

Folinic acid is ineffective for treating Kearns-Sayre syndrome[☆]



El ácido fólinico no es eficaz en el tratamiento del síndrome de Kearns-Sayre

Dear Editor,

It was with great interest that we read the case presented by Pardo Ruiz et al.¹ of an 8-year-old patient with Kearns-Sayre syndrome (KSS), with a single 6.4-kb mitochondrial DNA (mtDNA) deletion and a heteroplasmy rate of 27%. We would like to make the following observations.

Mitochondrial DNA deletions are rarely inherited.² Did the patient's mother present symptoms of mitochondrial disease? Did she undergo studies aimed at detecting mtDNA deletions?

A heteroplasmy rate of 27% is low, and unlikely to fully explain the patient's severe, progressive phenotype. Although muscle biopsy was not performed, we wonder whether the heteroplasmy rate was determined in other tissues, particularly in muscle tissue, where the rate is usually higher.

There are several possible explanations for the ineffectiveness of folinic acid. Firstly, the dose may have been too low. The authors do not indicate the daily dose administered to the patient, treatment duration, or whether the dose changed during the treatment period. Secondly, folinic acid is unable to cross the blood–brain barrier. Were CSF folinic acid levels determined at the end of the treatment period? Third, the ineffectiveness of the treatment may be explained by malabsorption of oral folinic acid. Did the patient have any gastrointestinal diseases that may have interfered with drug absorption? Patients with mitochondrial diseases frequently display such gastrointestinal manifestations as gastroesophageal sphincter dysfunction, constipation, dysphagia, vomiting, gastroparesis, gastrointestinal pseudo-obstruction, diarrhoea, and pancreatitis.³ Were folinic acid levels determined before and after treatment? Furthermore, treatment adherence may have been poor. Did the patient's carers supervise medication?

Although treatment had no clinical effect, it may have had a subclinical effect, reducing the heteroplasmy rate. Was the heteroplasmy rate determined before and after treatment?

KSS is frequently associated with high lactate concentrations in the serum or CSF. Was the lactate level determined before and after treatment?

Some studies with small samples of patients with KSS support the benefits of folinic acid⁴ while others have found no effect⁵; no clinical trial has provided evidence that folinic acid is effective for treating KSS.

Given that patients with KSS usually present mitochondrial multiorgan disorder syndrome, the authors should have provided information on any other medications the patient may have been taking. Was the patient receiving mitochondrial-toxic drugs? Mitochondrial dysfunction may constitute an adverse reaction to a concomitant medication.

In any case, the article by Pardo Ruiz et al.¹ is interesting in that it shows that folinic acid may be ineffective in patients with a single mtDNA deletion. The ineffectiveness of the treatment has several potential explanations, which should be considered in our communication with patients.

References

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