Cystinosis encephalopathy: MRI perivascular enhancement with micronodular T2* hypointensity

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Cystinosis is an autosomal recessive disease causing intracellular accumulation of cystine crystals [1]. Children involved by the disease are born normal but rapidly develop end-stage renal failure. Renal transplantation and cysteamine (which converts cystine into a soluble form) have recently helped to prolong these patients’ lives.

Symptomatic damage to the central nervous system [2] (cognitive and motor disorders and epilepsy) affects 2% of adult patients [3] although a few magnetic resonance imaging (MRI) observations have been reported. We describe the case of a patient suffering from encephalopathy secondary to cystinosis in whom encephalic MRI showed perivascular update of contrast associated with micronodular T2* hypointensity.

Case report

The patient was being followed up for childhood cystinosis and had a renal transplant at the age of 8 years old. Adherence to cysteamine treatment had always been poor with intralyzosomal cystine measurements between 2.5 and 6.4 demi-cystine/mg of protein (normal < 1). Clinically, the patient had complications of cystinosis with eye damage, thyroid failure, anemia, impairment of the renal transplant and cognitive disorders since adolescence.
At the age of 24 years, the patient had a transient episode of right brachial and facial deficit associated with aphasia. MRI (1.5 T, GE Medical System) (Fig. 1) showed diffuse atrophy and multiple areas of ischemic in the semi-oval centre, T2 hyperintensity in the periventricular areas, a few frontal sub-cortical T2* hypointensity and slight uptake of contrast in the perivascular spaces in the fronto-parietal white matter and central grey nuclei. Investigation of the intracranial arterial blood vessels was normal. The patient was started on treatment with 160 mg of lysine acetylsalicylate.

He gradually developed walking difficulties, together with a cerebellar and frontal pyramidal syndrome. Because of clinical worsening, a further MRI (3 T, Siemens verio) (Fig. 2) was performed 3 years later and showed persistent T2* hypointensity and increased contrast update in the perivascular stasis and T2 hyperintensity in the periventricular areas. Investigation of the intracranial arterial blood vessels was normal and the laboratory assessment showed no acute phase reaction. Adherence was still poor with an intraleukocyte cystine level raised at 6.4 nmol demi-cystine/mg of protein.

In view of the context of poor adherence to treatment, the clinical findings compatible with complications of cystinosis and the lack of an acute phase reaction, the MRI abnormalities were attributed to encephalopathy secondary to the cystinosis.

The patient was already being treated with immunosuppressive drugs and treatment therefore consisted of recommending that he improves his adherence to the cysteamine.

**Discussion**

Symptomatic central nervous system damage due to cystinosis is rare although their incidence is liable to increase because of new methods of management. Berger et al. [4] reported a patient suffering from cervical myelitis associated with internal capsule and hemisphere T2 hyperintensity lesions, some of which increased uptake after injection. Histological analysis showed a perivascular lymphocyte infiltrate associated with a cystine crystal deposition and a small and median diameter blood vessel vasculitis. In our case, contrast was taken up with the perivascular spaces located close to the areas of T2* hypointensity. The main reasons for increased uptake in the perivascular spaces are vasculitis and infectious inflammatory or malignant meningeal infiltration. In our case, the areas of increased contrast may have been due to vasculitic lesions in small diameter vessels, secondary to cystine crystals, which are known to cause an autoimmune reaction and explain the deep infarction in the initial neurological episode. CT angiography did not show stenoses although this is known to have poor spatial resolution distally [5]. The main differential diagnosis in young adults is granulomatous diseases (sarcoidosis, histiocytosis), although these are associated with pachymeningeal uptake and/or uptake in the pituitary stem. The T2* hyperintensity areas could represent microhemorrhagic lesions secondary to small vessel damage. Renal impairment can cause microangiopathy, which is responsible for white matter abnormalities and can also produce cerebral atrophy, although this has been shown to be more common in patients with cystinosis [2].

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**Figure 1.** Multiple nodular hyperintensities in the white matter (a: weighted diffusion sequences) (white arrows) with restricted diffusion (b). Periventricular hyperintensity areas on T2 Fluid Attenuated Inversion Recovery (FLAIR) (black arrows).
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The treatment of cystinosis encephalopathy was corrected adherence to cysteamine and immunosuppressant therapy. Broyer et al. [6] have shown that improving adherence to cysteamine can stop progression.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References


