Lesson of the month (1): Cabergoline – 'I eat funny on that'

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ABSTRACT

We present the case of a patient treated for hyperprolactinaemia with weekly doses of cabergoline for 12 years. Over this time she had suffered from binge eating and compulsive shopping which impacted on her weight and made her finances precarious. We discuss the features of impulse control disorders and suggest that seeking out these side effects in patients taking such agents is important. The behaviours may be embarrassing and patients may not volunteer them, likewise if the doctor dismisses them they may continue unabated, causing significant social harm.

Case history

A 44-year-old lady was referred to the neurology clinic because of head and neck pain. On listing her comorbidities and medications, she particularly mentioned cabergoline, which she had taken for 12 years for hyperprolactinaemia, initially at a dose of 0.5 mg once weekly between 2001 and 2005, which was then increased to 3 mg once weekly. The patient said, 'I hate that one, it makes me eat funny'. When asked to elaborate, she explained that she compulsively ate 'Jamaican bread' – a high-carbohydrate sweet food. On being asked about any other 'funny things' she may have noticed while taking the treatment, she immediately listed compulsively buying unnecessary volumes of sanitary towels and clothing, as well as downloading and playing a letter/number game, which she perceived as a useless compulsive behaviour, whipping out her iPad to show a screen full of similar games. She also mentioned that she had been having compulsive imposed thoughts about self-harm and recognised that they were irrational and not her own. Cabergoline was stopped, and a week later she abruptly became aware that she was in debt and is currently seeking bankruptcy. This case history represents classic dopaminergic impulse control disorder. Now the cabergoline has been stopped, her prolactin levels are being monitored. The patient's neck and head pain ceased to be a problem. However, she has had to have counselling to help adjust to the upset of her financial situation.

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Discussion

Hyperprolactinaemia

Hyperprolactinaemia is the most common endocrine disorder of the hypothalamic–pituitary axis. In the general adult population, the prevalence of hyperprolactinaemia is about 0.4%.[1] Women present with galactorrhoea and secondary amenorrhoea, while men present with impotence and infertility.[2]

Hyperprolactinaemia can result from reduced secretion of dopamine from the hypothalamus and insufficient action of dopamine on the pituitary.[3] The multitude of causes can be categorised as physiological, pathological and pharmacological. The most common cause in clinical practice is reduced levels of dopamine due to pharmacotheraputic agents.[3]

Treatment aims to reduce levels of prolactin, which can be achieved by medical or surgical approaches. Medical therapy uses dopamine agonists that act on D_2-type receptors, which lead to a reduction in synthesis of prolactin. The three dopamine agonists currently licensed for endocrine use in the *British National Formulary* are bromocriptine, cabergoline and quinagolide.[4] Successful medical therapy for hyperprolactinaemia has limited the need for destructive surgical procedures.[3]

Limitations of dopamine agonists include possible teratogenicity in pregnancy and reduced lactation during the breastfeeding period.[4] In addition, there is a risk of inducing a psychotic episode in patients taking concurrent psychoactive medications.[5] Common side effects include nausea, constipation and headaches, while other reported side effects include hypotension, dyskinesia and impulse control disorder.[4]

Impulse control disorders

Epidemiology

Impulse control disorders are a group of pathological behaviours that have seen a notable increase in recognition over the past 10 years with regard to the use of levodopa and high doses of dopamine agonists to treat Parkinson's disease. They are less common and less recognised in endocrinology, where doses of dopamine agonists are lower and not given daily.[6]

Most of the literature describes impulse control disorders in patients with Parkinson's disease treated with dopamine agonists, in whom the prevalence is 17% in the UK and USA compared with 6% in patients with Parkinson's disease who have impulse control disorders but are not on dopamine agonist treatment.[7,8] This case report looks at impulse control disorders

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related to dopamine agonist treatment in a patient with hyperprolactinaemia. In this setting, one paper that looked at impulse control disorder in three groups of patients – those taking dopamine agonist treatment for adenoma-related or idiopathic hyperprolactinaemia, those with hyperprolactinaemia alone, and those with a hypothalamic lesion without high levels of prolactin – found a small increase in some measures of impulsivity in the first group.[9]

Definition and behaviours

The international and statistical classification of diseases and health-related problems, tenth edition (ICD-10) describes habit and impulse disorders as: 'repeated acts that have no clear rational motivation, cannot be controlled, and generally harm the patient's own interests and those of other people. The patient reports that the behaviour is associated with impulses to action'.[10] The main behaviours seen in impulse control disorders include excessive shopping, binge eating, pathological gambling, hypersexuality, punding and dopamine dysregulation syndrome.[7,11]

Excessive shopping and binge eating

Excessive buying and binge eating on certain foods that is impulsive and repetitive often centres around items that the patient does not necessarily need. This can cause patients and families to go into debt.[11]

Pathological gambling

Numerous forms of gambling are available to affected patients, such as casinos, betting shops and scratch cards. Recent access to online gambling has made it easier to hide this behaviour from others. Pathological gambling has led to people losing their houses; in one case, a patient lost up to $100,000 (about £60,000).[11]

Hypersexuality

This can start as an increase in libido and can result in inappropriate behaviours such as paraphilia, paying for sex and exhibitionism. These behaviours can affect a person's image in society and put a great deal of stress on a partner due to increased and inappropriate sexual demands. In one such case, a man demanded sex from his partner 5–6 times a day; when she eventually refused, the man decided to find a sexual partner who would satisfy his needs.[6]

Punding

Patients carry out repetitive, aimless behaviours and excessive hobbyisms from which it is hard to disengage and which are not done for pleasure.[11] Examples described by Evans *et al* include dismantling cars, lawnmowers and even fridges; senseless paper shuffling; filling pockets with useless things; and constant tidying and reorganising.[12]

Dopamine dysregulation syndrome

Dopamine dysregulation syndrome (DDS) is the compulsion to seek and overuse dopaminergic medications despite a lack of need or when use results in excessive dyskinesias.[7,11]

Management

The first step is to reduce the likelihood of impulse control disorders developing. Risk factors such as alcohol addiction and use of illicit drugs should be assessed, as should a positive family history of addictive behaviour, especially with regard to developing DDS. Single status and the lack of a support network puts patients at a higher risk of impulse control disorders. Hypersexuality and pathological gambling are seen more in men, whereas compulsive shopping and binge eating are more common in women.[7]

The next step is patient education. Particular types of behaviours related to impulse control disorders should be explained, so that the patient and their family members can identify and recognise them as side effects of the drug. The doctor should describe risk factors, and routine monitoring of the patient should be arranged after dopamine therapy is started. Particular attention should be paid to patients with Parkinson's disease who request frequent rescue doses and fast-acting levodopa or to patients who develop dyskinesias. This may be a sign of an impulse control disorder, particularly DDS,[7] but has not been described for patients with prolactinoma on dopamine agonists.

If impulse control disorders have been identified, doses of dopamine agonists should be tapered down until they can be stopped.[7,11] Cognitive behavioural therapy may be useful in patients with DDS to help them gain insight into their situation.[11] It is important to recognise the effect that impulse control disorders can have on patients and their families, so the availability and importance of counselling and psychological support should be mentioned.

Conclusion

Impulse control disorders can be triggered in patients taking low, intermittent doses of cabergoline used for hyperprolactinaemia and are a particular concern for patients taking high doses for Parkinson's disease. With an increase in recognition of these pathological behaviours, it is easier to identify symptoms in other patient groups taking regular dopamine agonist treatment (eg hyperprolactinaemia). This is important as they can be socially disruptive for patients and their families. ■

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Clinical Medicine 2014 Vol 14, No 2: 207–9 **LESSON OF THE MONTH**

Lesson of the month (2): All that glitters is not stroke

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Case presentation

A 62-year-old man was admitted via the emergency department having been found unresponsive with clenched teeth and open eyes. His family reported deterioration in speech over the previous 7 days that had worsened in the preceding 48 hours. They also reported complaints of dizziness and vertigo. The only past medical history of note was depression and anxiety that had been treated with gabapentin and mirtazapine. At presentation he was hypothermic with a temperature of 34.2°C, maintaining his airway, breathing spontaneously, cardiovascularly stable and with no identifiable biochemical or metabolic cause for a Glasgow coma scale (GCS) of 6. Neurological examination revealed normal tone and intact reflexes; however, power and sensation could not be assessed due to low GCS. The pupils were bilaterally equal and reactive to light.

Initial bloods were unremarkable. Non-contrast head computed tomography (CT) scan revealed bilateral occipital infarcts (Fig 1). Magnetic resonance imaging (MRI) was recommended by the radiologist to ascertain the diagnosis. Unfortunately the patient deteriorated into status epilepticus which could not be controlled by lorazepam. His airway was secured by rapid sequence intubation and he was invasively ventilated, sedated with propofol and paralysed with atracurium. A contrast CT angiogram was performed; this demonstrated bilateral ill-defined, non-enhancing areas of low attenuation within the posterior regions of parietal lobes in addition to similar bilateral lesions in the occipital lobes.

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Differential diagnosis included:

- cerebrovascular accident (CVA)
- infective encephalitis
- autoimmune encephalitis
- vasculitis.

Treatment

The patient persisted in status epilepticus with no improvement in GCS in the inter-ictal period. Given the absence of a definitive diagnosis and the suspicion of autoimmune or infective cause for his deterioration, intensive care was provided with a view to establish the diagnosis in the interim by further investigation. Sedation, paralysis and ventilation were continued in addition to the institution of the following neuroprotective strategies;

- head up tilt of 15–30 degrees
- put in neutral position with no restriction to head and neck venous drainage
- MAP of 80–90
- haemoglobin of 80–110 gm/l
- partial pressure of oxygen (PaO_2) of >13 kPa
- partial pressure of carbon dioxide ($PaCO_2$) of 4.5–5 kPa
- controlling of pyrexia and seizures.

He received a loading and maintenance infusion of phenytoin and sodium valproate to treat status epilepticus. Cerebral oedema, either due to infective or autoimmune origin, as well as status-related persistent hypertension, could not be ruled out. Therefore an infusion of 1 g/kg of mannitol along with dexamethosone was also administered.

Following a discussion with the neurologist and microbiologist (due to the suspicion of meningitis and encephalitis), antimicrobial therapy with aciclovir and cefotaxime were initiated. To establish the diagnosis a

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