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Short communication

Hair loss with levetiracetam in five patients with epilepsy

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ABSTRACT

Purpose: To report cases of hair loss with levetiracetam (LEV) in epilepsy patient and summarise their demographic and clinical features.
Method: All patients reported attended the epilepsy outpatient clinic of the West China Hospital, Sichuan University. Demographic and clinical information was obtained from medical records and by interview. All the patients were under regular follow up.
Results: Five epilepsy patients (4 females and 1 male) are reported. All developed hair loss within two months of starting LEV treatment. Three had idiopathic epilepsy, two symptomatic epilepsy. Three patients received LEV monotherapy, two combination treatment. None decided to switch away from LEV to another drug after developing hair loss, although the dose of LEV was reduced in one patient.
Conclusion: Hair loss may be a rare side effect of LEV treatment in patients with epilepsy. LEV-related hair loss appears reversible if the dose is reduced or treatment is stopped.

1. Introduction

Levetiracetam (LEV) is a second-generation anticonvulsant approved by the Federal Drug Administration in 1999 for the treatment of epilepsy. It has been reported that LEV has a low incidence of both adverse effects and interactions with other antiepileptic drugs.[1] Well-known adverse effects of LEV include somnolence, dizziness, and behavioural abnormalities. In the treatment of patients with antiepileptic drugs (AEDs), hair loss or alopecia had commonly been reported in association with valproate (VPA),[2] occasionally with carbamazepine (CBZ)[3] and lamotrigine (LTG),[4] and only rarely with LEV[5]; to our knowledge, hair loss or alopecia has not been previously reported in Asians patients. Here, we present five patients who developed hair loss after starting LEV therapy and summarise their demographic and clinical features.

2. Case reports

All patients attended the epilepsy outpatient clinic of the West China Hospital, Sichuan University. Demographic and clinical information (Table 1) was obtained from medical records and by interview.

2.1. Case 1

A 24-year-old woman was diagnosed with generalised epilepsy at the age of 21. Her habitual seizures were generalised tonic–clonic seizures (GTCSs). Cranial MRI was normal and routine electroencephalography (EEG) showed generalised epileptiform activity. After the third seizure, the patient started LEV (750 mg/day) treatment. Two months after starting LEV therapy, the patient developed appreciable diffuse hair loss, and she was referred to a dermatologist at our hospital, who then excluded the most common causes of hair loss, including dermatological problems, thyroid disease, nutritional deficiency and autoimmune disturbances such as systemic lupus erythematosus. The patient was not pregnant and did not receive any other medications than LEV at the time. Although the patient was told that the hair loss may have been caused by LEV intake, she was so worried about a recurrence of her seizures that she decided to continue LEV (750 mg/day). In the following year, her seizures were controlled well but the hair loss continued. The dose of LEV was gradually reduced and stopped over six months, by which time her hair loss demonstrated improvement and had almost recovered.

2.2. Case 2

A 26-year-old woman was diagnosed with generalised epilepsy at the age of 24. Her habitual seizures were GTCSs. Cranial MRI was normal and routine EEG showed generalised epileptiform activity. After more than one year of TPM (100 mg/day) treatment, the patient continued to experience regular seizures. LEV (500 mg/day)

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Table 1
Demographic and clinical characteristics of the five cases.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Age (years)	24	26	21	39	31
Gender	Female	Female	Male	Female	Female
Onset age (years)	21	24	12	6	29
Aetiology of epilepsy	Idiopathic	Idiopathic	Symptomatic	Symptomatic	Idiopathic
Seizure type	GTCSs	GTCSs	CPS, GTCSs	CPS, GTCSs	GTCSs
Frequency of seizures (before LEV intake)	Weekly	Monthly	Weekly	Weekly	Monthly
Epilepsy duration (years)	3	2	9	33	2
MRI	Normal	Normal	Abnormal	Abnormal	Normal
EEG	Abnormal	Abnormal	Abnormal	Abnormal	Abnormal
Number of AEDs	1	2	1	3	1
Drugs taken	LEV	TPM, LEV	LEV	VPA, OXC, LEV	LEV
Dose of LEV (mg/day)	750	1000	1000	1000	500
Time to notice hair loss (weeks)	8	6	8	6	3
Type of hair loss	Diffuse	Diffuse	Diffuse	Diffuse	Diffuse
Drugs adjusted	No	Yes	No	No	No
Outcome					
Seizure control	Well	Lower frequency	Well	Lower frequency	Well
Hair loss	Remitted	Improved	Improved	Improved	Remitted

Abbreviations: GTCSs, generalised tonic–clonic seizures; CPS, complex partial seizure; AEDs, antiepileptic drugs; VPA, valproate; OXC, oxcarbazepine; LEV, levetiracetam.

was added and increased to 1000 mg/day two weeks later, after another seizure. One month after starting LEV (1000 mg/day), the patient noticed increasing hair loss. She was referred to a dermatologist, who excluded the most common causes of hair loss. The hair loss was considered to be secondary to LEV. Due to the good treatment response, LEV was not stopped but was decreased to 750 mg/day. At a four-month follow-up, seizures had not recurred, but her hair loss had improved, although it had not remitted completely.

2.3. Case 3

A 21-year-old man was diagnosed with partial epilepsy and had suffered from complex partial seizures (CPSs) and secondarily GTCSs since the age of 12. Cranial MRI showed changes in the right occipital lobe most likely to have been caused by a dysplasia, and routine EEG showed focal epileptiform activity mainly in the right occipital zone. The patient had taken VPA (1500 mg/day) since the age of 14. This treatment had been stopped approximately two years previously, at which time the LEV (1000 mg/day) treatment had been started. Two months after starting LEV treatment, the patient noticed appreciable hair loss. As the most common causes of hair loss had been excluded by a dermatologist, the hair loss was considered most likely to be associated with the LEV treatment. However, the patient decided to continue the LEV (1000 mg/day) treatment, as it seemed effective for his seizures. In the following months, the hair loss continued, but his seizures were well-controlled. After the patient had been seizure free for one year, the dose of LEV was reduced to 750 mg/day, and at three-month follow-up, his hair loss demonstrated improvement.

2.4. Case 4

A 39-year-old woman was diagnosed with partial epilepsy at the age of 6. Her habitual seizures were CPSs and secondarily GTCSs. Cranial MRI showed changes in the left temporal lobe most likely to have been caused by a dysplasia, and routine EEG showed focal epileptiform activity mainly in the left temporal and frontal zone. The patient had been treated with VPA (1000 mg/day) in combination with clonazepam (2 mg/day) since the age of 26, and oxcarbazepine (600 mg/day) was added and clonazepam was stopped two year prior to her presentation. However, she continued to experience frequent seizures and LEV (1000 mg/day) was started as add-on therapy. At a two-month follow-up, the patient reported no seizures but had developed diffuse hair loss approximately six weeks after starting LEV. The hair loss was considered due to LEV, as the most common causes of hair loss had been excluded by a dermatologist. However, as her epilepsy had proven refractory to other treatments and appeared to be responding to LEV (1000 mg/day), the patient agreed to continue this treatment. At a three-month follow-up, although the hair loss continued, the seizures were controlled well, and the patient continued treatment despite continuing hair loss.

2.5. Case 5

A 31-year-old woman was diagnosed with generalised epilepsy at the age of 29 when she had two GTCSs at night during sleep in a one-month period. Cranial MRI was normal and routine EEG showed generalised epileptiform activity. The patient was given LEV (500 mg/day) after the second seizure. At two-month follow-up, the patient complained that she noticed increasing hair loss approximately three weeks after LEV was initiated. She went to see a dermatologist, who excluded the most common causes of hair loss, and the association of the hair loss with the administration of LEV was noted. However, as the patient worried more about the risk of seizure recurrence and she did not find the hair loss intolerable, she agreed to continue to take the treatment. In the following year, the hair loss continued, but she did not become bald, and her seizures were well-controlled. Thereafter, the dose of LEV was gradually tapered and the drug was stopped altogether six months later. Her hair loss gradually stopped and her hair recovered completely.

3. Discussion

As there was a plausible temporal relationship between hair loss in these five patients and the administration of LEV, and as the most common causes of hair loss had been excluded, we suggest that our patients' hair loss was induced by LEV. However, LEV-induced hair loss appears reversible, as is observed in our patients that hair loss was improved or settled after the LEV treatment was stopped completely in two cases and reduced in another two.

Drugs can affect hair follicles primarily through two mechanisms: (i) by inducing an abrupt cessation of mitotic activity in rapidly dividing hair matrix cells, namely anagen effluvium, which is a prominent adverse effect of antineoplastic agents, or (ii) by inducing the premature rest of follicles, namely telogen effluvium,

which may be a consequence of a large number of drugs including anticoagulants, interferons, antihyperlipidaemic drugs,[6] and AEDs.[7,8] Accordingly, the hair loss in our report could be due to telogen effluvium. Although the mechanism by which AEDs causes hair loss remains unclear, zinc depletion has been reported to be the likely mechanism through which VPA causes alopecia,[2,9] which is similar to the LEV-induced hair loss.[5] This is supported by the finding that LEV enhances GABAergic transmission by contrast to zinc antagonism at $GABA_A$ and glycine receptors,[10] and phenytoin, the only other AED preventing zinc antagonism that is similar to LEV, has also been associated with hair loss.[10] However, two of the five patients in our report did not developed hair loss over a long period of VPA treatment, indicating that the hair loss induced by LEV and VPA does not necessarily share a common mechanism; this needs to be further investigated.

In summary, patients and clinicians should be aware of hair loss as a possible rare side effect of LEV treatment. As the LEV-induced hair loss improved after drug tapering or withdrawal, patients and clinicians should consider whether to reduce or stop LEV if they experience hair loss. If severe hair loss occurs, the dose should be adjusted or a switch to another therapy is warranted; in this way, patients' compliance is likely to be much better – a phenomenon which is likely to contribute to the effectiveness of antiepileptic medication.

Conflict of interest statement

None of the authors have any conflict of interest to disclose.

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