Childhood alopecia areata (AA) is associated with a poorer prognosis than adult AA (1). In 2011, we reported the results of a retrospective study conducted between November 2005 and December 2009 and evaluated the efficacy and tolerability of methotrexate (MTX) in severe childhood AA (S3–S5 according to Olsen et al. [2]) (3). Prior to treatment with MTX, some children had been treated with topical and systemic steroids. Of the 13 evaluable children, MTX was associated with hair regrowth of >50% in 5 children, but treatment failed in the remaining 8 patients. The maximal dose of MTX was 0.38 mg/kg weekly and the mean duration of MTX therapy was 14.2 months. MTX was given in the children together with once a week folate. There is a lack of alternative systemic treatment, therefore we concluded that MTX should be considered in severe and resistant childhood AA. However, long-term assessment of MTX therapy is lacking in childhood AA. The objective of this report was to assess the long-term outcome of patients from our previously published series.

MATERIALS AND METHODS

This was a long-term follow-up cohort study. Assessments were carried out between January 2010 and April 2014. Data were recorded from hospital records and patients’ photographs, which were collected during a regular medical follow-up. Patients were also contacted by phone to obtain missing data.

RESULTS

With regard to the 8 patients who did not have successful results from the previous MTX therapy in 2009, none were retreated with MTX and no hair regrowth was observed. The data from the 5 patients who experienced successful initial treatment in 2009 are shown in Table I. In 2 of these patients (patients 2 and 3), no relapse occurred after stopping MTX; follow-up after last MTX dose was conducted at 6 and 4.3 years, respectively. In the 3 remaining patients (patients 4, 5 and 14), no sustained hair regrowth was observed, even though 2 of them (patients 4 and 14) were successfully treated again with MTX (retreatment after AA relapse) (Fig. 1). Regrowth was observed in patient 14, but MTX was stopped because of recurrent nausea. In patient 4, regrowth (A4) was noted after the first retreatment, but relapse occurred when MTX was gradually tapered to 10 mg/week. Therefore, MTX was restarted, but no regrowth was observed after a second retreatment, despite a higher dose of 25 mg/kg being administrated intravenously. Similarly to the first study, no serious side-effects were observed under treatment.

The 3 patients who were not treated successfully (patients 4, 5 and 14) were asked for their opinions of the treatment. Patient 5 reported that MTX was important to get through adolescence. In contrast, patient 4 reported that if she could do things differently, she would not have undergone treatment because of the final failure of the treatment. Patient 14 had no opinion because his main problem was related to tolerance (nausea).

DISCUSSION

This is the first study to report the long-term effectiveness of MTX in childhood AA. Importantly there was an absence of spontaneous regrowth in the 8 patients in whom MTX treatment failed. This is in accordance with the fact that long-term severe AA is rarely associated with spontaneous regrowth (<10%) (4).
study suggests that the effectiveness of MTX in childhood AA can be maintained in the long term (several years), in contrast to other treatments with a high rate of relapse or no data on long-term effects, such as boluses of methylprednisolone (5) or diphencyprone (6). Nevertheless, this long-term effectiveness concerns only a minority of patients. Unfortunately, at initial examinations it is not possible to identify patients who are likely to benefit from MTX treatment. Comparison of responses to MTX in children with adult’s responses is difficult. In a series by Chartaux & Joly (7), after a short-term follow-up (30 months), 80% of the patients showed relapse after stopping or tapering MTX. Our study provides information regarding retreatment with MTX. Patient 4 noted an absence of hair regrowth after the third treatment with MTX, despite significant regrowth during the 2 previous MTX therapies. We are unsure whether this was because of a worsening of AA over time, as previously suggested (1), or a reduction in the efficacy of the treatment over time. To date, no other treatment is available for childhood AA, but new therapies with JAK1/2 inhibitors, such as ruxolitinib or tofacitinib, are under development (8).

In conclusion, MTX has possible long-term effectiveness, but it occurs in only a minority of patients. These novel data are important in helping clinicians with initial counselling of children and families and in deciding whether MTX should be prescribed for severe and resistant childhood AA.

Based on the fact that treatment with MTX may fail in most patients, or that its effectiveness will disappear with time, it seems reasonable not to use MTX too early in life, but to wait for adolescence, which is a difficult period for coping with AA.

REFERENCES