Wilson's disease: A pictorial essay

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Authors: J. A. Borges, A. A. S. M. Santos, M. L. O. Santos; Rio de Janeiro/BR
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Learning objectives

- Wilson's Disease is an autosomal recessive disorder and must be a part of the differential diagnostic of chronic liver disease and extrapiramidal symptoms.
- This study discuss the main signs in brain Computed Tomography (CT) and specially in Magnetic Resonance Imaging (MRI).
- Will be related the most common places of disease and the patterns in several images sequences.

Background

- Wilson's disease is the result of a genetic alteration that affects 1:30000 people no matter their race, nationality or sex.
- It is transmitted by an autosomal recessive gene located on chromosome 13. The ATP7B gene is characterized by accumulation of copper in the tissues (mainly liver, basal ganglia and cornea) due to a defect in the excretion of this element.

Neurologic signs:

- Rest and intention tremors, dystonia, hypertonia, muscle spasms, Choreia, rigidity, salivation, dysphagia and dysarthria.
- Initial changes: flexo-extensor tremor of the wrists, faces, difficulty in writing and unintelligible speaking ("juvenile parkinsonism").
- Spasticity of the muscles of the larynx and pharynx leads to dysarthria and dysphagia.
- Dystonic facies, excessive salivation.
- Difficulty in writing can be an early sign.

Kaiser-Fleischer's rings:

- As one of the criteria for diagnostic confirmation is the examination of slit lamp to visualize the Kayser-Fleischer's rings, who is typical of Wilson's disease.
- Were described by Kayser in 1902, and in 1909 Fleischer reported a patient with corneal ring, cirrhosis and pseudoesclerose.
- The rings are pigmented alterations, located in Descemet's membrane, mainly in the limbic region of the cornea (Fig 1).
• Kaiser-Fleischer's rings are present in 95% of patients with neurological manifestations.
• It should be remembered that the rings Kayser-Fleischer can be the first manifestation of Wilson's disease, discovered by chance in a routine eye examination, hence the importance of its recognition by ophthalmologists, who may be the first to suggest this diagnosis.
• It wasn't proven the relationship between the reduction in ring size and neurological improvement.
• It should be remembered that the presence of the Kaiser-Fleischer's rings and low serum ceruloplasmin level (less than 20 mg / dL) are sufficient for the diagnosis of Wilson's disease.

Other manifestations:

• One of hepatic manifestations of Wilson's disease, the most benign, is described as an acute hepatitis, self-limited and often confused with viral hepatitis or infectious mononucleosis.
• Can be observed renal manifestations such as hematuria, aminoaciduria, renal glycosuria, phosphaturia, hypercalciuria or renal tubular acidosis, with or without nephrolithiasis, by glomerulopathy or renal tubular disease, such as Fanconi syndrome. These changes probably due to the deposition of copper in the renal proximal.
• Skeletal changes, such as demineralization, premature osteoarthritis, cysts subarticular and fragmentation of the bones around the joints can be observed.
• Other much more rare manifestations include gallstones, cataracts, heart disease and a blue color in the nail lunulae.

Images for this section:
Fig. 1: Kayser-Fleischer's Ring
Imaging findings OR Procedure details

**IMAGING FINDINGS:**

- Imaging tests are not part of the diagnostic protocol of the classic disease. However, it should be emphasized its importance due to the difficulty and delay in clinical diagnosis. Furthermore, the disease, if untreated, has a bad prognosis.

**Computed Tomography:**

- CT is much less sensitive than MRI in cases of Wilson's disease, may be normal or show only a mild generalized atrophy and ventricular dilatation.
- The most frequent findings are putamina bilateral hypodensity.
- CT can be improved by using thin slices (1 or 2 mm) in the levels of the basal ganglia.
- It is important that the radiologist when faced with a CT scan showing signs of brain atrophy, especially in young patients, make the correlation with clinical data, which may include Wilson's disease as a diagnostic possibility, requiring further research imaging, indicating the MRI.

**Magnetic resonance imaging:**

- The findings on MRI depend on some factors such as disease duration, duration of treatment and presence or absence of significant liver disease.
- The most signs observed on MRI is hyperintense on T2 and hypointense on T1 in the basal ganglia, thalamus, stem and dentate nucleus. May be bilateral and symmetrical involvement (Fig 1-6).
- In studies where patients are examined at various stages of drug therapy, the most common injury is lenticular nucleus, more specifically in the lateral portion of the putamen, which is the site of injury are common according to the general literature. The second most affected site is the pons (Figs 7-9).
- Edema, gliosis, necrosis and cystic degeneration due to copper toxicity or secondary to ischemia explain these signal characteristics on T2 images.
- In patients without treatment and those with longstanding disease, the paramagnetic effect of copper may promote a reduction of signal on T2.
- Another explanation for this change of sign is the deposition of iron in place of copper after chelation therapy.
- The hypointense signal in T1 is due to deposition of manganese, copper and / or iron at concerned sites in patients with liver failure.
- If a patient with asymptomatic Wilson's disease have high signal on T1, one should be aware of the severity of liver damage.
- It is reported also cerebral atrophy and white matter lesions in cortical.
• It is important to mention that after treatment the lesions may regress significantly and then the MRI a useful tool to control response to drug therapy used (Fig. 10).

Another presentation possible is described as a sign of "Face of the Giant Panda" in the midbrain (Fig. 11):

• This image consists of normal signal intensity in red nucleus and pars reticulate of the substantia nigra, hyperintensity of the tegmentum and hypointensity of the superior colliculus in T2.
• This hypointensity, as discussed, is likely to be due to the paramagnetic effect of copper and iron.
• There is also a description of the "Faces of the Panda" in miniature on the pons, represented by the hypointensity of the medial longitudinal fasciculus and central tegmental tract (panda eyes) in contrast to hyperintensity of the aqueduct opening in the fourth ventricle (nose and mouth), limited in the lower portion by the superior spinal veil.

• Restricted diffusion observed in the putamen, may precede the neurological manifestations of Wilson's disease. Important in early detection of disease (Fig 12).

• In spectroscopy observed reduction of NAA / Cr in frontal white matter and parietooccipital and basal ganglia, suggesting neuronal loss.

Images for this section:
Fig. 1: Unenhanced T1: low signal in the basal ganglia. Signs of cerebral atrophy and mild dilatation of the ventricular system.
Fig. 2: Axial enhanced T1: No significant enhancement in the lesions in the basal ganglia.
Fig. 3: FLAIR AXIAL: Hyperintense signal in lenticular nuclei and mild dilation of ventricular system
Fig. 4: T2 AXIAL: areas of hyperintensity lenticular nuclei and thalamus bilaterally.
Fig. 5: FLAIR CORONAL: areas of hyperintensity in the basal ganglia and the cerebral peduncles bilaterally.
Fig. 6: T2 CORONAL: High signal in the lenticular nuclei bilaterally.
Fig. 7: IR AXIAL: Hypointensity in the brain stem (pontocerebellar tract: anterior pontine fibers, pontine tegmental reticular nucleus and middle cerebellar peduncles).
**Fig. 8:** IR AXIAL: Hypointense signal in the basal ganglia bilaterally. Note also the cortical sulci, suggesting signs of cerebral atrophy.

**Fig. 9:** Acquisitions axial T2 (right) and T1 (IR) with foci of hyperintensity on T2 and hypointense on T1 (IR) in the cerebral peduncles. Furthermore, there was moderate dilatation of IVo. ventricle.
**Fig. 10:** Control after treatment, shows marked reduction of areas of hyperintensity in the basal ganglia, both in FLAIR axial and coronal T2.

**Fig. 11:** Sign of "Face of the Giant Panda" in the midbrain
Fig. 12: Restricted diffusion observed in caudate and lenticular nuclei bilaterally.
Conclusion

• The Wilson's disease is a relatively rare disease, little known and difficult to diagnosis.
• Although imaging studies are not part of the diagnostic protocol of the disease, they may be critical to the suspicion and diagnostic elucidation.
• It is for radiologists to recognize the main radiological signs, thinking about the hypothesis and alerting attending physicians.
• It also emphasizes the importance of MRI in evolutional monitoring. Furthermore, studies of diffusion and spectroscopy are underway, becoming increasingly used as an auxiliary tool in early diagnosis of this disease.

Personal Information

1. Juliana Aguiar Borges:
   • Specialization Course in Radiology of IPGMCC (Institute of Postgraduate Medical Carlos Chagas). Rio de Janeiro. Brazil
   • Radiologist of HCN (Clinical Hospital Niteroi) and VOT-IMAGE (Venerable Third Order of St. Francis), Rio de Janeiro, Brazil

2. Alair Augusto Sarmet M.D.Santos:
   • Professor and Chief of Radiology Service HUAP-UFF (Antônio Pedro University Hospital - Federal Fluminense University). Rio de Janeiro/Brazil.
   • Master and PhD in Radiology from the Federal University of Rio de Janeiro (UFRJ)
   • Vice-President of the Brazilian College of Radiology (CBR) - Rio de Janeiro
   • See e-curriculum: http://buscatextual.cnpq.br/buscatextual

3. Maria Lúcia de Oliveira Santos:
   • Professor of Radiology Departament HUAP-UFF (Antônio Pedro University Hospital - Federal Fluminense University).
   • PhD in Radiology from the Federal University of Rio de Janeiro
   • Radiologist of HCN (Clinical Hospital Niteroi). Rio de Janeiro.Brazil
   • See e-curriculum: http://buscatextual.cnpq.br/buscatextual
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