CASE PRESENTATION

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Case Presentation

Clinical History

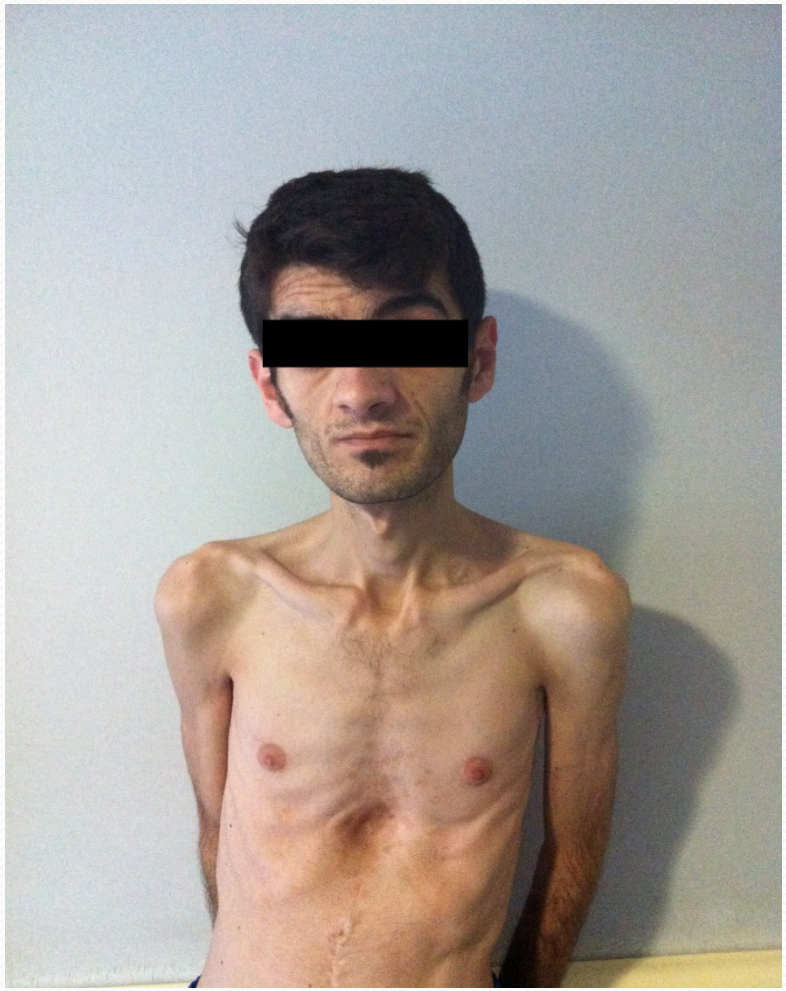
- 28 years old male
- Symptoms has begun in 2005 as nausea, vomiting and weight loss.
- Upper and lower endoscopy were performed 3 years later because of abdominal pain and vomiting
  - Lower endoscopy: Hyperemic mucosa on ileoceacal region, edamatous and ulcerative
  - Pathology: Crohn disease.
- On the third day of therapy because of acute abdominal symptoms, intestinal resection has performed due to diverticulosis.

Clinical History

- Pathology: Not compatible with Crohn disease, reported as acute diverticulosis.
- In the third postoperative day he was reoperated because of small intestinal perforation.
- After discharge, symptoms of diarrhea following constipation periods, nausea and vomiting have continued intermittently.

Current Admission

- He was admitted to our outpatient clinic with nause, vomiting, diarrhea and ileus. He was hospitalized for further investigation.
- Physical
  - T:36.5°C HR:78/min BP:125/70 mmHg RR:16/min
  - Cachexia, pectus carinatum
  - Ptosis
  - Hyperactive bowel sounds, diffuse abdominal tenderness, no defence, no rebound
  - Drop foot on the left side (after intestinal operation in 2008)
  - Anxiety



Laboratory Results

- Hgb:13.8 g/dl (11.7-15.5)
- WBC:11,600/mm3 (4100-11200)
- Plt:170,000/mm3 (159,000-388,000)
- ESR: 16 mm/hr (0-20)
- **CRP: 1.13 mg/dL (0-0.8)**
- Liver enzymes – Renal function tests , lipid levels normal
- Gaita parasite/culture: -/-
- Hepatite markers: - (no vaccination)
- Immun globulin levels: normal
- **Prealbumin: 11.4 mg/dl (20-40)** albumin: 4.3 g/dl (3.4-4.8)
- Brucella agglutination: -

Imaging

Plain Abdominal Graphy: Air-fluid levels

Abdominal CT : Hepatomegaly, smoothening in proximal jejunal segments

Differential diagnosis

- Crohn disease
- Diverticulosis
- Malabsorption syndrome (celiac sprue)

Drop foot???
Mental and psychiatric problems??

- EMG: Diffuse demyelinated polyneuropathy in sensory and motor nerves of lower extremity

- Enteropathy due to constrictive pericarditis??
- Echocardiography: EF: %50, constrictive pericarditis ?

- Cardiac MR: Not compatible with constrictive pericarditis

Any diagnosis?

Further investigations ?

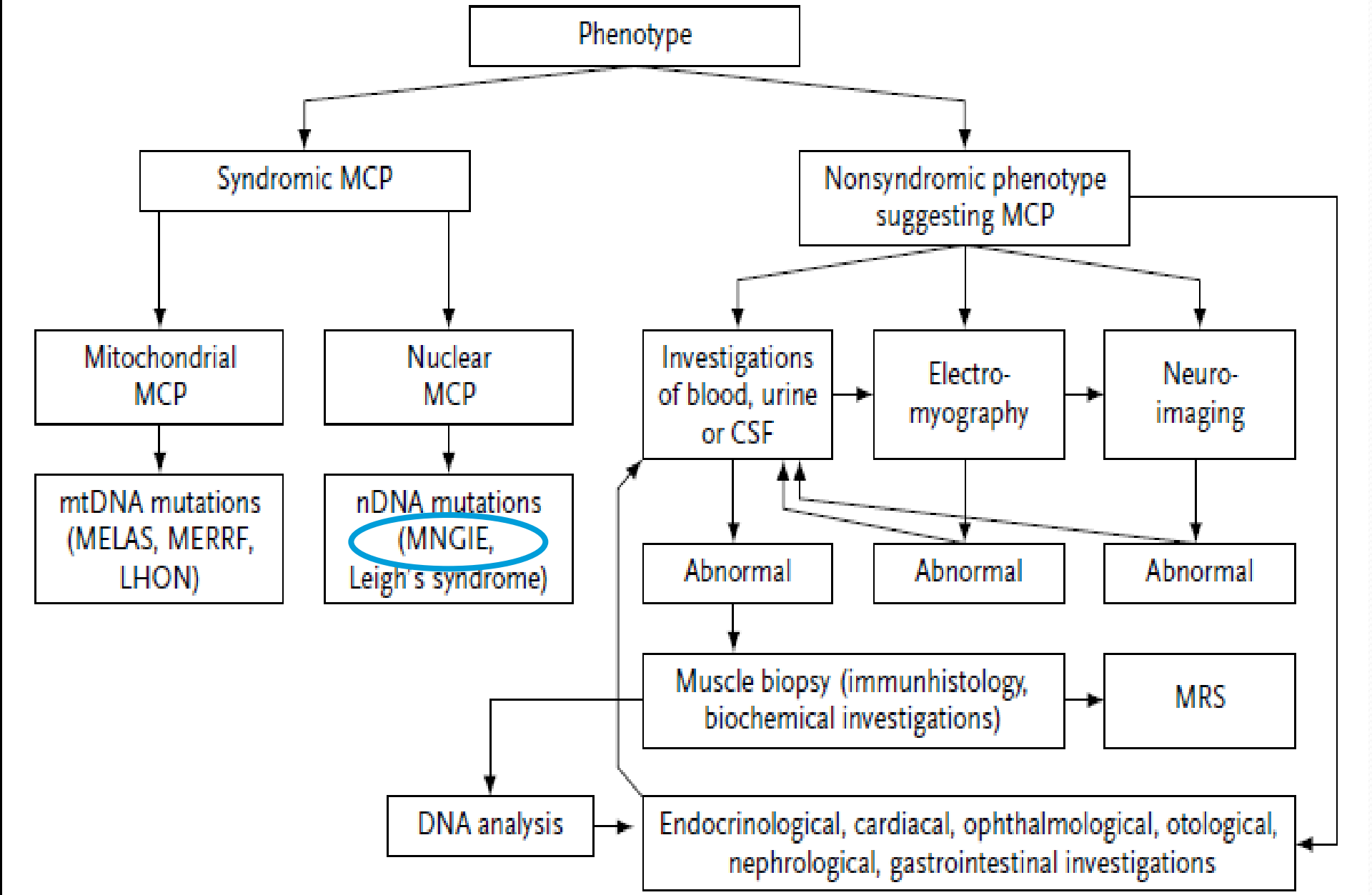
- Cranial MR: Hyperintense lesions as patchy infiltration in peridentate , pontine, basal ganglia and thalamus; diffuse involvement in cerebral white matter, internal and external capsules. It is compatible with mitochondrial neurogastrointestinal encephalopathy

MNGIE SYNDROME

- Biceps muscle biopsy: Low degree neurogenic changes, compatible with mitochondrial myopathy

- Genetic testing sent to Dr. Hirano

Figure 1. *Stepwise procedure for the diagnostic work-up of mitochondriopathies*



PATHOPHYSIOLOGY of MNGIE SYNDROME

- Mutations in the gene encoding thymidine phosphorylase.
- Accumulation of thymidine and deoxyuridine in blood and tissues
- Toxic levels of nucleosides → mitochondrial DNA abnormalities leading to an abnormal intestinal motility.
- Intergenomic communication between nuclear and mitochondrial genomes

MNGIE

Polyneuropathy
Ophthalmoplegia
Leucencephalopathy
Intestinal **P**seudoobstruction

- Multisystemic involvement
- Autosomal recessive
- 20 years old

SYMPTOMS

- Episodic nausea and vomiting
- Gastroparesis
- Progresive intestinal pseudoobstruction
- Abdominal pain
- Gastrointestinal dismotility and dilatation
- Diarrhea and malabsorbtion
- Progresive malnutrition
- Mortality at 40 years

SYMPTOMS

- Myopathy, chronic progresive ophtalmoplegia (CPEO)
- Glaucoma like optic neuropathy
- Cognitive dysfunction due to leucoencephalopathy
- Retinitis pigmentosa
- Deafness
- Disartria
- Polineuropathy

DIAGNOSIS

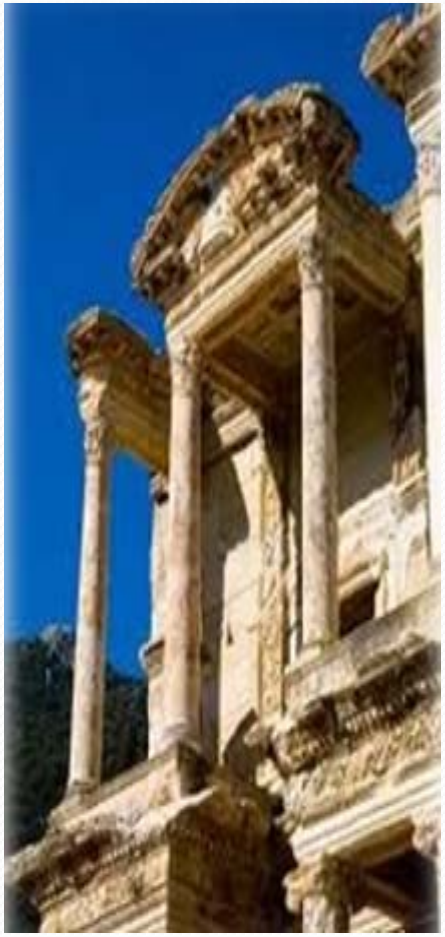
- Increase in plasma thymidine and deoxyuridine levels
- Thymidine phosphorylase (TP) enzyme activity in leukocytes <10%
- Molecular genetic testing of TYMP, mtDNA defects in peripheral blood or muscle biopsy specimens
- Brain MR demonstrating leukodystrophy.
- Hirano et al :
    1. Ptosis and/or ophthalmoparesis
    2. Gastrointestinal dysmotility
    3. Peripheral neuropathy
    4. Ragged-red fibers or succinate dehydrogenase activity in muscle biopsy

TREATMENT

Treatment supportive

- Carnitine - CoQ
- Antiemetic
- Pancreatic enzyme replacement
- Prokinetic agents
- Total parenteral nutrition
- Pain relief
- Treatment of infections
- Platelet infusions transiently provide TP activity and reduce plasma thymidine and deoxyuridine levels
- Allogeneic hematopoietic stem cell transplantation

Thanks for your patience and attention…



Türkiye

See you in ESIM 2012 in Kuşadası, Türkiye