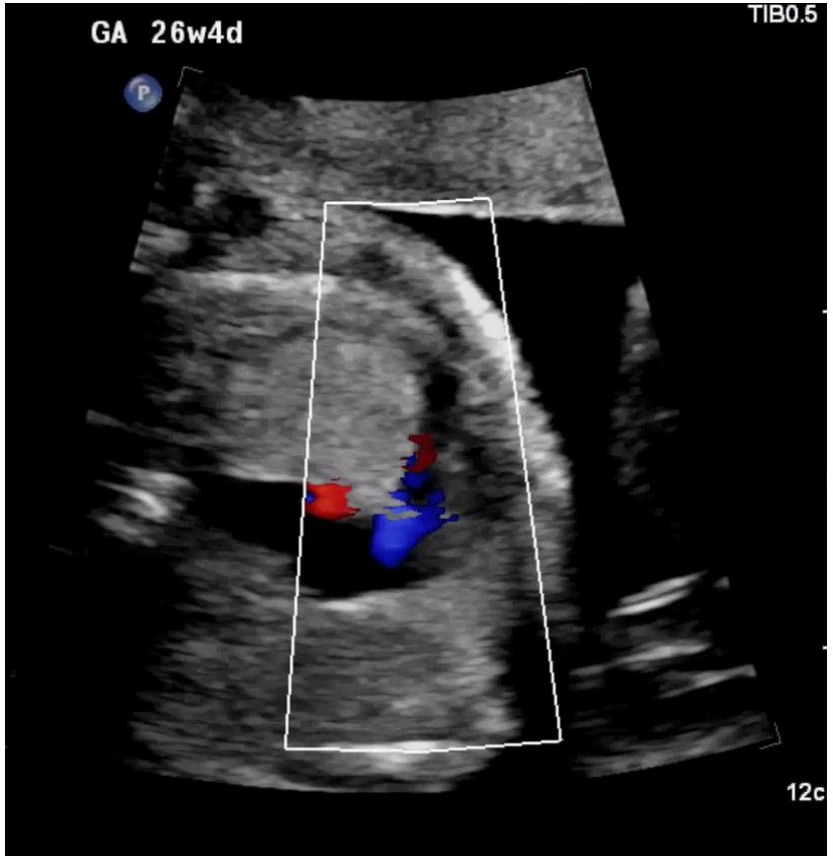
Rhabdomyoma

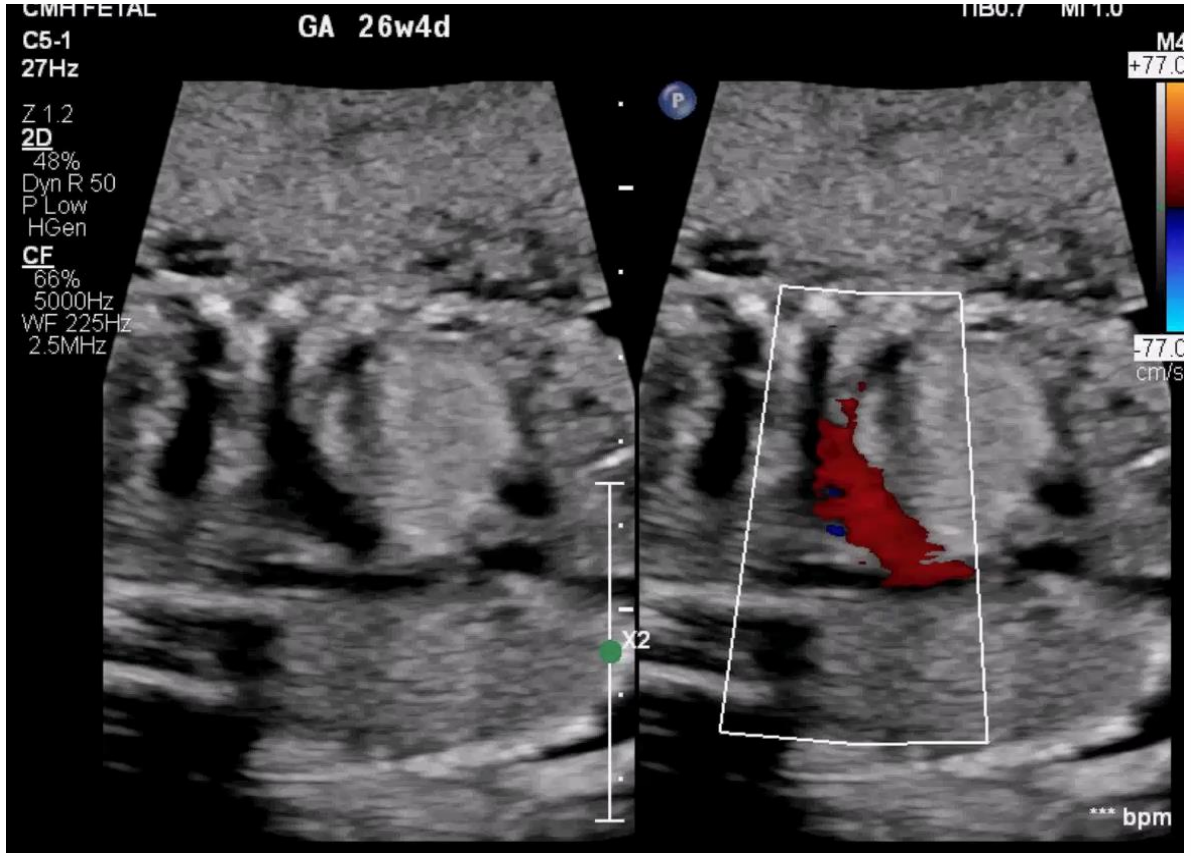




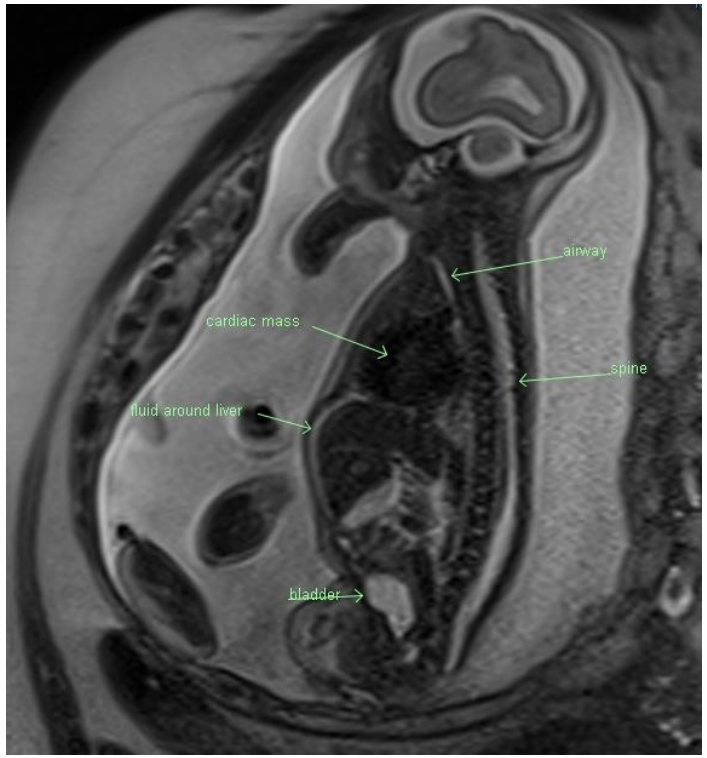


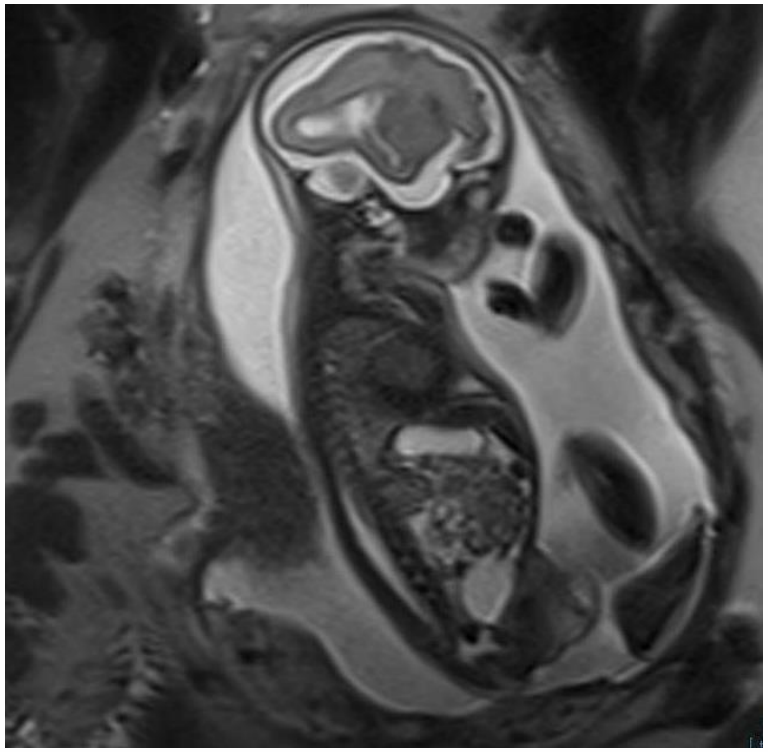
Rhabdomyoma





Rhabdomyoma – Prenatal Management



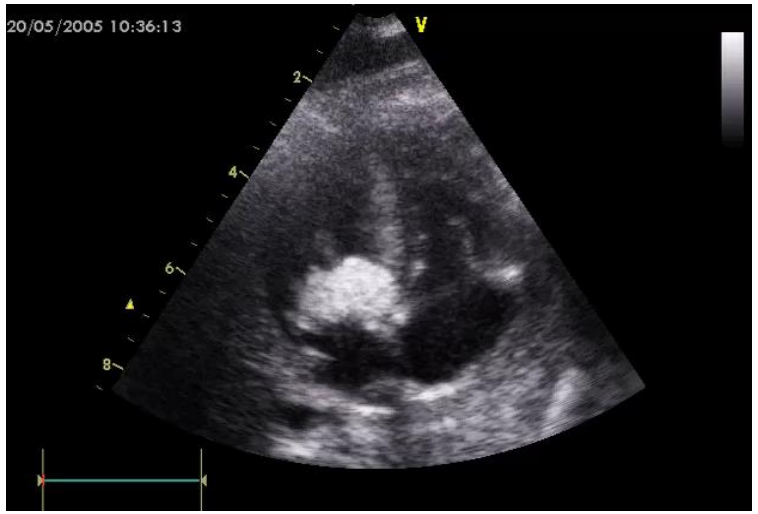


Rhabdomyoma – Postnatal Management

- The location and the size of the tumor will affect the hemodynamics
- PGE might be needed if there is a ductal dependent physiology
- If inflow or outflow obstruction is significant 4-6% will need intervention
- Arrhythmias and conduction abnormalities are not uncommon
- Sudden death may occur
- In asymptomatic cases no intervention is the preferred approach since most rhabdomyomas regress over time (most often regression happens within the first year of life and is independent of tumor size or number).

Rhabdomyoma – Postnatal Management

- Rhabdomyomas usually have a favorable outcome with survival after prenatal diagnosis ranging from 94-100% in various reports in the literature
- Predictors of unfavorable outcome are
  - Large cardiac tumor size
  - Fetal dysrhythmias
  - Fetal hydrops
- The greatest impact is associated with TSC and involves neurocognitive complications
  - In CNS involvement up to 80% of involved patients might have seizures (1/3 infantile spasms)
  - Neurodevelopmental delay up to 68%, including spectrum of autism disorder
- The spectrum of neurocognitive abnormalities differs between prenatal and postnatal diagnosis (40% with symptoms with 71% having CNS findings vs 88% of postnatal diagnosis)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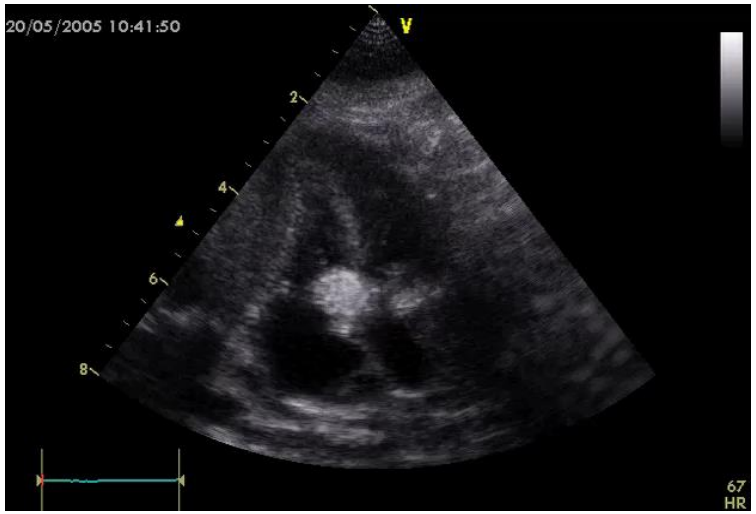
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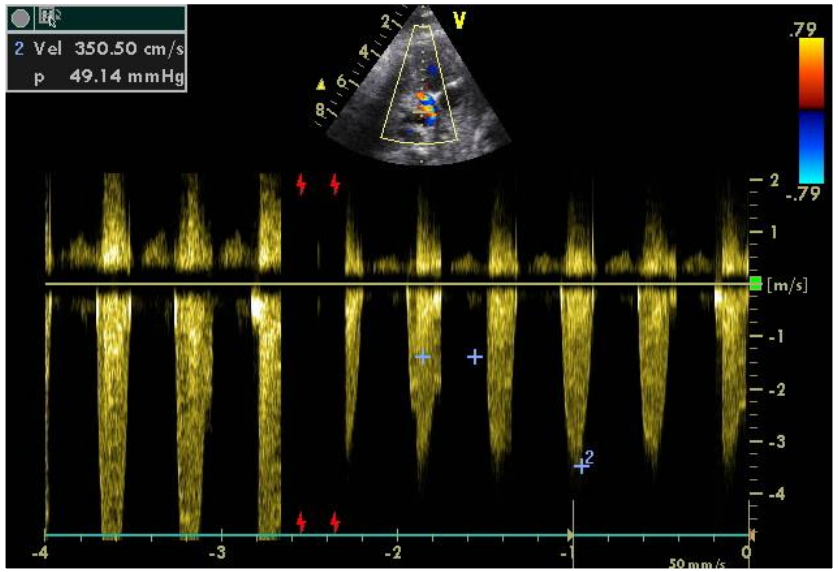
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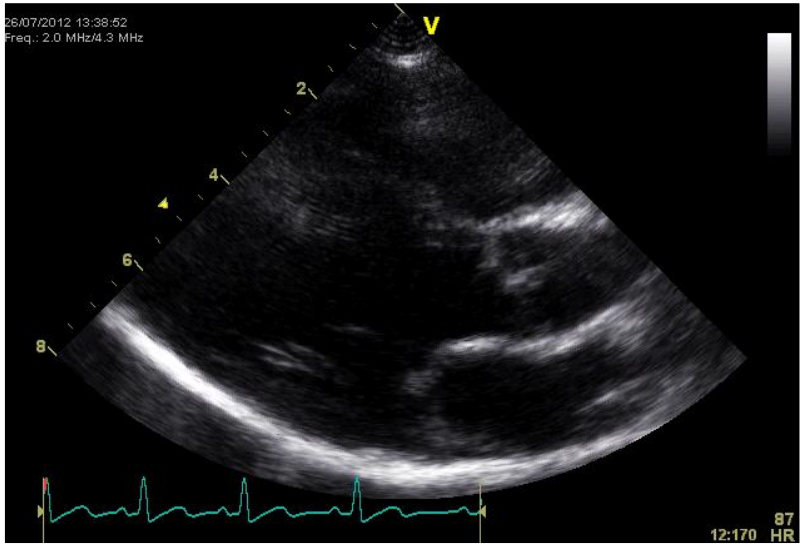
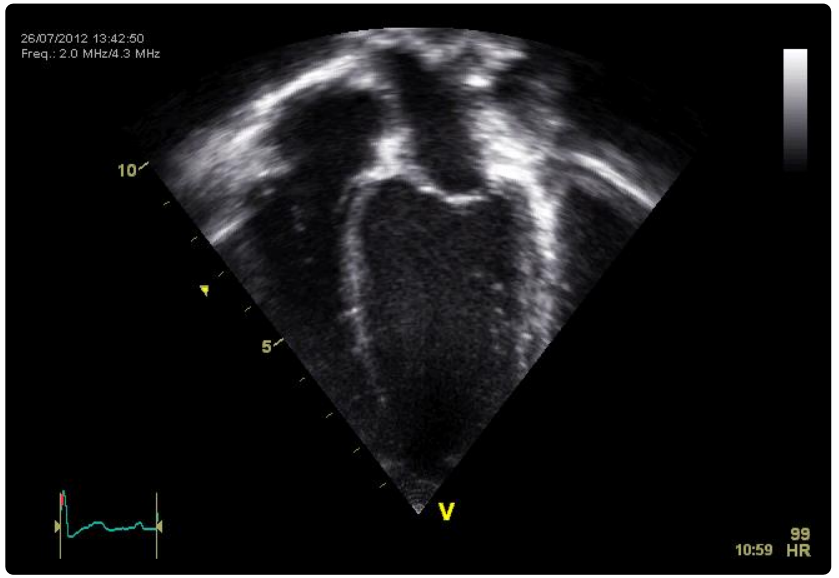
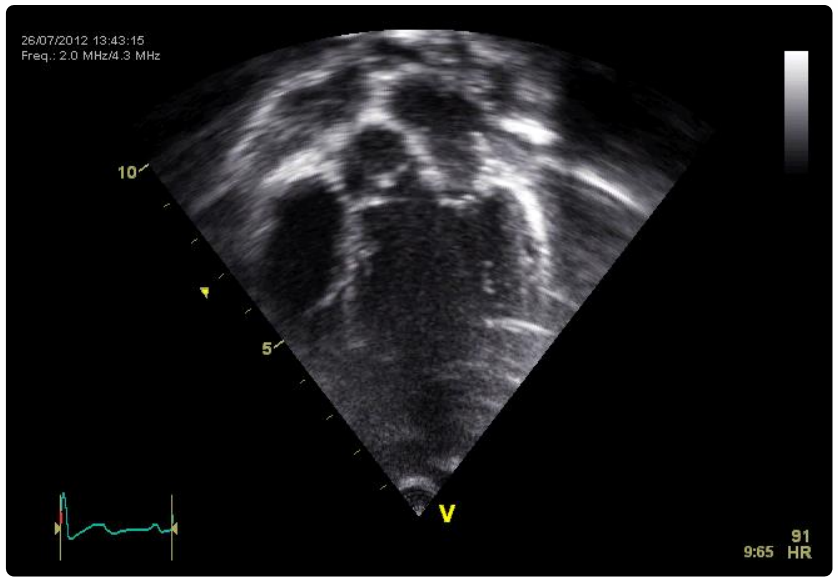
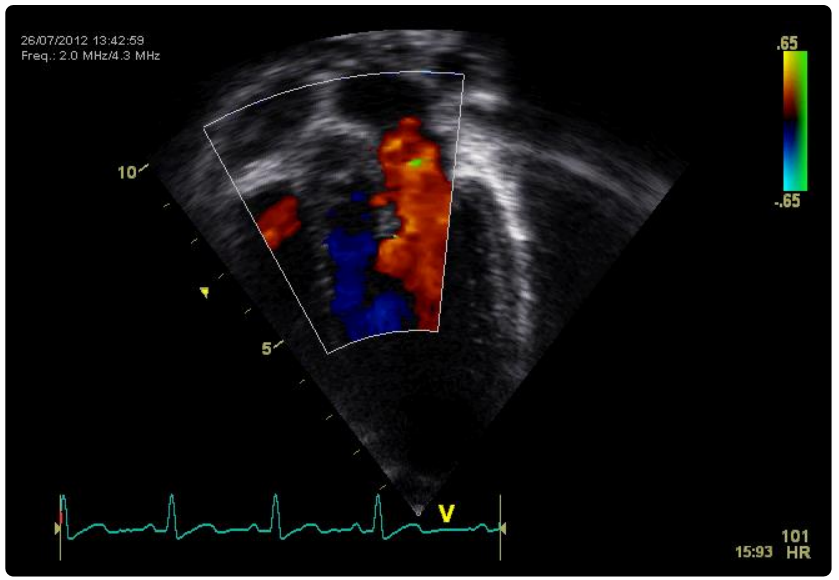
Rhabdomyoma - Outcome



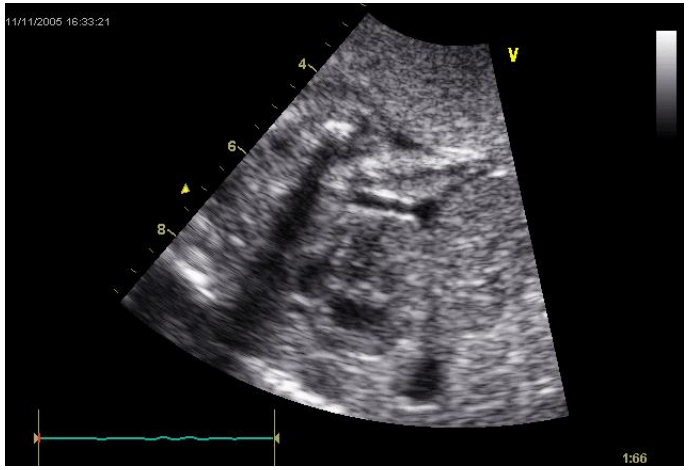


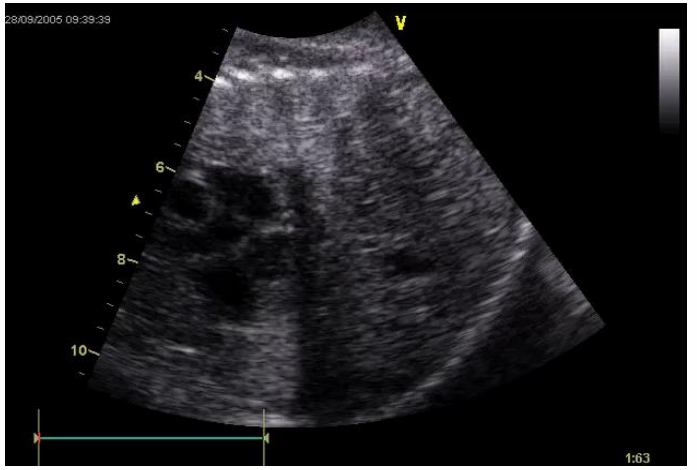




Myocardial Fibroma

- Myocardial fibromas account for 10-15% of cardiac tumors diagnosed in fetal life
- They are connective tissue tumors deriving from fibroblasts and myofibroblasts.
- Other names used are fibrous hamartomas, congenital mesoblastic tumors, fibromatosis, myofibromatosis
- **Echocardiographic features**
  - Typically they are found within the ventricular septum, but frequently they are found within the left or right ventricular wall (intramural)
  - They are usually single
  - They are more echogenic than the surrounding myocardium, but more so than the rhabdos
  - Maybe cystic (degeneration)
  - Usually they are large

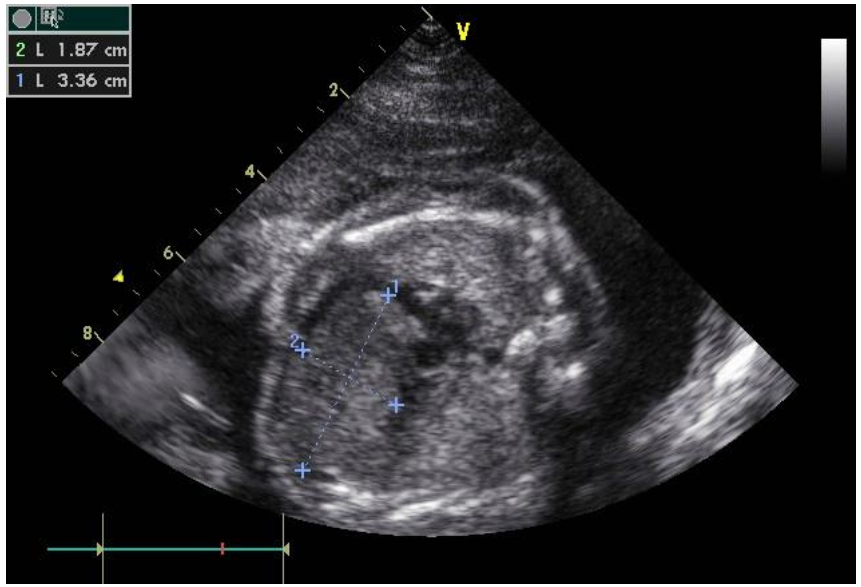




Myocardial fibroma

- May cause ventricular inflow or outflow obstruction, and since they don't regress in size, they might need resection postnatally
- May distort the AV valves and lead to insufficiency
- Can cause heart failure
- They are often associated with arrhythmias
  - Ventricular ectopy
  - Ventricular tachycardia
  - Atrioventricular block
- Postnatally they are associated with emboli

- ***Fibromas do not regress in size***



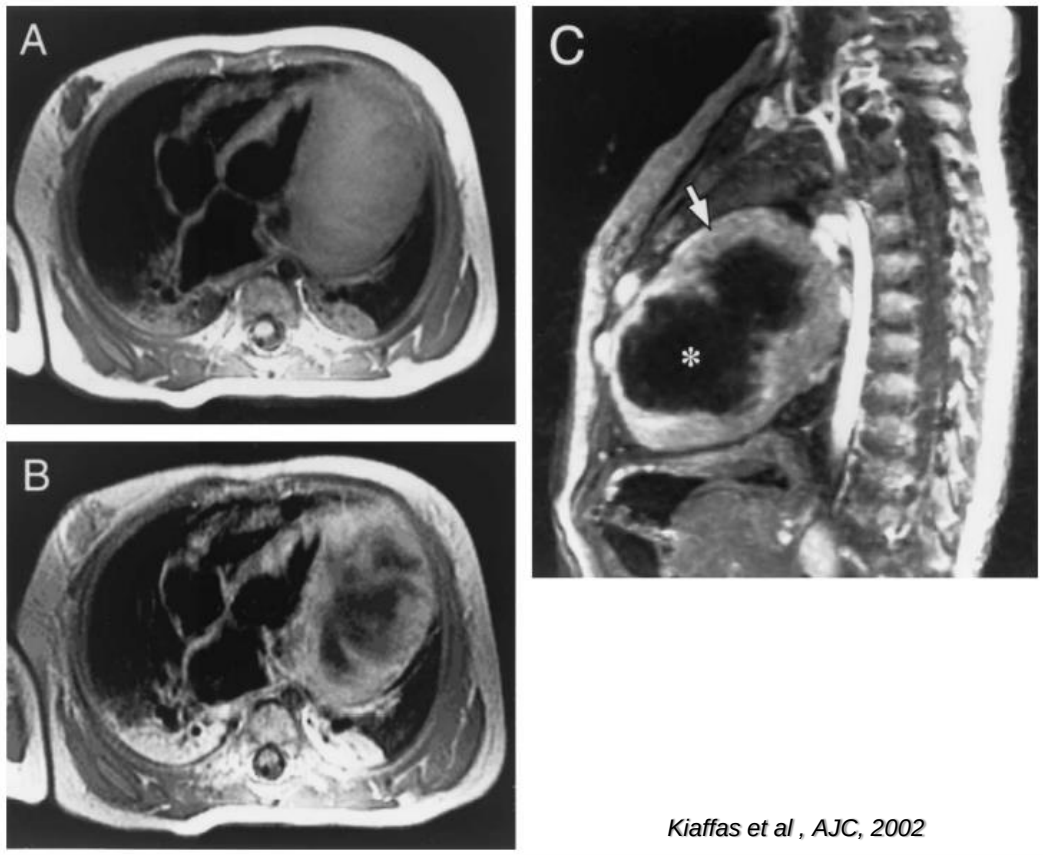
Fibroma – Anatomical Associations and Genetics

- Rarely associated with CHD.
- Extracardiac pathology associated with cardiac fibromas
  - Cleft lip and palate
  - Hydrocephalus
  - Cystic renal dysplasia
  - Beckwith-Wiedeman syndrome
  - Gorlin syndrome (nevoid basal cell carcinoma syndrome)

Fibroma – Postnatal Outcome

- Arrhythmias – PVCs, Ventricular tachycardia are common
- Obstruction of inflows or outflows
- AV valve regurgitation
- Size regression is rare so need for surgical resection, SV palliation when causing VOTO or transplant may be needed
- Survival rate in neonatal life ranges from 29%-50%

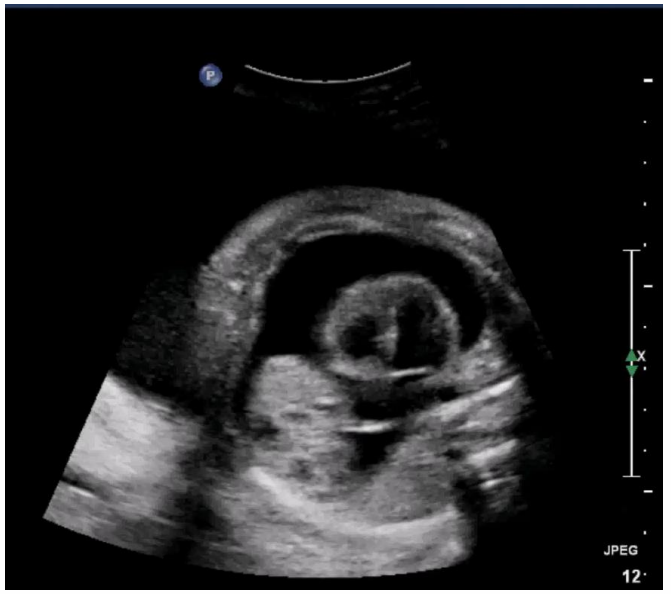
Fibroma – Postnatal Outcome

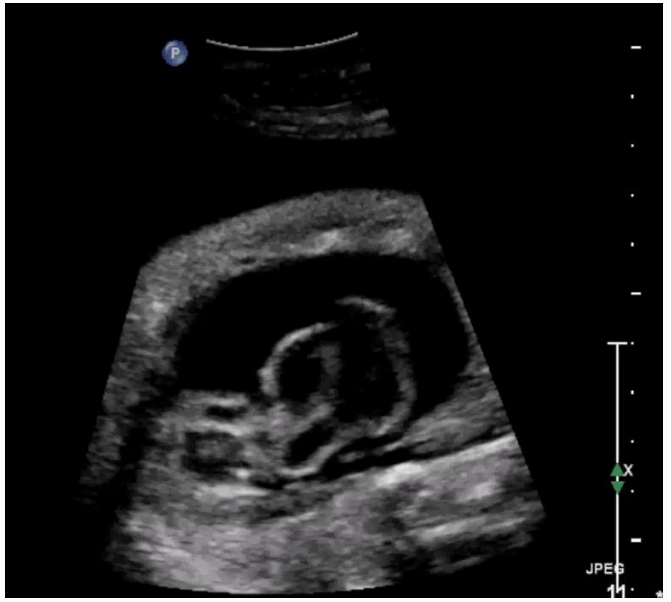


Kiaffas et al , AJC, 2002

Pericardial Teratoma

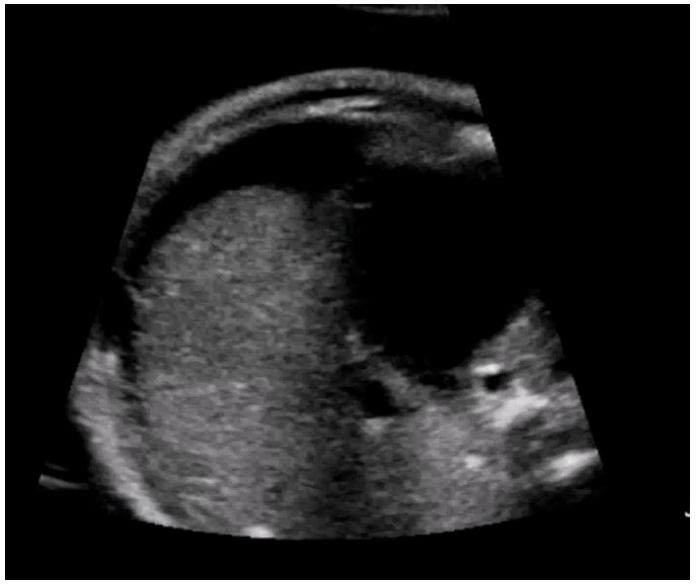
- Pericardial teratomas account for 10-15% of cardiac tumors diagnosed in fetal life
- Consist of endodermal, mesodermal and ectodermal germinal cell layers.
- They develop from the pericardium and attach to the roots of the great arteries
- **Echocardiographic features**
  - Typically are found in the pericardial reflection at the junction of SVC, RA, AsAo
  - Might be identified in the mediastinum – rarely intracardiac
  - They are usually single
  - They are encapsulated
  - Heterogeneous masses with calcified and cystic elements
  - Consistently associated with pericardial effusion

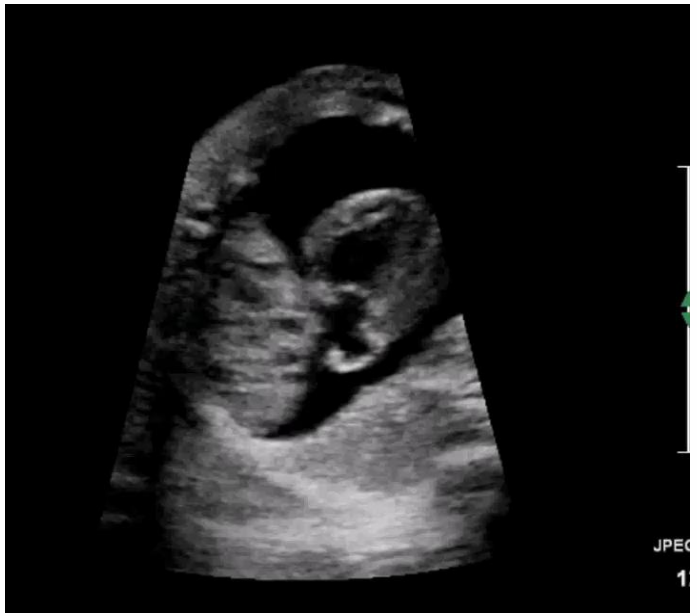




Pericardial Teratoma

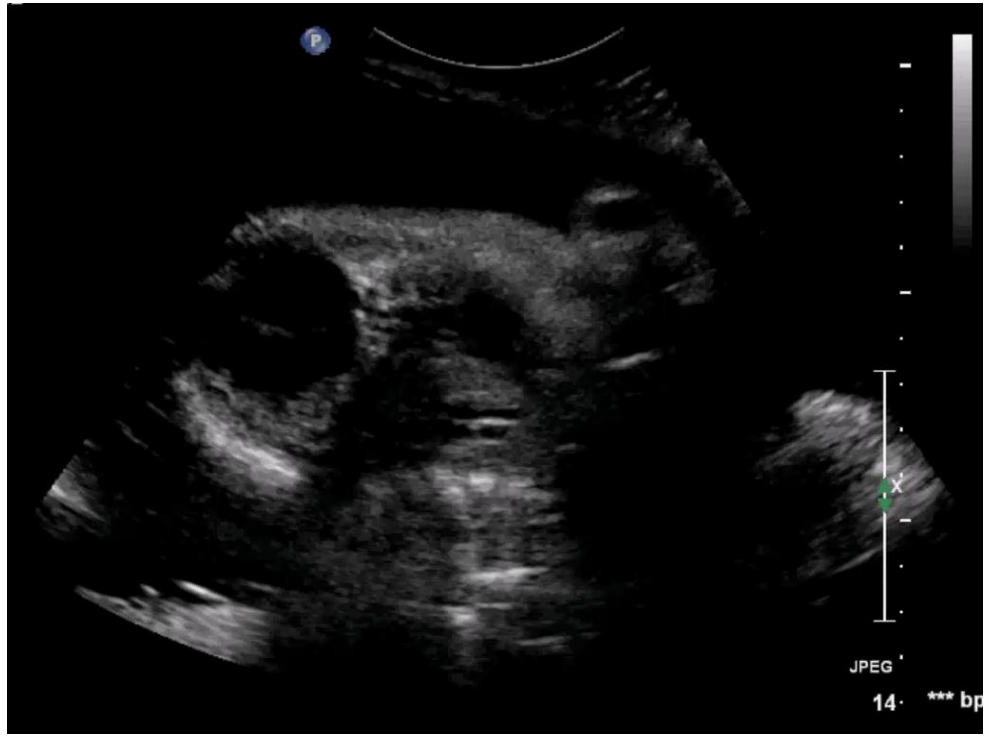
- Typically occur in the second and third trimester
- Usually they have hemodynamic consequences in utero
- When pericardial they may cause tamponade and are associated with hydrops up to ~80%
- They can grow rapidly
- They cause compression of the SVC, great arteries and cardiac chambers
- When intracardiac they can cause obstruction of the inflows and outflows, pulmonary or systemic emboli
- When intrathoracic they might compress airway and cardiac structures





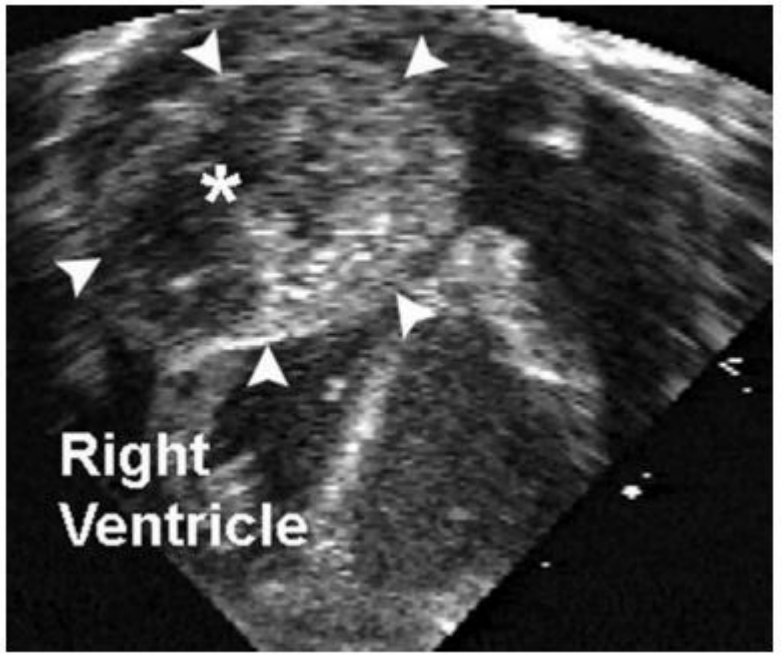
Pericardial Teratoma - Outcome

- Recent review of 67 published cases
- 68.7% presented with hydrops and 25.4% with polyhydramnios
- Prenatal intervention in 26 (20 with hydrops) including pericardiocentesis, shunt placement, open fetal surgery in 3
- 72% liveborn (58% of those with hydrops and 95% without)
- Survival in 88% with vs 68% without prenatal intervention were liveborn



Hemangioma

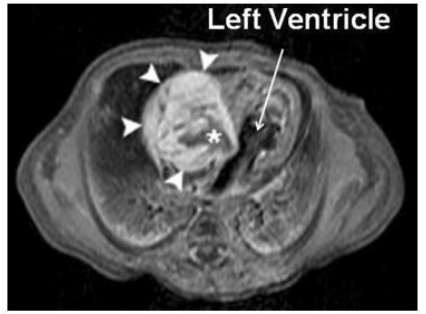
- Very rare tumor in fetuses/neonates observed in 6-7%
- They are vascular tumors and can be classified
  - Cavernous – consisting of many thin-walled vessels
  - Capillary – composed of lobules of smaller vessels
  - Mixed – composed of both types
- The most common place is
  - the base of the heart adjacent to the right atrium
  - may be endocardial or in the myocardium
  - may be associated with the pericardium
- **Echocardiographic features**
  - Most are located in the RA
  - They are secretory and can be associated with pericardial effusion
  - The feeding vessel may be visible by color Doppler – power Doppler
  - Mixed echogenicity – they have cystic and solid parts, occasionally calcifications

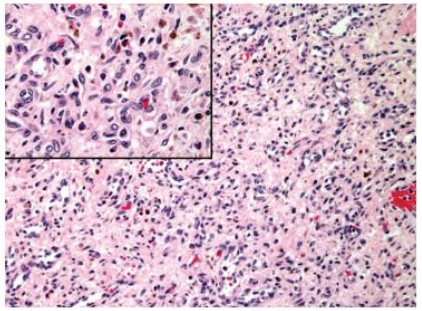


Roman et al, Card Young 2005

Hemangioma

- When large they can be associated with heart failure, either high output or due to compression
- They are associated with dysrhythmias
- When with effusion they might cause tamponade
- Consumption of blood products
- Rarely they have been described to regress





Outcome

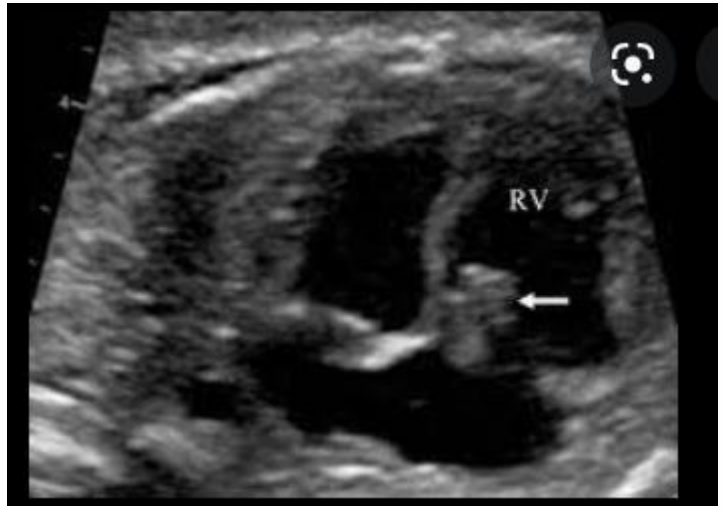
- In the majority of cases surgical resection will be needed
- Good early and long-term outcomes in the literature with at least 85% survival
- Small risk for recurrence

Roman et al, Card Young 2005

Myxomas

- They are composed of primitive connective tissue
- They are rare in fetal life
- Usually single
- Although mainly seen in the atria postnatally, in fetal life they might be seen in the ventricles (LV)

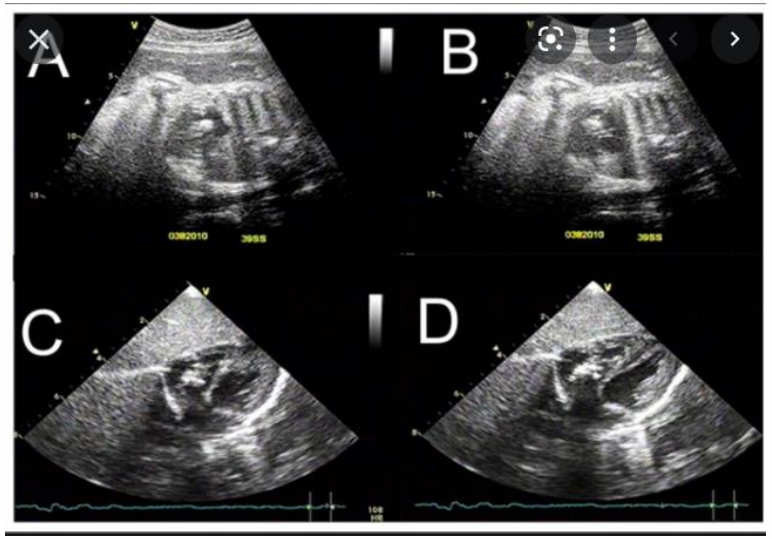
- **Echocardiographic features**
  - May be intracavitary or intramural and occasionally epicardial
  - May be often pedunculated and mobile, also sessile
  - Rarely associated with pericardial effusion



Fetal Cardiac Myxomas, Thieme

Myxomas

- They might cause AV valve or VOT obstruction
- May cause AV valve insufficiency
- Postnatally they are associated with emboli



Outcome

- Surgical resection is the choice
- Often familial or genetic as in the Carney complex, they have a risk for recurrence

Rare Fetal Cardiac Tumors

- Hamartomas
- Lipomas
- Malignant tumors
  - Rhabdomyosarcomas
  - Fibrosarcomas
  - Lymphosarcomas
  - Giant cell sarcomas
  - Fibromyxosarcomas
  - Leiomyosarcomas
  - Neurogenic sarcomas
  - Undifferentiated sarcomas

Fetal tumors - Overview

- Detailed evaluation of atria, ventricles, septum and myocardium
- Description of number, location, tissue characteristic and size
- Potential for obstruction of ventricular inflow or outflow
- Risk of compression and cardiovascular compromise
- Cardiac output assessment may be considered
- Assessment of venous flows, extracardiac Dopplers (DV, UA/UV)
- Assessment of fetal arrhythmias and conduction
- Serial assessment to evaluate tumor growth
- In certain cases consider MRI

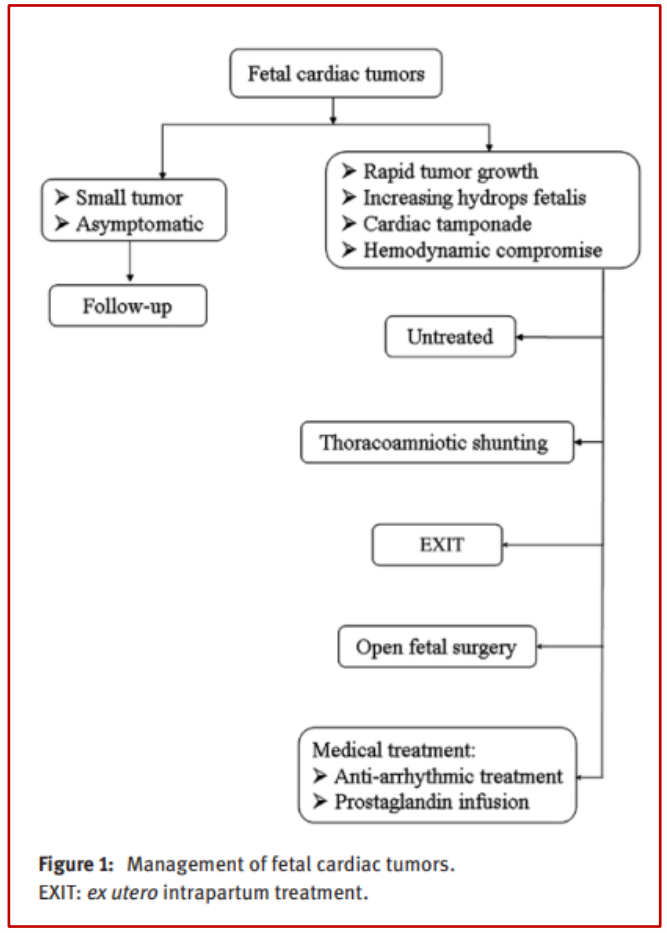


Figure 1: Management of fetal cardiac tumors.
EXIT: *ex utero* intrapartum treatment.

Yuan SM, Card Young 2018


LOVE WILL.