Short Communication

Wien Med Wochenschr
https://doi.org/10.1007/s10354-022-00943-0

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Wiener Medizinische Wochenschrift

Anti-MDA5 antibody-positive dermatomyositis with mild encephalopathy with reversible splenial lesion: a possible rare association?

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Received: 18 November 2021 / Accepted: 25 May 2022

Summary Central nervous system (CNS) involvement in dermatomyositis (DM) is seldom observed. However, there are very rare case reports of CNS involvement with juvenile dermatomyositis. Encephalopathy in DM may occur for a number of reasons, such as cerebral vasculitis and hypoperfusion/hypertensive encephalopathy, but mostly as a consequence of immunosuppressant treatment. We report here for the first time the case of a patient with two rare diseases, namely anti-MDA5 antibody-positive dermatomyositis and mild encephalopathy with reversible splenial lesion (MERS).

Keywords Encephalitis · Magnetic resonance imaging · Myopathy · Corpus callosum · Interleukins

Anti-MDA5-Antikörper-positive Dermatomyositis in Kombination mit leichtgradiger Enzephalopathie mit reversibler Milzläsion: eine mögliche seltene Assoziation?

Zusammenfassung Die Beteiligung des zentralen Nervensystems (ZNS) an einer Dermatomyositis (DM) wird selten beobachtet, und nur sehr selten gibt es Fallberichte über die Beteiligung des zentralen Nervensystems bei juveniler DM. Eine Enzephalopathie bei DM kann aus einer Reihe von Gründen auftreten, z. B. bei zerebraler Vaskulitis, Hypoperfusion/hypertensiver Enzephalopathie, meist aber als Folge einer immunsuppressiven Behandlung. In der vorliegenden Arbeit wird erstmals über einen Fall berichtet, in dem bei einer Patientin zwei seltene Krankheiten vorkommen, und zwar eine Anti-MDA5-Antikörper-positive DM und eine leichtgradige Enzephalopathie mit reversibler Milzläsion („mild encephalopathy with reversible splenial lesion“, MERS).

Schlüsselwörter Enzephalitis · Magnetresonanztomographie · Myopathie · Corpus Callosum · Interleukins

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We describe the case of a 20-year-old woman with no past medical history. She presented to our emergency department with a week-long history of irritability followed by altered mental status and fever. Patient history revealed that the patient had developed a non-pruritic reddish rash in her face and on the back of her metacarpophalangeal and interphalangeal joints without muscle weakness or arthralgia 2 months prior. The physical examination at that time of admission showed a confused patient with a Glasgow Coma Scale (GCS) score of 11/15, temperature 39.0 °C, blood pressure 110/68 mm Hg, heart rate 130 beats/min, SpO_2 99%, and respiratory rate 16 breaths/min. We found stiffness of the neck with negative Brudzinski's and Kering's signs. On dermatological examination, we found heliotrope rash (Fig. 1a) and periungual telangiectasias (Fig. 1b) with Gottron papules (Fig. 1c) on both hands.

Brain computed tomography (CT) revealed no abnormalities. Cerebrospinal fluid (CSF) was clear with normal protein at 0.28 g/l and glucose at 0.91 g/l, 3 leucocytes per mm^3, negative Gram stain, and sterile culture. Laboratory blood analysis revealed elevated

Published online: 21 June 2022

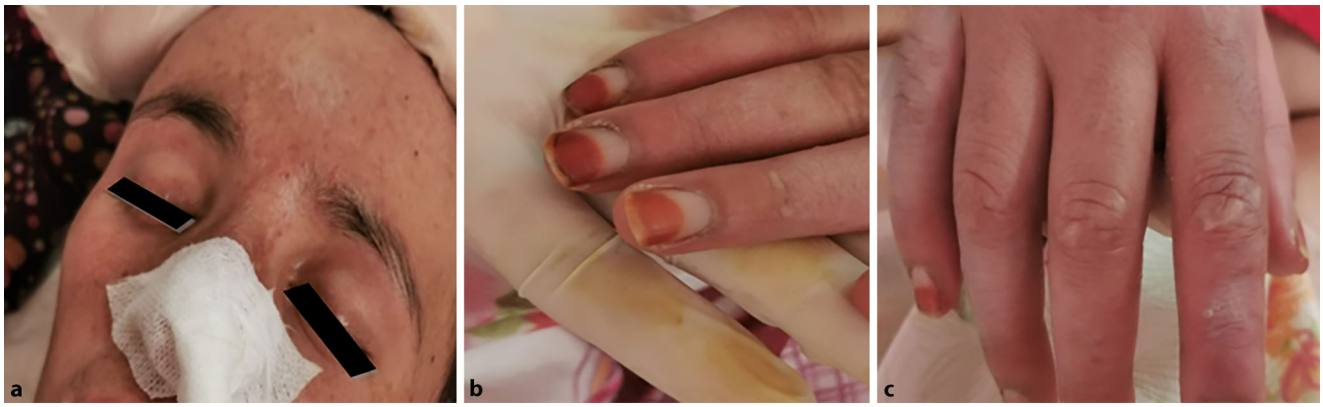

Fig. 1 Cutaneous manifestations suggestive of dermatomyositis. **a** Heliotrope rash. **b** Periungual telangiectasias. **c** Gottron papules

C-reactive protein and erythrocyte sedimentation rate (ESR; 11.5 g/l and 70 mm, respectively) with negative procalcitonin. Complete blood count (CBC), renal function, and serum electrolytes were normal with negative oropharyngeal swab for SARS-CoV-2 and ELISA SARS-CoV-2. Brain magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) were done 2 days after admission, revealing an oval-shaped focal lesion in the splenium of the corpus callosum, measuring 7 mm in diameter. The lesion was hyperintense on T2-weighted, fluid-attenuated inversion recovery (FLAIR) (Fig. 2a) and diffusion sequences (Fig. 2b), with restriction on the apparent diffusion coefficient (ADC) sequence (Fig. 2c). Dermatomyositis (DM) test panel was positive, showing an elevated creatine kinase (CK) of 3030 UI/L and positive anti-melanoma differentiation-associated gene 5 (MDA-5) antibody. Based on the EULAR/ACR classification criteria, we concluded that the patient had confirmed DM. After 1 week of hospitalization, the patient regained consciousness with a GCS of 15/15 without receiving any specific treatment. Follow-up brain MRI done after 7 weeks showed complete resolution of the corpus callosum lesion (Fig. 2d–f). The whole picture was in favor of mild encephalopathy with reversible splenius lesion (MERS). We concluded that the patient had anti-MDA-5 antibody-positive DM together with MERS.

Discussion

Mild encephalopathy with reversible splenial lesion (MERS) is a clinical-radiological syndrome that was first described by Kim et al. in 1991 [1]. MERS is commonly seen in Asian pediatric populations, less frequently among adults [2]. It is characterized by encephalopathy with altered consciousness, irritability, delirium, seizures, and fever, with typical reversible brain MRI images. Our patient had a similar clinical presentation, warranting brain imaging which showed characteristic findings compatible with the diagnosis of MERS.

The lesion is hyperintense on T2-weighted and FLAIR sequences, with diffusion restriction and no contrast enhancement [3]. It is located in the center of the corpus callosum for MERS type 1, or involves the corpus callosum and the periventricular white matter in a symmetrical pattern, so-called MERS type 2. Usually, the lesion resolves completely after a couple of weeks [3], as was the case of our patient.

The underlying pathogenesis of MERS is still unknown; however, infection, especially viral agents, are the main triggers, particularly influenza A and B and the rotavirus [4–6]. Recently, a few cases of MERS in patients with COVID-19 have been published [7–9]. In a case study of four children with MERS associated with H1N1 influenza, no viral RNA was found in their CSF, which suggests an indirect implication of viral agents in triggering MERS [5]. Other studies conducted in patients with MERS have shown associations with elevated leucocytes as well as elevated IL-6 and IL-10 levels in CSF [2, 10]. This points to a pathogen-induced myelin-specific response triggered by an infectious agent which activates the immune system and thereby the participation of inflammatory cytokines and generation of oxidative stress, subsequently leading to the reversible white matter lesions seen in MERS [6, 10, 11].

To the best of our knowledge, the association of MERS with autoantibodies has been reported in only two cases. Fujiki et al. described the case of an adult male with MERS and positive antiglutamate epsilon 2 receptor antibodies [12], and Oger et al. reported the case of 10-year-old boy with MERS and anti-GFAP astrocytopathy [13]. The presence of autoantibodies in CSF supports the theory that an autoimmunological mechanism is behind developing MERS. Bacterial agents such as *Mycoplasma pneumonia, Legionella pneumonia, Staphylococcus aureus Escherichia coli,* and *Klebsiella pneumonia* can also trigger MERS [6]. Other possible causes include administration or withdrawal of antiepileptic drugs, high-altitude exposure, and metabolic disturbances [1, 4].

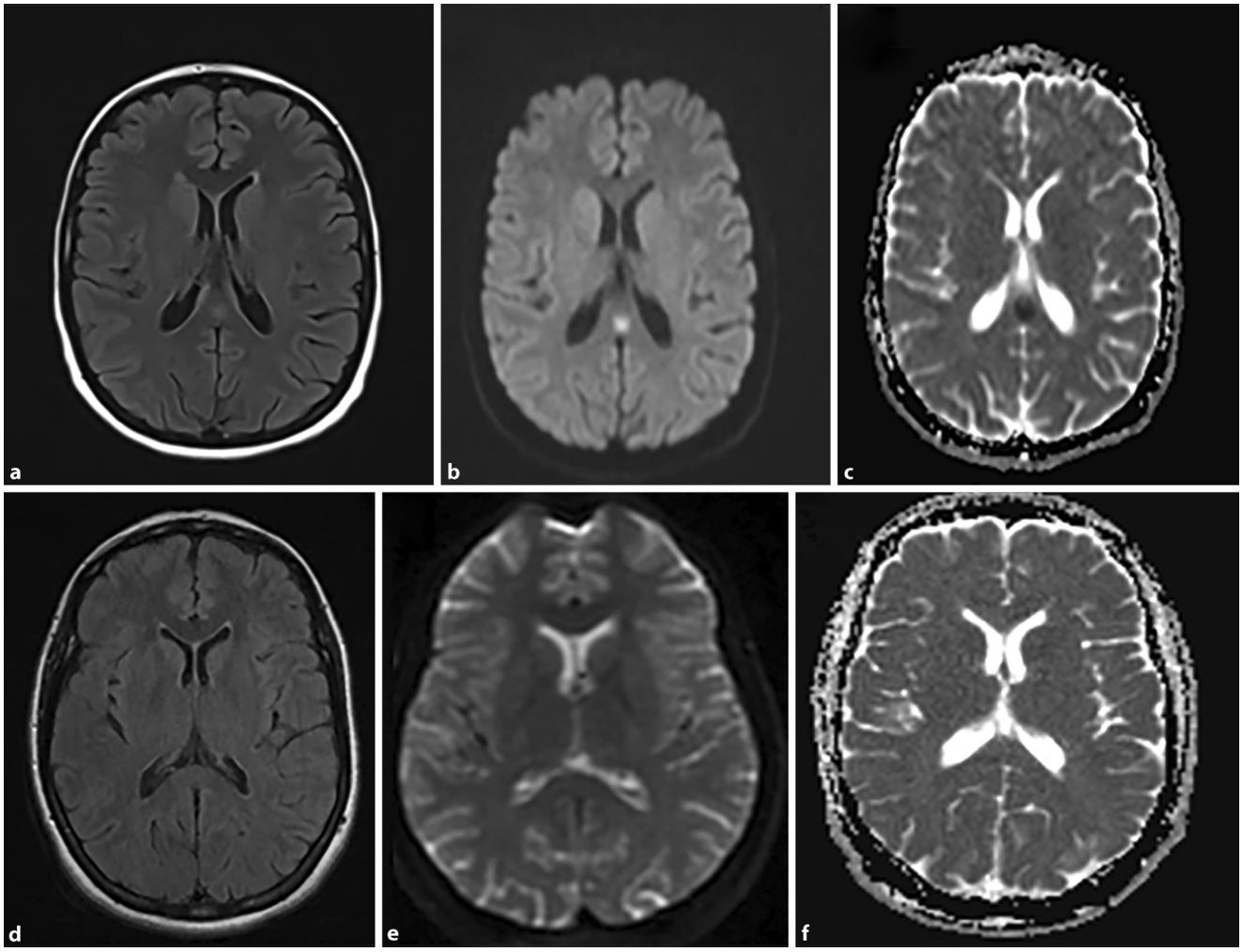

Fig. 2 Axial MRI of the brain demonstrates an ovoid lesion in the splenium of the corpus callosum, hyperintense on fluid-attenuated inversion recovery (FLAIR; **a**) and diffusion-weighted imaging (**b**), with diffusion restriction on apparent diffusion coefficient (ADC; **c**). Follow-up MRI after 7 weeks shows complete resolution of the lesion in the splenium on FLAIR (**d**), diffusion-weighted (**e**), and on ADC sequences (**f**)

Dermatomyositis (DM) is a rare idiopathic myopathy with muscle weakness and characteristic cutaneous manifestations [14]. Central nervous system (CNS) involvement in DM is seldom observed. However, there are rare case reports of CNS involvement with juvenile dermatomyositis (JDM) [15, 16]. Regan et al. described the first case of CNS vasculitis with refractory DM in adults [17], and Delman et al. reported a case of DM with positive anti-MDA-5 antibody associated with neuromyelitis optica spectrum disorder, probably due to the fact that the two diseases are both B cell-mediated autoimmune diseases [18].

Encephalopathy in DM may occur for a number of reasons, such as vasculopathy as a part of cerebral vasculitis of small or medium-sized vessels, hypoxic ischemic encephalopathy secondary to cerebral hypoperfusion/hypertensive encephalopathy, but mostly as a consequence of immunosuppressant treatment [14]. While MERS is supposed to be a post-infectious disease, its pathogenesis remains unclear. Our case of a patient with positive anti-MDA-5 antibodies in DM suggests that immune response may be the underlying mechanism of developing MERS.

Conflict of interest K. Saghir, M. Chraa, N. Kissani, H. Joulal, l. Essaadouni, and N. Louhab declare that they have no competing interests.

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