## DEPARTMENT OF MOLECULAR BIOLOGY AND HUMAN GENETICS

### 22. GENETIC ASPECTS OF THE HUNTINGTON DISEASE

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**Background.** Huntington disease (HD) is an incurable, adult-onset, autosomal dominant inherited disorder associated with cell loss within a specific subset of neurons in the basal ganglia and cortex. HD is named after George Huntington, the physician who described it as hereditary chorea in 1872. Characteristic features of HD include involuntary movements, dementia, and behavioral changes.
**Case report.** Purpose and objectives: This study focuses on the variability of the HTT gene expression and its correlation with the onset of the disease. It also outlines the genetic aspects of the disease: types of inheritance, anticipation and the frequency of new mutations in the population. Etiology: The selective neuronal dysfunction and subsequent loss of neurons in the striatum, cerebral cortex, and other parts of the brain can explain the clinical picture seen in cases of HD. Several mechanisms of neuronal cell death have been proposed for HD, including excitotoxicity, oxidative stress, impaired energy metabolism, and apoptosis. Treatment: In a study published recently in the New England Journal of Medicine, researchers from UBC and their colleagues have demonstrated for the first time that the drug IONIS-HTTRX (now known as RO7234292) successfully lowered the levels of the mutant huntingtin protein - the toxic protein that causes Huntington disease -- in the central nervous system of patients. The treatment is designed to silence the gene. On the trial, 46 patients had the drug injected into cerebrospinal fluid. The first in-human trial showed the drug was safe, well tolerated by patients and crucially reduced the levels of huntingtin in the brain. Experts say it could be the biggest breakthrough in neurodegenerative diseases for 50 years.
**Conclusion.** Taking into consideration the above description of the new trial treatment of the disease, the studies made in this field could be crucial for the next generations.
**Key words:** Huntington's disease, anticipation, penetration, treatment, mutation

### 23. RECURRENT AORTIC DISSECTION: A PECULIAR COMPLICATION OF MARFAN SYNDROME

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**Background.** Marfan syndrome (MFS) is an autosomal dominant disorder caused by a mutation in FBN1 gene which involves abnormal connective tissue. MFS affects different parts of the body such as bones, joints and eyes, but the most serious complication involves cardiovascular system. Acute aortic dissection (AD) is a life-threatening condition caused by a tear in the intimal layer of the aorta or bleeding within the aortic wall, resulting in the separation of the layers of the aortic wall. Even though AD is a characteristic complication of the MFS, recurrent aortic dissection (RAD) is a rare phenomenon where MFS is a strong independent

risk factor. As many as 15% of aortic dissections are painless and often the signs on presentation are subtle and easily overlooked, RAD require a multidisciplinary approach and a complex treatment strategy.

**Case report.** We present the case of a 47-year old female with a history of MFS since 1976, admitted for retrosternal chest pain worsening with activity, associated with shortness of breath and radiation of the pain over the abdominal area, for over a month. Her pathological background included: aortic dissection (ascending and descending thoracic aorta) in 2005, dilated cardiomyopathy, stage 3 hypertension, class IV NYHA chronic heart failure and superior and inferior vena cava thrombosis. The transthoracic echocardiography revealed an intimal flap and two lumina were visualized in the thoracic aorta under the origin of the left subclavian artery (LSA), bicuspid valve with severe aortic regurgitation, tricuspid insufficiency and a left atrial appendage thrombus. The thoraco-abdominopelvic CT has exposed an aortic dissection involving both the ascending and the descending aorta (Stanford A/DeBakey I). Under both medical and surgical treatment consisting in valvuloplasty and angioplasty the patient evolution was improving.

**Conclusions.** RAD remains a challenging entity regarding both the diagnosis and management, but its incidence at patients with MFS may be reduced by regular clinical examination, screening and by imaging at the time of diagnosis and during follow-up.

**Key words:** Marfan syndrome, recurrent aortic dissection

## 24. A RARE CAUSE OF EPISTAXIS: OSLER–WEBER–RENDU DISEASE

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**Background.** Rendu-Osler disease is a rare genetic disease, with suggestive clinical manifestations: recurrent epistaxis, telangiectasias and visceral vascular abnormalities.

**Case report.** A 40-year-old patient presents to the emergency room for asthenia, dyspnea, recurrent epistaxis and headache. Patient's history revealed that her mother and aunt died from a liver disease and the two also presented epistaxis. At the physical examination, pallor, discrete edemas, tachycardia and systolic murmur were noticed. Biologically, there was an iron deficiency anemia. The ENT examination revealed a vegetative nasal septum formation, which was biopsied. Abdominal ultrasound revealed a hypoechogenic formation, in the proximity of the pancreas tail, for which angioCT was performed, describing several splenic aneurysms and a particular aspect of hepatic vascularization. This pattern is suggestive for intrahepatic arteriovenous malformations. For the differential diagnosis: bacterial endocarditis, cirrhosis, connective tissue disease or vasculitis were taken into consideration. Resumption of the clinical examination allowed the discovery of a small telangiectasia of the upper lip. Based on the Curacao criteria, the diagnosis was established (3 out of 4: epistaxis, telangiectasia and a positive family history of a relative of the first degree). Further investigations were made in order to detect other possible abnormalities. Signs of pulmonary hypertension and heart failure were identified, complications secondary to the liver arteriovenous malformations. The patient received treatment with iron, initially parenterally, later orally. Selective embolization of the largest of the splenic artery aneurysms was performed, taking into account the risk of rupture. Iron therapy was maintained as a primary treatment. The patient is monitored biannually for the liver and heart disease. Screening for the family members was recommended.