STATE UNIVERSITY OF MEDICINE AND PHARMACY
„NICOLAE TESTEMITANU” FROM REPUBLIC OF MOLDOVA

MYOCARDITIS AND CARDIOMYOPATHIES IN CHILDREN

CHISINAU 2013
DEFINITIONS

- Dictionary: Myocarditis - inflammation of the muscular walls of the heart.
- 1984: a process characterized by inflammatory infiltrate of the myocardium with necrosis and/or degeneration of the adjacent myocytes not typical of the ischemic damage associated with coronary artery disease.
- Cardiomyopathy - structural and/or functional abnormalities of the myocardium that are not secondary to hypertension, valvular or congenital heart disease, or pulmonary vascular disease.

PATHOGENESIS

- Virus binds to myocardial receptors - CAR: Coxsackie B and Adenovirus Receptor
- Viruses encode proteases that cleave cardiac dystrophies
- Immune mediated injury: Cytokines
  - Anti-myocyte antibodies
- Myocyte dysfunction: increased cell permeability and decreased contractility

ETIOLOGIC AGENTS

- Viral agents: Enteroviruses, Coxsackie B- serotype 1-6; Adenoviruses type 1 and; HIV, EBV, CMV. hepatitis with viral RNA or DNA
- Bacterial agents
  - N. meningitidis, S.typhi, S.aureus
- Toxin mediated
  - C.diphereriae, C.tetany, S.pyogenes
- Parasites: Trypanosoma cruzi (Chaga’s), Leishmania, Toxoplasma, Trichanella, Larva migrans.
- Fungal - Aspargillus, Candida, Coccidiodes, Cryptococcus, Histoplasma
- Non-infectious
  - Drugs hypersensitiveness - antibiotics, diuretics, digitalis et al.
  - Autoimmune - SLE, hyperthyroidism, infant of diabetic mother.

CLINICAL MANIFESTATIONS

- Ppodromal symptoms: highly variable
- URI symptoms in last 1-6 weeks
- Fatigue, dyspnea, chest pain
- CHF, pulmonary edema, cardiogenic shock
- Neonates: may appear septic - fever/hypothermia; Poor feeding, anorexia, listless, lethargic

MYOCARDITIS: IMAGING STUDIES

- Chest X-ray: Cardiomegally (CI>0.58), pulmonary edema
- ECG: ST-T changes, LVH, arrhythmias
- EcoCG- shortening fraction (SF-N=30%) ejection fraction (EF-N=>55-65%), cardiac index (CI=3-4l/m2), mean VCF shortening=1-1.2cinc/sec.
  - dilated poorly contracting LV
  - pericardial effusion, MV regurgitation

LABORATORY DATA

- Cardiac enzymes normal value: Troponin 1-0.052ng/ml; CPK-MB-N<24 un, LDH total <480un-elevated titer in patients
- Elevated ESR, WBC, CRP>6mg/ml

OTHER DIAGNOSTIC METHODS

- Myocardial biopsy- storage disease, mitochondrial defects
- Histology: Lymphocytic infiltrate, PMN’s
- PCR for viral agents
- Recover agent from stool or throat cultures
- Indirect serologic evidence: IgM, IgG
• Scintigraphy with Technetium 99 evidence the inflammatory regions

**MYOCARDITIS: SUPPORTIVE THERAPY**

• Pressors: Milrinone, Dopamine 1-5-20mg/kg/day, Epinephrine
• Diuretics: Lasix, Spironolactone
• Afterload reduction: Nipride, ACE Inhibitors or antagonists
• Beta blockers: Inderal, Atenolol, Carvadilol
• Anti-arrhythmics- Amiodarone
• Digitalis in half of normal dosage
• Steroids 2mg/kg/daily, tapered to 0.3/mg/kg/dayily over of 3 mo and Immunosuppressive agents

**SPECIFIC TREATMENT OF MYOCARDITIS**

• IV Immunoglobulin- 2g/kg
• IFNa, IFNb, Pleconaril for enterovirus, Acyclovir for Epstein-Barr virus
• Extra-corporal membrane oxygenation (ECMO)
• Heart transplantation

**FOLLOW-UP**

• One visit in 3-6mo to monitoring heart function: ECG, Holter, ECHO, serum marchers, immunological tests.
• All patients will be monitoring 3 years after acute myocarditis.

**CARDIOMYOPATHY**

**DEFINITION**: Expert consensus panel 2006

• Heterogenic group of myocardium diseases
• Mechanistic or electrics disturbances,
• Hypertrophic or dilated manifestation
• Multiple causes, often genetics
• Functional manifestation:
  1. Dilated Cardiomyopathy
  2. Hypertrophic Cardiomyopathy
  3. Restrictive Cardiomyopathy

**ETIOLOGY ASSOCIATED DISORDERS**

• Genetic- mitochondrial abnormalities
• Fatty acid metabolism
• Protein abnormalities of cardiomyocyte
• Glycogen storage disease
• Infections
• Viral
• Bacterial
• Parasitic
• Nutritional factors
• Arrhythmias- tachyarrhythmia
• Brady-arrhythmias
• Familial cardiomyopathy (20-30%), Friederich’s ataxia
• Carnitine deficiency-CoA dehydrogenase deficiency
• Duschenne muscular dystrophy, Fabry’s disease
Pompe disease type II, III
Myocarditis Coxsackie B, Adenovirus, Parvovirus 19, HIV
Rheumatic fever, Sepsis, Diphtheria
Trypanosomiasis
Calcium, cooper, iron, selenium deficiency
Superventricular, ectopic, ventricular tachycardia Complete heart block

DILATED CARDIOMYOPATHY
Final common pathway for many disorders which result in heart failure.
Year incidence in children 0.56/100 000, 75% of them need heart transplantation.

Common other causes of heart failure:
- Decrease beta receptors
- Increase catecholamines
- Decrease Nor-epinephrine stores
- Cardiomyocyte dysfunction

CLINICAL MANIFESTATION
- Symptoms: Feeding intolerance, fussy/irritable, respiratory distress, exercise intolerance, chest pain, failure to thrive, abdominal pain (liver congestion).
- Signs: BP may be low, narrow pulse pressure, tachycardia, large liver, Gallop-pre-systolic murmur, AV regurgitation (MR>TR), signs of systemic emboli (LA and LV thrombus)

DCM - IMAGING STUDIES
- Increase BUN/Cr, plasma carnitine/acyclamitine
- ECG- Pompe disease, arrhythmias, left/right ventricular hypertrophy, T-wave abnormalities
- EcoCG- aortic valve and mitral regurgitation, left atrium/ventricle dilatation
- Chest X-ray: cardiomegaly, pulmonary congestion, presence of pleural effusions, pneumonia
- Cardiac catheterization: SF and CI decreased, increase LVED pressure; on biopsy- areas of fibrosis are present

DCM - LABORATORY DATA
- Increase BUN/CR, plasma carnitine/acyclamitine
- ABG: metabolic acidosis, anion gap, lactic acidosis.
- Urine organic acids and amino acids,
- Viral origin- ELISA; PCR- ARN, ADN

DCM - MANAGEMENT OF CHF
- Critically ill children: intubation, IMV, IV inotropes (Dobutamine, Milrinone)
- Digoxin, vasodilators, diuretics 1-2 mg/kg/day;
- b-adrenergic blocking agents –Metoprolol 1-5 mg/kg/day;
- ACE inhibitors- Captopril 0.5-0.6mg/kg/day for <1yr age;
  1-3 mg/kg/day in older children; Enalapril 0.1-0.5mg/kg/day;

Supportive treatment
- Bed rest or restriction of activity
- Immunosuppressive agents, steroids are controversial.
- In arrhythmia (Amiodarone); syncope- implantable pacemaker
- Anticoagulation with aspirin or warfarin, in risk of thrombosis
- Cardiac transplantation in a pediatric center (Maisch B et al, 2006, Herz,31(9)

HYPERTROPHIC CARDIOMYOPATHY
HCM is a primary, often familial cardiac disease with a diverse clinical and morphologic expression that is characterized by a hypertrophied and non-dilated left ventricle in the absence
of another cardiac or systemic disease that is capable of producing LVH

- Incidence 1:500 in the community, more undiagnosed
- Occurs equal in both sexes
- Pathophysiology is diastolic dysfunction, unlike systolic dysfunction in DCM

**HCM - ETIOLOGY**

- Mutation of the any one of the 10 genes:
  most common are myosin heavy chain, troponin T, α-tropomysin, and cardiac myosin-binding protein C
- Autosomal dominant transmission
- Underlying cause of hypertrophy unknown:
  - abnormal myocardial calcium kinetics
  - abnormal sympathetic stimulation
  - coronary abnormalities in coronaries
  - subendocardial ischemia

**HCM - MORPHOLOGY**

- LVH: gross anatomic- marker and a major determinant of the clinical feature of the disease
- Disorganized muscle fibers
- Intramural coronary artery with narrowed lumen and thickened wall
- Children with HCM may progress in LV hypertrophy
- Asymmetric LV hypertrophy primarily is confined to the anterior/posterior portion of the septum
- Extensive scarring of the ventricular septum
- Mitral valve enlarged, elongated and thickening

**HCM – PATHOPHYSIOLOGY**

- Anatomic variations: hypertrophic obstructive cardiomyopathy (HOCM), idiopathic hypertrophic subaortic stenosis (IHSS), asymmetric septal hypertrophy (ASH)
- Systolic LV volume is in related with obstruction
- Mitral regurgitation: mild, moderate, severe
- Myocardial ischemia: increase ventricular pressure, oxygen demand =>anginal chest pain, syncope, repetitive NSVT, sudden death (SD)
- Myocardial fibrosis decreased compliance
- Diastolic dysfunction: abnormal LV relaxation (stiffness) =>LA enlargement and pulmonary venous congestion (dyspnea, orthopnea, paroxysmal nocturnal dyspnea)

**HCM – PECULIARITY IN INFANTS**

- Malignant genotype, asymptomatic or mild symptom
- Familial or primary genetic forms occurring in 1/500
- Patients with other conditions=>Noonan’s syndrome; glycogen storage disease (Pompe), infants of diabetic mother=> all without LVOT obstruction
- Poor prognosis with heart failure, syncope, SD
- In infants of diabetic mother LV mass may regress in several months

**HCM – IMAGING STUDIES**

- ECG signs=>ST-T changes, prominent R in V1&V2, abnormal Q in II,III,avF and V4-6; deep S in V1-3, WPW- syndrome may be present
- ECG signs appear before EcoCG (important in familial)
- EcoCG- systolic anterior motion of the mitral valve
- Asymmetric septal hypertrophy, subaortic stenosis,
- LVH outflow tract gradient- (>50mmHg)
- Chest X-ray: cardiomegaly with prominence of the LV
- Cardiac catheterization in patients for surgery
- Genetic screening- defect of contractile protein of 4(6) chromosomes 14.1, 15.1- about 50
NATURAL HISTORY

- Clinical variability and difficult to predict natural course, annual mortality from sudden cardiac death in 2-4%, typical age is 12-35 years
- Syncope is related to sudden death (SD)
- LVOT obstruction does not correlate with SD
- Cardiac arrest/sustained recurrent VT
- Familial history of SD from HCM
- Patients with extreme thickness of LV wall >or=30mm with or without arrhythmia
- Long-term athletic training produces increases in LV diastolic dimension, LVED >45mm

MANAGEMENT AND TREATMENT OF HCM

- Discontinue sports/physical activities
- Pharmacological therapy: Propranolol 2mg/kg/day, Atenolol 1-2 mg/kg/day, Verapamil 2-4mg/kg/day, Nifedipin 0.6-0.9mg/kg/day, Amiodaron 5-10mg/kg/day
- Digitalis, diuretics, Isoproterenol are contraindicated
- rise outflow tract gradient
- Surgical IV septum myotomy, replacement of MV
- In recurrent syncope- implantable pacemaker
- Heart transplantation

HCM - PROGNOSIS

- Treatment of HF result in temporary remission
- High risk patients in familial forms
- Sudden death (50-90% in effort)
- Screening of ECG and EcoCG in children <12yr; and between the ages 18-21=>greatest risk

RESTRICTIVE CARDIOMYOPATHY

- Idiopathic or associated with a systemic disease: scleroderma, amyloidosis, sarcoidosis; errors of metabolism (mucopolysaccharidosis); hypereosinophilic syndrome; malignancies; radiation therapy; congenital: non-compaction of the left ventricular myocardium
- Diastolic ventricular compliance decrease in RCM
- Systolic function may be maintained
- Clinical: dyspnea, edema, ascites, hepatomegaly, increased venous pressure, and pulmonary congestion, high risk of pulmonary vascular disease; the heart moderately enlarged, murmurs absent; in pulmonary hypertension second heart sound is loud

RCM – IMAGING STUDIES

- ECG- markedly prominent P waves, often normal QRS voltage, ST depression, T-wave inversion
- Chest X-ray: moderate cardiomegaly
- EcoCG- markedly enlarged atria (two- to threefold larger than small/normal- sized ventricles, endocardial fibrosis
- Differential diagnosis from constrictive pericarditis
- MRI scan: diagnosing a thickened pericardium, delineate the fibrosis of endomyocardium

RCM – TREATMENT

- Differential diagnosis from constructive pericarditis – pericardietomy.
- Heart failure management: diuretics; antiarrhythmic drugs; anticoagulation (aspirin, warfarin)-risk of mural thrombosis and stroke.
- Cardiac transplantation if systemic disease is not present

**Bibliography:**
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