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Case of alopecia universalis associated with alemtuzumab treatment in MS

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Alemtuzumab (Lemtrada®) is a monoclonal antibody recognizing CD52 that selectively depletes T- and B-lymphocytes[1] and is indicated for the treatment of relapsing-remitting MS (RRMS). Although it is highly efficacious, its use is associated with secondary autoimmune phenomena, such as thyroid dysfunction, immune thrombocytopenia, and glomerulonephritis.[2]

Alopecia areata is a form of autoimmune hair loss that can progress to the point of global hair loss, after which it is known as alopecia universalis.[3]

Here, we report a case of alopecia universalis in a young woman being exposed to alemtuzumab as treatment of highly active RRMS.

Case report

We report a 29-year-old woman with active RRMS, diagnosed in November 2014, who was otherwise healthy with no history of other autoimmune disorders and normal thyroid function. She had aggressive disease suffering 2 severe clinical relapses presenting with internuclear ophthalmoplegia and sensorimotor hemiparesis accompanied by a high and active lesion load on MRI. This prompted initiation of alemtuzumab treatment. Sixty milligrams of this antibody were applied over 5 consecutive days IV. Alemtuzumab was tolerated well. Since December 2014, her MS has remained clinically silent with no further relapses or disability progression. As expected, monthly laboratory controls revealed severe lymphopenia with total lymphocyte counts around 100/μL during the first months after commencing treatment. Six months after the last infusion, the patient noticed regional hair loss cumulating in generalized complete hair loss, including scalp, eyebrows, and pubic hair, within the following 3 months (figure). Otherwise, the patient was healthy. After 12 months, total lymphocyte counts were within the lower normal range (1,200/μL), with slightly decreased CD3 and CD4 counts and an increased CD19 count. A detailed laboratory workup showed normal values for all measures of thyroid functioning and absence of antithyroid antibodies. A large screening for autoantibodies revealed only low-titer antinuclear antibodies (indirect immunofluorescence test). A broad serum hormonal profiling was normal as well. A skin biopsy was performed 12 months after treatment initiation, which did not reveal any signs of local inflammation. Without any specific intervention, hair regrowth was first observed 15 months after the last infusion of alemtuzumab. At that time, all lymphocyte counts, including CD3, CD4, and CD19 subtypes, were within the normal range. Complete hair regrowth in all affected regions was seen 2 years after the last infusion.

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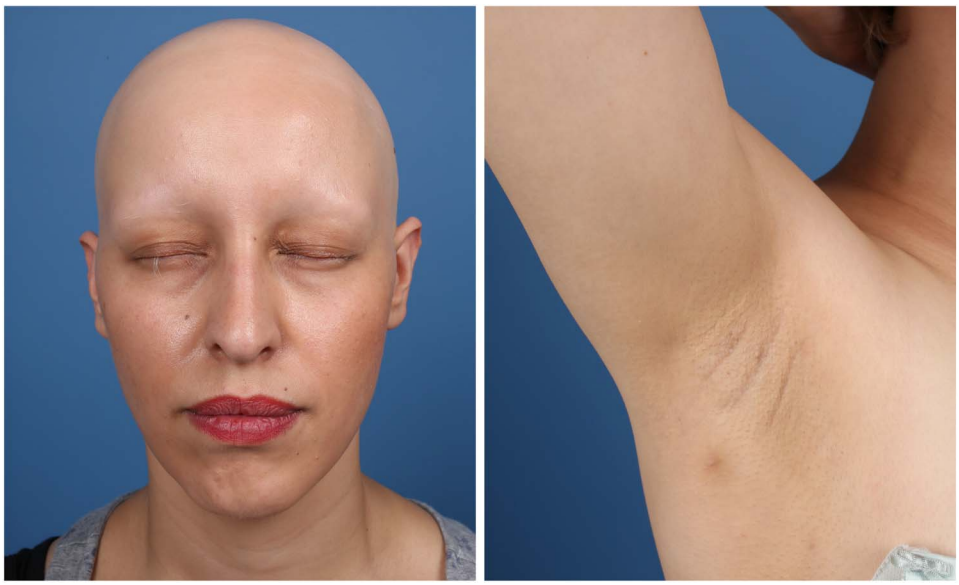
Figure Alopecia universalis 12 months after treatment initiation with alemtuzumab



Discussion

Alopecia is stated as a common adverse event in patients treated with alemtuzumab in the respective Summary of Product Characteristics published by the European Medical Agency; however, a case of generalized alopecia has not been reported in the literature so far.

The exact cause of alopecia areata is still unknown. Increasing evidence supports an autoimmune origin in the context of a genetic predisposition, modified by unknown environmental factors.[4] Cytotoxic T-lymphocytes are believed to mediate damage to hair follicles.[5] Because our patient did not have an additional autoimmune disease before treatment initiation, it is tempting to speculate that a secondary autoimmune phenomenon trigged by treatment with alemtuzumab may have caused the hair loss described. Alemtuzumab-associated secondary autoimmunity has been reported in up to 48% of patients and encompasses B-cell–driven disorders.[2,6] The high prevalence of this complication points to a potential predisposition in patients with MS.[1] In our patient, we were able to detect slightly elevated antinuclear antibodies, which may be reflective of B-cell activation, but could also represent a nonspecific finding. It is important to note that to date, a dominant hairy cell–specific B-cell autoantigen has not been identified and a primarily B-cell–driven autoimmune response causing hair loss has not been established.

Depletion of CD52-positive cells by alemtuzumab is incomplete.[2] It can therefore be anticipated that nondepleted cells could drive an early T-cell reconstitution through expansion, which would be in favor of immune populations that respond to self. This may explain, at least in part, the observed development of secondary autoimmunity after alemtuzumab.[7] It is difficult to judge whether such an expansion would be significant enough to cause hair loss already 6 months after the last infusion of alemtuzumab. The skin biopsy may have been performed too late to detect lymphocytic infiltrates.

In conclusion, alopecia universalis in this patient with MS may have been triggered by the therapeutic application of the monoclonal antibody alemtuzumab. The time course and the exclusion of other differential diagnoses would support this view. Our observation re-emphasizes that pharmacovigilance is crucial when treating patients with innovative therapies.

Author contributions

V.I. Leussink treated the patient, analyzed and interpreted the data, and wrote the manuscript. H.-P. Hartung critically revised the manuscript and provided important intellectual content. J. Reifenberger treated the patient, acquired, analyzed, and interpreted additional data.

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Disclosure

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