CASE REPORT

Alopecia areata and narcolepsy: a tale of obscure autoimmunity

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SUMMARY

Alopecia areata is an autoimmune dermatological disorder characterised by loss of hair in one or more discrete patches over the scalp. It has been linked to multiple disorders having an autoimmune origin. Like many autoimmune disorders it tends to be more common in females. To date, only five cases have been reported where alopecia has been associated with narcolepsy. Male gender is less commonly affected by alopecia areata. No case of alopecia areata in males has been associated with narcolepsy to the best of our knowledge. The current case represents the first ever-reported case of alopecia areata in a male patient with narcolepsy type 1. This coexistence is most likely the manifestation of a common underlying pathoimmunological mechanism that has not been completely understood, rather than a random association.

BACKGROUND

Alopecia areata is an autoimmune dermatological disorder characterised by loss of hair from the scalp or beard. A more severe and widespread type involves total loss of body hair including from the scalp, and loss of eyelashes and facial and pubic hair, this is called alopecia universalis. Alopecia areata has been linked to multiple other disorders of autoimmune origin. Speculation persists regarding association of alopecia and narcolepsy, given that both disorders could be related to autoimmunity and are prevalent in young adults. Narcolepsy in association with alopecia universalis, which represents a severe form of alopecia, has been reported in few male patients.¹ However, it has not been reported in association with alopecia areata in males. The current case represents the first ever-reported case of alopecia areata in a male patient with history of narcolepsy type 1. This case report supports the notion that along the 'alopecia spectrum', autoimmune activation does not necessarily have to be profound and widespread (such as that witnessed in alopecia universalis) to bear an association with narcolepsy, as even localised forms of the disorder (alopecia areata) can coexist with narcolepsy.

CASE PRESENTATION

A 25-year-old Hispanic man with a medical history of migraines presented to the sleep disorders centre for evaluation of fatigue and excessive daytime sleepiness ongoing for 5 years prior to presentation. The patient endorsed symptoms of cataplexy, which was manifested as sudden onset of weakness

in the knees bilaterally, during episodes of uncontrollable laughter. He also reported hypnagogic hallucinations, sleep attacks and sleep paralysis, all ongoing for the past 5 years. He recalled that, growing up in Mexico, he had experienced a few episodes of minor head injuries. Also, he reported having recently seen a dermatologist for hair loss from the scalp for 5 months. He was not using any rapid eye movement (REM) suppressing medications. He denied smoking, drinking alcohol or use of recreational drugs. He worked normal daytime hours as a construction worker. He denied any accidents during driving or at work, although his Epworth sleepiness score (ESS) suggested severe daytime sleepiness at a score of 20/24.

His body mass index was 31 kg/m². Physical examination of his scalp revealed a 6 cm×3.5 cm patch of non-scarring hair loss on the right occipitoparietal scalp with a few short 'exclamation point' hairs within it. Pull test at periphery was negative. No evidence of hair loss elsewhere in the scalp, or from the beard, eyebrows, eyelashes or other areas of the body, was noted. The patient's dermatologist had diagnosed him as having alopecia areata. Oral examination revealed modified Mallampati class 2 with no crowding of the airway.

INVESTIGATIONS

The patient underwent an attended, in-laboratory baseline polysomnogram (PSG), which showed mild obstructive sleep apnoea (OSA), with an apnoea-hypopnoea index (AHI) of 14.3, supine AHI of 13 and minimum oxygen saturation of 89%. It was felt that his degree of sleepiness was beyond what could be totally explained by the presence of mild OSA, which was predominantly positional in nature. Hence the PSG was followed by a daytime multiple sleep latency test (MSLT), which showed mean sleep latency of 2.8 min and 5 out of 5 sleep onset REM periods (SOREMP; figure 1).

TREATMENT

Given these clinical findings (presence of excessive daytime sleepiness, almost daily for over 3 months along with cataplexy) and polysomnographic findings (mean sleep latency of less than 8 min with presence of 2 or more SOREMP), the patient was diagnosed with narcolepsy type-1. He was started on oral methylphenidate 10 mg controlled release tablets once a day along with a recommendation for taking scheduled naps every day. Also, in light of the diagnosis of mild OSA, he was offered continuous positive airway pressure (CPAP).

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Figure 1 Daytime MSLT hypnogram following the overnight PSG. The patient fell asleep on all 5 nap opportunities. Notice the presence of sleep onset REM period (SOREMP) on all five nap opportunities. This is highly suggestive of narcolepsy. MSLT, multiple sleep latency test; PSG, polysomnogram; REM, rapid eye movement.

He declined using CPAP and instead opted for positional therapy (avoidance of supine sleep position).

OUTCOME AND FOLLOW-UP

At 6 months follow-up, the patient's excessive daytime sleepiness was under good control with daily use of oral methylphenidate. He had not experienced any new episodes of cataplexy although he continued to have occasional episodes of hypnagogic hallucinations. Also, regrowth of scalp hair was noticed after he had completed two rounds of intralesional corticosteroid injections in the dermatology clinic. Driving and workplace safety precautions were reviewed with the patient before he left the sleep clinic.

DISCUSSION

Alopecia areata is considered to be a T-cell mediated and natural killer cell facilitated autoimmune disease in which there is insidious collapse of the hair follicles' 'immune privilege'. Compared

with the general population, patients with alopecia areata are at increased risk of other autoimmune disorders such as vitiligo, systemic lupus erythematosus, psoriasis, thyroid diseases and allergic rhinitis.² Lately, evidence is accumulating to suggest an association between alopecia areata and narcolepsy.^{1 3} This is the sixth case in the literature reporting the autoimmune association between alopecia and narcolepsy (table 1). At the same time, the current case is unique as it represents the first ever-reported case of alopecia areata in a male patient with narcolepsy type 1.

Narcolepsy type 1 is characterised by specific loss of hypothalamic hypocretin-producing neurons.⁴ Given the strong human leucocyte antigen (HLA) association in narcolepsy, there is a hypothesis that type 1 narcolepsy involves autoimmune destruction of these neurons. One study found that 25% of patients with recent-onset narcolepsy type 1 produce autoantibodies against Tribbles homologue 2—an antigen also targeted in autoimmune uveitis.⁵ Whether these or other antibodies destroy hypothalamic hypocretin-secreting neurons has not been proven.

It is to be noted that the Chu *et al*² study analysing autoimmune disorders associated with alopecia areata made no mention of narcolepsy. This could be related to multiple factors. Narcolepsy type 1 is an uncommon disease with a prevalence of 0.02–0.18% and can have a bimodal peak for prevalence.⁴ Unless specific clinical questions are asked at the right time to the right patient, and objective sleep data collected simultaneously on PSG with MSLT, narcolepsy will be missed. Also, there is a social stigma associated with reporting of cataplexy, hallucinations and even excessive daytime sleepiness. Hence reporting bias can lead to underestimation of symptoms. Under-reporting of symptoms might also be related to presence of depressive symptoms, which are common in patients with narcolepsy.⁴ Another striking feature is that the association between these two autoimmune disorders in prior reports has been primarily found in non-Asian patients, which might explain why the Taiwanese study failed to find this obscure association. A narcoleptic patient with excessive daytime sleepiness might not be aware of asymptomatic, insidious hair loss, and many times hair regrowth might occur spontaneously before even discovering the earlier existence of alopecia. This will lead

Table 1 All reported cases of alopecia associated with narcolepsy

Subject (n)	Age in years at clinical presentation	Sex	Type of Alopecia (alopecia areata* vs alopecia universalis†)	Type of narcolepsy (type 1‡ vs type 2§)	Documentation that multiple sleep latency test (MSLT) was preceded by overnight polysomnogram (PSG)¶
1 ²	18	Male	Universalis	Type 1	No
2 ²	54	Female	Areata	Type 1	No
3 ²	39	Male	Universalis	Type 1	No
4 ³	19	Female	Initially areata but later progressed to universalis	Type 2	Yes
5 ³	20	Female	Areata	Type 2	Yes
6 ^{Present case}	25	Male	Areata	Type 1	Yes

*Alopecia areata: loss of scalp or beard hair in distinct patches.

†Alopecia universalis: loss of all scalp and body hair.

‡Narcolepsy type 1: Meeting clinical and polysomnographic criteria for narcolepsy along with cataplexy (or if CSF was tested, CSF hypocretin-1 concentration, measured by immunoreactivity, is either ≤ 110 pg/mL or $1/3$ of mean values obtained in normal patients with the same standardised assay regardless of symptoms of cataplexy).⁴

§Narcolepsy type 2: Meeting clinical and polysomnographic criteria for narcolepsy without cataplexy (and if CSF was tested, CSF hypocretin-1 concentration, measured by immunoreactivity, is either >110 pg/mL or $>1/3$ of mean values obtained in normal patients with the same standardised assay).⁴

¶Documentation that multiple sleep latency test (MSLT) was preceded by overnight polysomnogram (PSG): Overnight PSG helps to rule out acute sleep deprivation and delayed sleep-wake phase circadian disorder, both of which can lead to false-positive MSLT and erroneous diagnosis of narcolepsy. Also, overnight PSG can supplant one sleep onset REM period (SOREMP) to give a total of at least 2 SOREMPs needed to meet polysomnographic criteria for narcolepsy. Hence, wherever possible, overnight PSG should precede daytime MSLT.

CSF, cerebrospinal fluid.

to inability to capture alopecia areata in the patient with narcolepsy.

A common immunogenetic process explaining the coexistence of narcolepsy and alopecia is likely, though not confirmed. It has been found that there is an overlap in the DQB1 regions of

Patient's perspective

I have been informed about my sleep disorders by my doctors. I consent to the reporting on medically relevant data, as this will enhance the understanding of these diseases in the future.

Learning points

- ▶ This is the first ever-reported case of alopecia areata in a male patient with history of narcolepsy type 1. To date, six cases (including the current case) have been mentioned in the literature reporting association of type-1 or type 2 narcolepsy with some subtype of alopecia.
- ▶ Although severe subtypes of alopecia such as alopecia universalis have been associated with narcolepsy in men, even mild, self-limited varieties such as alopecia areata noted in this patient can be associated with severe narcolepsy.
- ▶ Although few case reports have been presented, the autoimmune association between narcolepsy and alopecia has not been established definitively.
- ▶ The lack of a concrete association between the two is likely attributable to the inability to capture two fleeting, uncommon diseases at the same time in any given patient. Under-reporting of symptoms of narcolepsy and asymptomatic, transient hair loss in alopecia areata that resolves spontaneously, might be the barriers to proving a statistically significant clinical association between these two autoimmune disorders.
- ▶ A strong clinical index of suspicion should be maintained when evaluating a patient with excessive daytime sleepiness or focal hair loss to ask them targeted questions to rule out coexistence of the narcolepsy and alopecia.

the HLA alleles in narcolepsy and alopecia areata. In individuals heterozygous for HLA allele DQB1*0602, an increased risk for developing narcolepsy is attributed to presence of DQB1*0301.⁶ Increased risk of developing alopecia areata is also associated with presence of DQB1*0301. Recently, a genetic link has been suggested between narcolepsy and a gene encoding T-lymphocyte receptor α that interacts with HLA proteins to generate an immune response.⁷ Both the brain parenchyma and proximal epithelium of hair follicle are sites of immune privilege where a downregulation or absence of major histocompatibility complex (MHC) class Ia expression prevents tissue destruction by autoreactive CD8+ T cells.⁸ Could there be an immunogenetic mechanism similar to the collapse of immune privilege at the hair follicles (that leads to alopecia areata) occurring at the hypothalamic hypocretin secreting neurons leading to narcolepsy?⁹ Rigorous histological experimental investigations are required to provide definitive answers to such questions.

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