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Late diagnosis of narcolepsy with cataplexy;

A novel case of cataplectic facies presenting in an elderly woman.

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ABSTRACT:

Cataplectic facies is an unusual feature described in children with narcolepsy and cataplexy. The typical manifestations of cataplectic facies consist of repetitive mouth opening, tongue protrusion, and ptosis. An interesting observation is that the usual emotional triggers associated with cataplexy such as laughter and joking are not always present, thus hampering diagnosis of the underlying syndrome. Cataplectic

facies is thought to be a phenomenon observed in the early stages of narcolepsy with cataplexy and is thought to disappear by the time the patient reaches puberty. We present a unique case of an elderly woman with narcolepsy and cataplexy demonstrating cataplectic facies. The novel circumstances of this case highlight that facial cataplexy can present later in life, in contrast with previous descriptions which report resolution of cataplectic facies before puberty. Wider recognition of these features throughout the life-course may aid in accurate diagnosis and thereby ensure swift access to appropriate treatment.

INTRODUCTION:

Cataplectic facies are increasingly recognised as an important indicator of underlying narcolepsy with cataplexy in children[1,2]. They include orofacial automatism, ptosis, tongue protrusion and asymmetrical facial twitching. This has hitherto been described as a feature commonly seen in the childhood disease, and in this group it may be mistaken for tics and focal seizures[2]. The clinical course and severity of narcolepsy in children is comparable to that in adults[3].

Cataplectic facies is a distinguishing feature of narcolepsy in early childhood[1,2,4] as it is thought to generally resolve prior to puberty[2,5]. Here we present a case of an older adult with diagnostic features of narcolepsy with cataplexy, including a long history of hypersomnolence and highly fragmented sleep and typical cataplectic facies. The patient was initially diagnosed with complex partial seizures and subsequently non-epileptic attack disorder before being referred to our unit.

To our knowledge this is a unique case of cataplexy with facial manifestations in an elderly patient, which was initially misdiagnosed for years as epilepsy and then non-epileptic attack disorder. The correct diagnosis guided subsequent treatment,

leading to a marked improvement in her life-limiting symptoms. The case highlights the importance of recognising signs of cataplectic facies in later life, in order to ensure accurate diagnosis and swift access to treatment.

CASE REPORT:

LD is a 77 year old right handed Caucasian lady who lives with her husband. She is a retired carpet machinist who worked in a local factory, all her working life from age 15 to 60.

She presented with a long history of poor, unrefreshing fragmented sleep, daytime hypersomnolence and the onset of paroxysmal episodes described as “funny turns”, all of which began 32 years ago (age of onset around mid-30s). The semiology of these episodes consisted of sudden collapse or slumping with no prior warning or subjective aura. She described the sensation of her legs ‘going to jelly’ and having to hold onto objects to avoid falling. An important diagnostic observation is her retained consciousness and full awareness of her surroundings during events. There is no associated amnesia; however she is unable to speak during the episodes. These events are brief lasting between a few seconds to 2 minutes. The onset and offset are abrupt, with a quick recovery and no associated cognitive deficits. Prior to treatment, the frequency of these attacks varied between 3-6 attacks per day.

In the medical history, she suffers from chronic ailments including essential hypertension, ischaemic heart disease, hypercholesterolemia and hypothyroidism. She had an acute myocardial infarction in 2001. She also underwent total abdominal hysterectomy surgery in 1985. She is an ex-smoker and gave up smoking over 5 years ago. She does not drink alcohol. There is no history of excessive tea or coffee intake.

Collateral history from LD's husband described her going limp and slumping down to the ground. An important observation is that the attacks typically begin with unilateral facial twitching (usually on the right) as well as tongue protrusion (a phenomena commonly observed in cataplectic facies in children[1,3]. During the attack her husband stated her head and jaw may drop and her eyes close, at which point she tends to hold on to something. If the attack progresses she will then slump to the floor. The attacks are triggered by tiredness or sudden loud noises (surprise). These tend to occur mostly when she is startled by a sound of a door bell or the phone ringing. The attacks can also be triggered by laughing and sometimes appear to be spontaneous. There are no other clear emotional triggers such as anger or stress and no hypnagogic hallucinations, but she reported having very occasional episodes of sleep paralysis.

In hindsight, it appears that her tongue protrusion and lateralised facial twitching were mistaken for focal epilepsy when she initially presented to neurologists over 20 years ago. She had been treated for presumed epilepsy since 1998, and was prescribed several different anti-epileptic medications (Lamotrogine, Carbamazepine, Valproate and Leviceracetam, Topiramate, Ethosuximide), to no effect. She stopped her anti-epileptics in 2013. Interestingly, she had experienced attacks in clinic settings which were witnessed by general physicians and other hospital doctors.

She was subsequently referred to the tertiary neurology centre and underwent ambulatory EEG. She was reviewed by another neurologist at this point and her diagnosis was revised to non-epileptic attack disorder (NEAD) in 2017. She was then referred to our centre for management of 'non-epileptic attacks.' However, the

clinical history raised strong suspicions of narcolepsy with cataplexy. She was booked for OPSG (overnight polysomnography) with video and Multiple Sleep Latency Test (MSLT) to confirm the diagnosis. Her sleep was staged according to Rechtschaffen and Kales, Hobson 1969[6].

In the clinic, the patient completed the Epworth Sleepiness Scale[7]: 11/24, and Insomnia severity index[8]: 20/28. Her Routine bloods were done including HLA typing. Notably, she was positive for the HLA-DBQ1*06:02 allele[9].

Investigations:

Previously, she had undergone several routine outpatient EEGs (EEG, Electroencephalography) which were all reported as normal. She had an ambulatory 72hr EEG in 2015 which captured several of her habitual events with no abnormal EEG correlates. Also, her 24 hour electrocardiogram was reported as normal and there was no postural drop in blood pressure during her attacks. Her brain MRI (Magnetic Resonance Imaging) scan (2014) showed moderate small vessel disease with a small amount of generalised brain atrophy but no focal pathology.

Prior to the OPSG, LD underwent 7 days of actigraphy (mean sleep latency 7 min, mean actual sleep time 6 hours 9 minutes, mean sleep efficiency 76.01%, mean fragmentation index 54.46). Subsequently, she attended for an overnight inpatient OPSG (see table 1) with video, and MSLT.

The daytime OPSG record demonstrated brief day time sleep on day one with some SOREM (sleep onset rapid eye movement sleep) noted. On day two, LD completed an MSLT which demonstrated short sleep latencies and SOREM (see table 2 and figure 1). During her admission the patient had three typical daytime episodes of

right facial twitching and tongue protrusion and drooping of the eyelids. These episodes demonstrated clear atonia on the EMG electrodes. One of these episodes was associated with laughing where the patient also went weak at the knees. There were no paroxysmal EEG changes associated with these events.

The night time OPSG record demonstrated short sleep latencies and SOREM (see table 1). There was fragmented sleep with a high wake after sleep onset index (WASO) of over 200, with anything above 50 being regarded as above average fragmentation. Although her sleep was poor with efficiencies of around 50%, all sleep stages were still present including N3 and REM (Rapid eye movement sleep). Over night, her Apnoea Hypopnia Index (AHI) was 12 (normal range < 5). Likewise, the Periodic Limb Movement index (PLMi) was 1.1 (normal range < 5). Overall, her OPSG, MSLT and video findings were consistent with a diagnosis of narcolepsy with cataplexy and cataplectic facies.

Outcome:

Following the test she was seen in clinic and commenced on a combination of low dose Modafinil 50mg and Venlafaxine 37.5mg. She showed a remarkable response with improvement in hypersomnolence and cataplectic attacks, which went into full remission. Although her tongue protrusion persisted, these were not troublesome to her. Her Epworth sleepiness score reduced significantly to 6/24. Moreover, her blood pressure remained stable. She remarked “I’ve got my life back.”

At 3, 7 and 12 months follow up, she maintained improvement in her symptoms and is ‘attack free’ on Ventalfaxine 75mg and Modafinil 150mg. However, she has had a longstanding problem of initial insomnia and remains on Clonazepam 1mg and Phenegran 10mg initiated by her GP.

Table 1 here.

Table 2 here.

Figure 1 here.

DISCUSSION

Cataplexy is typically defined as an “episodic, bilateral loss of muscle tone, triggered by emotions and with preserved consciousness”[10]. The clinical presentation of cataplexy in children can differ significantly from adults[3]. In children, cataplexy presents with a prominent facial involvement, for which the term ‘cataplectic facies’ has been coined.

Cataplectic facies have been described in children[1] and can confound or delay diagnosis of narcolepsy[2]. This may result in delays to treatment, as was demonstrated in the case of LD. The presence of asymmetrical facial twitching and tongue protrusion can cause diagnostic confusion.

In our case, the diagnosis of narcolepsy with cataplexy was established based on a long standing history of excessive daytime sleepiness; description and observation of the patient’s habitual episodes from the patient and her partner; as well as from using video OPSG. The presentation of tongue protrusion and asymmetrical facial twitching is atypical for narcolepsy with cataplexy in adults and is mostly seen in children[1,5] .

The novel circumstances of this case highlight that facial cataplexy can present late in life, in contrast with previous descriptions which report resolution of cataplectic facies before puberty[5]. Wider recognition of these features throughout the life-course may aid in accurate diagnosis and thereby ensure swift access to appropriate treatment.

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Figures and tables.

Table 1- Overnight PSG Sleep study statistics

***Sleep latency to N1 6.1 min**
***Latency to REM from N1 4.8 min**
Sleep efficiency 50.8%
Total sleep time 340 min
N1 sleep 29.4%
N2 sleep 43.1%
N3 sleep 11.2%
REM Sleep 16.3 %
AHI 12
PLM 1.1
WASO 216

Table 1 above shows the sleep statistics for the overnight polysomnography. *Short sleep and REM latencies are noted (normal sleep latencies are 10 minutes or more and normal REM latencies are greater than 20 minutes after sleep onset).

Table 2- MSLT Results

Start Time	Sleep onset latency	Non-REM Sleep stage entered	SOREM Present	SOREM latency
8.04	8min 41 sec	**N1 and N2**	**Y**	06 min 47 sec
10.05	4 min 21 sec	**N1 and N2**	**Y**	08 min 07 sec
12.10	4 min 05 sec	**N1**	**Y**	17 min 47 sec
14.10	01 min 52 sec	**N1 and N2**	**Y**	10 min 19 sec
Mean sleep latency	**4 min 45 sec**		**Mean SOREM latency**	**10 min 45 sec**

Table 2 above shows the results of the multiple sleep latency test for LD. It can be seen the mean sleep onset (4 min 45 sec) and REM (10 min 45 sec) latencies are abnormally short (normal mean values > 8 mins for sleep onset and > 20 minutes post sleep onset for REM).

Figure 1- MSLT Hypnogram

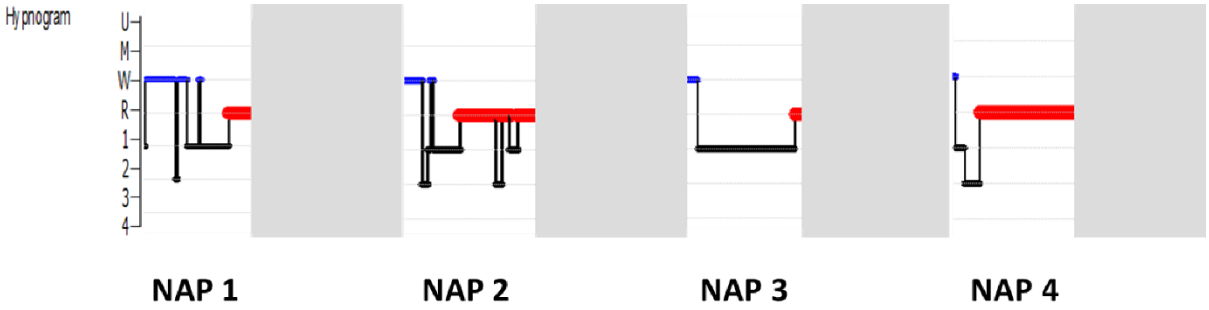

Figure 1 above is the hypnogram of the MSLT test. The blue line signifies awake and the red line SOREM. The numbers on the y-axis (U=unreadable, M=Movement, W=Wake, R=REM, 1, 2, 3, 4, represent sleep stages according to Rechtschaffen and Kales, Hobson 1969).The grey areas represent 2 hour periods of wakefulness between naps.