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MYOCARDITIS AND CARDIOMYOPATHIES IN CHILDREN

CHISINAU 2019

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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