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Letter to the Editor

Anti-NMDA receptor encephalitis: The importance of early diagnosis and aggressive immunotherapy in tumor negative pediatric patients

Dear Editor,

We read with interest the recent article by Kashyape et al. on the successful use of Cyclophosphamide in Anti-NMDA receptor encephalitis[1] and the related editorial in the same issue.[2] The authors of the article describe the clinical course and treatment of three female pediatric patients who had minimal response to first-line immunotherapy, including plasma exchanges for two of them, but dramatic clinical response after intravenous cyclophosphamide. They propose an early and aggressive approach when first-line immunotherapy, including steroids, immunoglobulins and plasma exchanges, fails. We report another interesting observation of a young girl, who showed an unexpectedly rapid clinical response and a complete recovery with a combination of plasma exchanges and rituximab started only three weeks after the onset of symptoms.

Our patient was a 7-year-old female child who presented to the emergency room with a history of behavioral changes (delirium, incoherent speech, auditory and visual hallucinations) and sleep disturbances since 10 days. On initial examination, choreiform movements of the upper and lower limbs, orofacial dyskinesia, and autonomic instability were observed. She also presented with a few self-limited seizures shortly after admission. Anti-NMDA receptor encephalitis was immediately suspected and rapidly confirmed with positive antibodies in both serum and cerebrospinal fluid. Cerebral MRI showed multiple patchy hyperintense T2 and FLAIR lesions. Tumor screening was negative. She was treated with a 5-day course of intravenous methylprednisolone from day 1 of her hospital admission (10 days after onset of symptoms) followed by oral prednisolone and intravenous immunoglobulins without any clinical response. Plasma exchanges were therefore started (at the beginning of the third week of symptoms), immediately followed by two doses of rituximab. Clinical improvement was observed 3 days after starting the plasma exchanges, with a rapid and progressive decrease in abnormal movements and agitation. She made continuous progress until she completely recovered, 8 weeks after her admission and a total of 10 cycles of Plasma exchanges. Repeat serum anti-NMDA receptor titers at 8 weeks were remarkably low (one tenth of the initial value), and her neurological examination was normal. On follow-up, 4 months after the onset of symptoms, she has resumed all her normal daily activities.

Anti-NMDA receptor encephalitis is a severe disorder with a dramatic clinical presentation, with often a purely initial neuropsychiatric phase, evolving into a severe encephalopathy accompanied by involuntary movements, seizures and autonomic instability; the disease course is typically prolonged and needs intensive care treatment.[3] Despite being highly suggestive on clinical grounds, the rarity of this entity makes it a diagnostic challenge, and a delay in the initiation of treatment may occur. An early diagnosis permits a rapid introduction of immunomodulatory therapy, and therefore, an early recovery.[4,5] There is no established treatment protocol for the management of anti-NMDA receptor encephalitis. Similar to the patients reported in the paper by Kashyape et al., our patient did not show any response to steroids and immunoglobulins used as first-line options; however, the aggressive initiation of plasma exchange and rituximab from the third week of symptoms were rapidly followed by favorable effects, and the recovery phase was considerably shorter than previously reported. These observations underline the importance of an early recognition, likely to be crucial in the management of these patients. They also speak in favor of an aggressive therapeutic approach in these patients, including early plasma exchanges, as described also by other authors.[6] The optimal type and mode of immunotherapy remain uncertain. Whether first-line steroids and immunoglobulin could even be avoided in favor of other therapeutic options needs further evaluation.

Yours sincerely

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Mary Kurian*, Joel Fluss, Christian Korff
Pediatric Neurology, Child and Adolescent Department, University Hospitals, 6 Rue Willy-Donzé, CH 1211 Geneva 14, Switzerland

*Corresponding author.
E-mail address: mary.kurian@hcuge.ch (M. Kurian).

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