

Alopecia and Mood Stabilizers: Two Case Reports

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Summary. Two cases of alopecia observed during treatment with lithium and valproate are described, and the recent literature on this subject is reviewed. Our clinical observations confirm earlier reports. These toxic alopecias are characterized by a diffuse but rarely total hair loss. After stopping medication, the hair grows back generally and completely. Two cases of toxic alopecia are presented where hair grew back following a substitution of lithium by valproate in the first case and after stopping valproate in the second. The evaluation and therapeutic attitude in the presence of alopecia in patients needing mood stabilizers are also discussed.

Key words: Alopecia – Lithium – Valproate – Carbamazepine

Introduction

Diffuse alopecia represents about 4–8% of dermatological pathologies; it is the most common disease of the scalp (Mackie, 1981). A hair loss of 50 hairs per day is considered to be normal (Anderson 1980, Touraine and Revuz 1982). Some alopecias are physiological, like seborrheic alopecia in males (effluvium telogenum). Hair loss as a consequence of a medical treatment is a well-known side effect. Anticancer chemotherapy, antithyroid drugs, anticoagulants, triparanol, and the antiepileptics or the analogues of vitamin A may produce a diffuse alopecia (Blankenship 1983). Alopecias induced by drugs are generally characterized by a diffuse, nonscarring hair loss and by its reversibility after stopping the treatment. The hair loss may be very discrete, but is sometimes pronounced, leading to complete baldness (Brodin 1987). Sometimes the patient is not aware of the beginning of alopecia and of its possible connection with medication. Therefore it is difficult to establish the real incidence of this side effect.

The use of mood stabilizers (lithium, carbamazepine, valproic acid) is now very frequent, not only for the

treatment of affective disorders, but also of other psychiatric diseases, such as behaviour disturbances or alcoholism. Many authors have described, among other side effects, the occurrence of diffuse alopecias in some very rare cases (Albrecht 1985, Warnock 1991). We present two cases and review the present knowledge about alopecias induced by mood regulators.

Lithium

This is the most commonly used drug for the treatment of cyclic affective disorders. Two studies (Orwin 1983, McCreadie and Morrison 1985) have revealed that 12–17% of their patients, mostly women, complained of hair loss, but in other patients an abnormally large amount of hair loss has been observed despite the absence of complaints (Dawber and Mortimer 1982). This brings us to believe that the real incidence of alopecias is higher than has been supposed.

A review of the literature (Table 1) shows that the first description (Vacaflor et al. 1970) deals with a case of hair loss which developed 4 months after the beginning of treatment and which stopped only after withdrawing lithium medication. Yassa and Ananth (1983) found evidence of the reversibility of this side effect in two cases. The use of lithium seems to affect both the growth and the size of the hair. Two cases of total alopecia have been described (Vacaflor 1975, Silvestri et al. 1988). Generally, regrowth is observed after stopping lithium therapy and within a lapse of time ranging from several weeks to several months. However, in some cases, regrowth is not regular (Silvestri et al. 1988). The most evident demonstration of a cause/effect relationship was made in two patients, whose hair loss occurred after reintroduction of lithium (Jefferson et al. 1979, Yassa and Ananth 1983). Acnea and psoriasis are two dermatoses which are most often associated with alopecias induced by lithium (Sarantis and Waters 1983).

The aetiological factors are unknown and it does not seem that an increased concentration of lithium in the hair root is a causal factor (Muniz et al. 1982). Kusumi (1971) has shown that lithium salts accumulate in the

Table 1. Case reports of hair loss and lithium (Adapted from Mortimer and Dawber 1984)

Authors	Publication year	No. of case	Gender	Age	Side effect	Duration (months)	Comments
Vacaflor et al.	1970	1	F	36	Alopecia	4	Partially reversible after stopping lithium
Vacaflor	1975	1			Diffuse alopecia progressing to a total alopecia		
Jefferson et al.	1979	6	F	21–38	Diffuse alopecia	5–54	Thyroid dysfunction in two cases Hair regrowing under lithium treatment in three cases Withdrawal and again hair loss after reintroduction in two cases
Muniz et al.	1982	1	F	27	Diffuse alopecia	6	Regrowing under lithium medication
Dawber and Mortimer	1982	7	F	39–50	4 diffuse alopecia 3 symptomatic alopecia	4–9	
Yassa and Ananth	1983	2	F	51–53	Diffuse alopecia	5 6	Regrowing under lithium medication Hair regrowing after lithium withdrawal and again hair loss after reintroduction of lithium
Shader	1983	2			Diffuse alopecia		
Orwin	1983	11	F		Diffuse alopecia		Hypothyroidism in 3 cases Hair loss of various parts of the body (one case of alopecia areata)
Ghadirian and Lalinec-Michaud	1986	1	F	56	Diffuse alopecia	5	Hair loss of various parts of the body, psoriasis
Eustace	1986	1	F	47	Diffuse alopecia	1,5	
Yassa	1986	3	F		Diffuse alopecia	5–14	
Silvestri et al.	1988	1	F	59	Diffuse alopecia	2	Total hair regrowing
Uehlinger et al.	This report	1	F	30	Diffuse alopecia	5	Regrow after stopping lithium. No hair loss after introduction of valproate

hair, but Mortimer and Dawber (1984), and Muniz et al. (1982) reported that hair loss happens with lithium levels within the therapeutic range. Hypothyroidism, sometimes observed during lithium therapy, has been claimed to be a causal factor, but this is not proven. According to this hypothesis, patients with a history of Hashimoto thyroiditis would mainly be affected (Shader 1983, Mortimer and Dawber 1984). Orwin (1983) has described 12 cases of alopecia caused by lithium treatment, three of which suffered from hypothyroidism. Two of these three cases were treated successfully with thyroxine.

Case Report (No. 1)

A female patient, 30 years old, unmarried and without a professional activity, had suffered from recurrent major depressive episodes for 8 years. Two years previously, she had tried to commit suicide by defenestration. She was hospitalized several times in psychiatric institutions, where she was treated with different antidepressants and sedative neuroleptics. During her last depressive relapse, which resulted in an admission to our psychiatric hospital, she agreed to a treatment with lithium carbonate (1200 mg per day). Unchanged additional medication was: fluvoxamine (100 mg/day) and chlorazepate (30 mg/day). Blood lithium levels reached 0.50 mmol/L maxi-

mum. Thyroid tests performed before and during lithium therapy gave normal values. Several weeks later, the patient complained of significant hair fall on her dress. In addition, when she washed her hair, she lost an abnormal quantity. Despite her early observation of this side effect, she only informed the nurses about 8 months later. The lithium medication was stopped and replaced by a treatment with sodium valproate. Within a few weeks and ever since then, the patient observed regrowth of her hair. Her depressive state also improved during hospitalisation, and she was able to restart an activity in a rehabilitation centre. Therefore, the replacement of one mood stabilizer by another had not effect on the favourable therapeutic outcome in this patient.

Carbamazepine

The utilisation of carbamazepine is well known for anti-epileptic treatments. However, for about the last 10 years, this drug has also been prescribed for mood disorders (Dose et al. 1987). A single case of alopecia associated with carbamazepine has been described in the literature up to the present day (Shuper et al. 1985). It was observed in an 8.5-year-old girl, whose pathological EEG led us to suspect a multifocal epilepsy, which was treated with doses reaching 300 mg/day carbamazepine. After 1

month of treatment, this young girl suffered from hair loss localised in the occipital region. Medication was gradually stopped and her hair grew back totally within 1 month. She had previously received propranolol for severe migraine. Propranolol is known to be associated with toxic alopecias (Martin et al. 1973), but it was readministered after stopping carbamazepine without consequent loss of hair. In this case, alopecia occurred at lower carbamazepine serum levels than those considered as therapeutic.

Valproate

Valproic acid or valproate is also an antiepileptic drug. In addition, this therapeutic effect has been shown in recurrent affective and schizoaffective disorders (McElroy et al. 1987, Pope et al. 1991). Alopecia has to be considered as part of the common side effects of valproate (Jeavons and Clark 1974, Jeavons et al. 1977, Völzke and Doose 1973, Sherard et al. 1980). Hassan et al. (1976) presented the cases of three patients complaining of hair loss in a study including 115 patients treated with varying doses of valproic acid (1200–1800 mg/day) for treatment-resistant epilepsy. Zaccara et al. (1987) reported about four cases of alopecia (three men and one woman). One of the patients received the drug alone and the others as part of a polymedication. In these subjects, hair loss was evident between the 12th and 20th week of treatment with a progressive aggravation. Herranz et al. (1981) described in a child both alopecia and a modification of the hair colour provoked by valproate. Finally, Covanis et al. (1982), in a study of 31 cases of alopecias due to valproate treatment, reported that the changes in hair thickness were temporary and that regrowth occurs generally despite continuation of the treatment.

Case Report (No. 2)

Mrs. B., a 50-year-old unmarried woman had been suffering from schizophrenia for 30 years. During her 7th psychiatric hospitalisation, she was treated with 10 mg/day haloperidol and 80 mg/day levopromazine. She showed manifest symptoms during a clinical evaluation. Consequently, valproic acid was gradually and successfully introduced 4 weeks later, in association with the neuroleptic. After 3 months of continuous treatment with a maximal dose of 1300 mg/day valproate, the nurses observed a significant deposit of hair in the bath after the patient had taken a shower. The persistence of alopecia over 2 months led to a dermatological examination which confirmed hair loss. Valproate was stopped and 8 weeks later the alopecia had completely disappeared, but the psychic state of the patient had clearly worsened. When evaluating the risk/benefit, it was decided to reintroduce progressively valproate to reach the same above-mentioned dose 2 months later. Her clinical state clearly improved, and surprisingly no further hair loss was observed from then on. During this time, the comedication

was not altered. This woman had been suffering from menopause for 5 years.

Conclusions

Several authors agree that the diagnosis of alopecia due to medication is difficult (Warnock 1981, Mortimer and Dawber 1984). Indeed, clinical evidence of a cause/effect relationship for a particular drug can only be established if alopecia occurs again after its readministration.

Our first observation shows that stopping lithium also halted alopecia and that the reintroduction of valproate was without side effects. In this patient, the fluvoxamine comedication could have played a role, as it has been shown that other psychotropic agents may provoke alopecias, especially some antidepressants (Warnock 1991, Jenike 1991). The mechanism of action which is responsible for alopecia during a treatment with mood stabilizers is not clear. One does not know whether it is a direct toxic effect or the result of a process comparable to that which occurs in the case of alopecia areata or hypothyroidism.

The evolution of the second case is surprising, as alopecia did not reappear when valproate was reintroduced, which would suggest that this drug was not the causal agent. However, hair loss stopped when this medication was withdrawn. It is possible that the comedication with haloperidol may have contributed to alopecia, but actually this medication was never withdrawn. Supposedly there were some momentary biological conditions which favoured alopecia (endocrinological factors, capillary metabolism such as effluvium telogenum, etc.). Also, in the case of hair loss observed during treatment with mood stabilizers, it is important to eliminate reactional factors (psychological, traumatic) and to proceed to routine laboratory examination, including the measure of the thyroid function. Moreover, it is recommended to stop the suspected medication.

In some patients it is, however, difficult to abandon the use of mood regulators. As an alternative treatment, the use of another agent proposed for the same indication (case No 1) is suggested. If the conditions are favourable or in the case of intolerance to other mood stabilizers, it may be possible to try to reintroduce the treatment with the same drug, progressively increasing the doses very cautiously.

In conclusion, toxic diffuse alopecia is mostly benign and reversible, but this side effect has to be very seriously taken into account, when a treatment with mood stabilizers is evaluated. Indeed, it could be easily the origin of a bad compliance and consequently lead to relapses.

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