# STATE UNIVERSITY OF MEDICINE AND PHARMACY

**„NICOLAE TESTEMITANU” FROM REPUBLIC OF MOLDOVA**

MYOCARDITIS AND CARDIOMYOPATHIES IN CHILDREN

# CHISINAU 2024

## 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.diphtheriae, 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=1-1.2circ/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, Spiranolactone
* 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 cacdiomyopathy (20-30%), Friederich’s ataxia
  + Carnitine deficiency-CoA dehydrogenase deficiency
  + Duschenne muscular dystrophy, Fabry’s disease
  + Pompe disease type II, III
  + Myocarditis Coxackie B, Adenovirus, Parvovirus 19, HIV
  + Rheumatic fever, Sepsis, Diphtheria
  + Trypanosomiasis
  + Calcium, cooper, iron, selenium deficiency
  + Superventventricular, 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

* Iincrease 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, a-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 progression 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 noctural dyspneya)

## 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 regresses 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

mutation

## 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 – pericardiectomy.
* Heart failure management: diuretics; antiarrhythmic drugs; anticoagulation (aspirin, warfarin)- risk of mural thrombosis and stroke.
* Cardiac transplantation if systemic disease is not present

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