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COVID-19

Chickenpox and asymptomatic COVID-19 after first cycle of alemtuzumab for multiple sclerosis

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A 28-year-old woman, kindergarten teacher, developed double vision on left gaze in May 2018. Neurological examination revealed right internuclear ophthalmoplegia. Brain and spinal cord MRI showed 15 T2 and FLAIR hyperintense periventricular, juxtacortical, and infratentorial lesions and 2 lesions in the cervical spinal cord; 2 brainstem lesions showed Gadolinium enhancement. Cerebrospinal fluid was positive for oligoclonal IgG bands, and she was diagnosed with relapsing remitting multiple sclerosis (RRMS). The patient fully recovered after pulse methylprednisolone treatment. In July 2018, she developed incomplete transverse myelitis with Th12 sensory level when she again received pulse methylprednisolone treatment. MRI performed in February 2019 showed 5 new supratentorial lesions. Because of the highly active RRMS and pregnancy planning, it was decided to start treatment with alemtuzumab. During the work-up before starting alemtuzumab, varicella zoster virus (VZV) IgG came back negative, and vaccination against VZV was recommended before starting treatment. However, it took three doses of live attenuated varicella virus (OKA strain) vaccine (Varilrix®) until a titer of VZV IgG was satisfactory for treatment start (0.87) (< 0.60 negative; 0.60—< 0.90 intermediate; ≥ 0.90 positive; enzyme linked fluorescent assay). From March 9 to 10, 2020, the patient received the first course of alemtuzumab. She developed a rash from day 2 through 5, which was symptomatically treated. The patient did not take any other concomitant treatments. Lymphocytes ranged from 0.32 in May 2020 to 0.88×10^9 in October 2020. After an outbreak of chickenpox in the kindergarten, the patient developed small, itchy blisters on the arms and back on November 20, 2020 (Fig. 1). Therapy with acyclovir, 400 mg 5 times a day through 7 days, was initiated, and she completely recovered. At the same time, her husband was diagnosed with COVID-19, and she spent 14 more days in self isolation. She never developed any symptoms characteristic for COVID-19, and she returned to work. Oropharyngeal swab during her husband's quarantine was not performed. In December 2020, serology for SARS-CoV-2 revealed the titer of antibody to spike protein titer of 102 U/ml (positive value ≥ 0.8 U/ml, Elecsys® anti-SARSCoV-2 S assay, Roche Diagnostics Int., Rotkreuz, Switzerland).In March 2021, VZV IgG titer was 3.89, and the patient received second cycle of alemtuzumab.

Alemtuzumab is an anti-CD52 humanized monoclonal antibody which, by depletion and consecutive repopulation of T and B cells, in many persons with RRMS leads to a long-lasting remission [1]. One of the possible complications associated with alemtuzumab is increased risk of infections, the most severe one usually happening in close temporal relation to alemtuzumab infusions. The majority of the infections reported were caused by herpesviruses; however, with more patients being exposed, reports of listeriosis and other rare bacterial, viral, or fungal infections after an alemtuzumab treatment cycle have emerged [2]. Based on this increased risk of infections, many neurological societies recommended against starting or continuing alemtuzumab during the COVID-19 pandemic [3]. However, initial reports indicated mild COVID-19 infection in persons with RRMS receiving alemtuzumab [4]. Another problem of high efficacy RRMS therapy is possibility of immune system to mount a response to an infectious agent or vaccination. Only limited evidence regarding this question exists on alemtuzumab. In a small study, serum antibodies against common viruses remained detectable after treatment, and vaccine responses were normal to T cell–dependent recall antigens (tetanus, diphtheria, and polio), a T cell–dependent novel antigen (meningococcus C), and T

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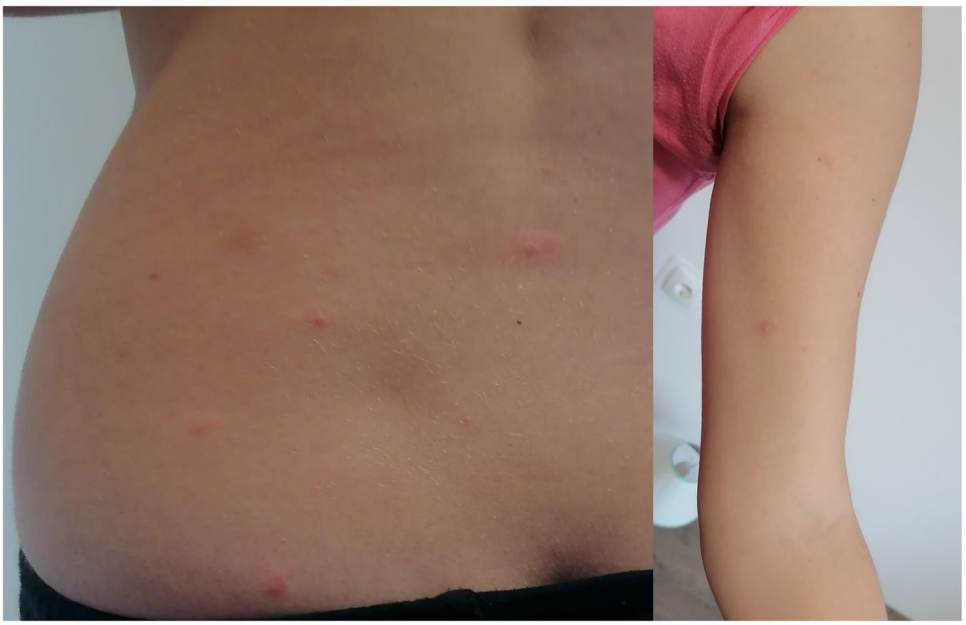

Fig. 1 Small, itchy blisters on the arms and back typical for chickenpox

cell–independent antigens (pneumococcal) [5]. Furthermore, there was no evidence for a diminished response to vaccinations in 5 patients studied within 6 months of alemtuzumab treatment [5]. So far, three cases of COVID-19 occurring in persons with RRMS from 1 week to 11 months after the last alemtuzumab cycle with positive SARS-CoV-2 IgG antibody were reported [6, 7].

The presented case had coexistent asymptomatic COVID-19 infection and very mild chickenpox 7 months after receiving the first cycle of alemtuzumab. The VZV vaccine effectiveness in a meta-analysis was 92% (95% CI: 88–95%), explaining the very mild clinical manifestation of chickenpox in the presented patient [8]. Furthermore, recently, a series on varicella-like exanthema as a specific COVID-19–associated cutaneous clinical picture has been described [9]. While the possibility that cutaneous manifestations in the presented case could be a consequence of COVID-19 cannot be excluded, the fourfold increase in the VZV IgG titer strongly argues for VZV infection. Finally, the main limitation of this case is that one cannot be certain that the patient developed the SARS CoV2 antibodies exactly during her chickenpox infection and her husband SARS CoV2 infection, although this is highly likely.

This case, together with previously published ones, suggests that appropriately selected persons with highly active RRMS benefit from treatment with alemtuzumab outweighs the risk, even in the time of COVID-19 pandemic.

Author contribution Study concept and design; acquisition of data; analysis and interpretation of data; drafting of the manuscript; critical revision of the manuscript for important intellectual content; administrative, technical, and material support: Habek.

Declarations

Ethical approval Not applicable.

Informed consent Not applicable.

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