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Conference case report

DULOXETINE-RELATED PANIC ATTACKS

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SUMMARY

Side-effects arising on the grounds of antidepressant administration pose as a substantial obstacle hindering successful depressive disorder treatment. Side-effects, especially those severe or those manifested through dramatic clinical presentations such as panic attacks, make the treatment far more difficult and shake patients' trust in both the treatment and the treating physician.

This case report deals with a patient experiencing a moderately severe depressive episode, who responded to duloxetine treatment administered in the initial dose of 30 mg per day with as many as three panic attacks in two days. Upon duloxetine withdrawal, these panic attacks ceased as well. The patient continued tianeptine and alprazolam treatment during which no significant side-effects had been seen, so that she gradually recovered.

Some of the available literature sources have suggested the possibility of duloxetine administration to the end of generalised anxiety disorder and panic attack treatment. However, they are outnumbered by the contributions reporting about duloxetine-related anxiety, aggressiveness and panic attacks. In line with the foregoing, further monitoring of each and every duloxetine-administered patient group needs to be pursued so as to be able to evaluate treatment benefits and weigh them against risks of anxiety or panic attack onset.

Key words: *duloxetine - side-effect - panic attack - anxiety*

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INTRODUCTION

Owing to the availability of a fairly large number of efficient antidepressants, depression can nowadays be successfully treated. Among antidepressants supplied to the market, a significant role is played by serotonin and noradrenalin reuptake inhibitors (SNRIs). This drug cluster sometimes also goes under the name "dual action antidepressants". One of the latest members of this cluster is duloxetine, which proved itself efficient in treating moderately severe and severe episodes of major depressive disorder (Nelson et al. 2010, Wise et al. 2009). Duloxetine is also administered to patients suffering from diabetic neuropathy (Goldstein et al. 2005) and stress urinary incontinence (Mariappan et al. 2005). Furthermore, duloxetine has proven itself effective in treating anxiety disorders, in particular those of a generalised type (Carter 2009), as well as in treating fibromyalgia (Arnold et al. 2004), chronic fatigue syndrome and musculoskeletal pain (Eli Lilly Ph 2006).

Based on its safety profile, duloxetine falls into the category of fairly safe antidepressants, most often associated with side-effects such as nausea, somnolence, insomnia, and dizziness reported by about 10% to 20% of patients (Wise 2009). Spontaneous post-marketing adverse event reports have brought forward a variety of other side-effects related to duloxetine administration; nevertheless, prevalence rates of these side-effects were substantially lower than those of major side-effects listed above. For that matter, a decrease in sex drive, hyperhidrosis, fatigue, inappetence and constipation have been registered in over 5% of patients. Aggravation of the existent anxiety and agitation has been reported in roughly 5 % of patients (Elli Lilly 2006). To the best of our knowledge, the available literature lacks reports on duloxetine-related panic attacks. Data on side-effect prevalence rates quoted above apply to major depressive disorder only, while side-effects witnessed with duloxetine treatment administered based on other indications, as well as their statistics, are somewhat different.

CASE REPORT

This case report deals with a 61-year old female patient, married, mother of two adults. Two years ago, she retired from a clerk position (of note, a senior clerk one). She was satisfied with her job and appreciated by her colleagues; she was looking forward to the retirement and made numerous plans for it. Her husband is still an active employee; they get along well and live in harmony, having no major concerns. Their children are fully independent, live under their own roofs and have families of their own. The patient has two grandchildren mothered by her daughter. She lives in a city, but spends summers in her house in the woods. She takes interest in many things and is of a good financial standing. She describes herself as a happy person prone to socialising; she enjoys cooking very much. As of now, she has had no health problems at all, and, with the exception of her two deliveries, has never been hospitalised on any grounds.

Psychical complaints started half a year post retirement, i.e. one and a half year ago; she started feeling dissatisfied and unfulfilled. She believes that, since retired, she "did not quite manage to find her

way". She had so many plans for the retirement, but these plans never got to come true; she simply started watching over her grandchildren and ended up with no spare time just for herself. Even though she blames herself for being a bad person, she honestly thinks that she "deserves to get something out of her life just for herself". Her husband supports her, which is more than could be said for her daughter who persistently requires her assistance with the children.

A year ago, the patient's father, who was until then in good health, suddenly died of a malignant disease. She was very attached to him, and spent a lot of time with him and caring for him. When he passed away, she was grief-stricken; since then, she has had trouble sleeping and has complained about a gradual loss of interest, initiative and joy of life. She has lost her appetite, as well as a few pounds. She sought comfort in her husband, but decided to visit a GP as well. The latter prescribed oxazepam 15 mg ½ tbl in the evening hours, alprazolam 1 mg a day and B-complex vitamins, but the therapy in reference failed to yield improvement. The attending GP also suggested a control visit and the completion of tests descriptive of other organic systems' status (blood and urinalysis, thyroid gland testing, gynaecological examination), but the patient failed to comply because of her lack of drive, lethargy, and "fear of results".

Three months later, she referred to a psychiatrist because of further deterioration. The appointment was made by her cousin who is also a doctor. On the occasion of the visit in reference, the patient complained about lethargy and lack of joy, and cried now and then without reason. She was overwhelmed with depression and the feeling of inferiority. She was disappointed with what had become of her, and complained about tension episodes witnessed during the daytime; she claimed a variety of somatizations such as headaches, back and neck pain, bloating and constipation. She yammered about neglecting her housework and about her bad, "fast food" cooking, which was so nothing like her. The patient denied suicidal thoughts, although admitted that "she does not want to live like this".

She was diagnosed with a moderate depressive disorder (IDC Code F 32.1) featured by somatizations and pain syndrome. The following therapy was prescribed: Duloxetine 30 mg in the morning hours, alprazolam 1 mg and oxazepam 15 mg ½ tbl in the evening hours. The next control visit was scheduled in three weeks.

Four days later, the patient phoned to seek urgent appointment and referred to the office on the very same day. She stated that she started taking 30 mg Duloxetine three days ago in the morning hours as prescribed, but instantly felt weird and more tense than usually. She took an additional dose of alprazolam which calmed her down. The next day, round noon, she experienced a panic attack accompanied by suffocation, major fear of death, and an overwhelming feeling of panic. The repeated alprazolam dose managed to calm her down. The day after, she experienced as many as two panic attacks, the first one occurring round noon, and the next one three hours later. On both occasions, the panic ceased following an additional 0.5 mg alprazolam dose. Given the fact that these episodes took place over the weekend, the patient contacted the on-call psychiatrist at the Clinic, who suggested duloxetine cessation and advised her to refer to her attending psychiatrist as soon as possible.

On the occasion of the subsequent visit, the patient lacked any panic attack or severe anxiety symptoms, but was tense and frightened because of everything she had to go through in the last two days. Her psychical status was still dominated by depression, passivity, somatizations and gastrointestinal symptoms, while the symptom self-estimated as the most prominent was insomnia.

Following examination, the therapy was adjusted in the following manner: Duloxetine was withdrawn and, based on our positive experience with its efficiency and tolerability, replaced by tianeptine. Alprazolam was increased to 1 mg. The patient was also advised to take 1 tbl of 15 mg oxazepam in the evening hours. She was scheduled for a control visit in two weeks.

On the occasion of the control visit scheduled two weeks later as announced above, a substantial improvement was seen; panic attacks and anxiety were lacking, while the depression appeared to be less profound. The patient was in a much brighter mood and seemed more satisfied. Nevertheless, she still described herself as being in slow motion, half-hearted and inert.

On the occasion of the next control visit scheduled in a month, the patient stroke us as even more improved; depression/anxiety symptoms were almost gone and the patient seemed more occupied with everyday issues and plans. She was accompanied by her husband, who described her health as substantially improved.

DISCUSSION

Along the path of routine depressive patients' treatment, one gets to come across a series of possible obstacles and difficulties, spanning from unsatisfactory antidepressant efficiency over irresponsiveness to therapy to poor compliance and treatment side-effects. "Dramatic" and endangering side-effects pose as a major difficulty in this regard. They deeply shake patients' trust in both the drug and the prescribing physician, and have a direct impact on the treatment outcome.

In this particular case, the patient was prescribed duloxetine to the effect of treating a depressive episode featured by somatizations and pain syndrome. According to data offered by the available literature (Wise TN et al. 2009), such patients benefit from duloxetine treatment. On the other hand, upon the

therapy launch the patient had experienced three panic attacks in three days, unseen ever before (the patient had no prior record of a panic disorder). Contemporary medicine has witnessed an increasing use of Duloxetine to the end of general anxiety disorder treatment (Carter et al. 2009). It has also been suggested for use in panic disorder treatment; these suggestions have been underpinned by a number of real-life showcases. JC Nelson and co-workers (2010) suggested duloxetine efficiency in depressive disorder treatment independent of anxiety, arguing that anxiety has no impact on the response to duloxetine therapy. Nevertheless, the inconsistency of these results might be indicative of duloxetine superiority in depression cases, but also of its concurrent inefficiency in anxiety cases. This piece of information might be indicative of duloxetine efficiency in a selected group of patients suffering from depression accompanied by anxiety symptoms, or from a generalised anxiety disorder. In another patient group, however, anxiety or even a panic attack may arise on the grounds of duloxetine administration, manifested with a "dramatic" clinical presentation as with the case reported herein. Future work should shift its focus to the anxiety arising on the grounds of administration of either duloxetine or other antidepressants falling into the same pharmacological cluster.

CONCLUSION

Beyond a shred of doubt, side-effects arising on the grounds of administration of antidepressants tagged by literature sources as possible anxiety disorder or depression-induced anxiety treatment modalities and manifested in form of panic attacks as revealed by this case report, bring forward numerous questions and raise numerous doubts. A patient that has never suffered from an anxiety disorder suddenly developed as many as three panic attacks in response to duloxetine treatment. Once the treatment was withdrawn, the attacks ceased. These panic attacks were successfully resolved by virtue of anxiolytic drug alprazolam. Despite contributions published insofar, the aetiology of the side-effect in reference and its underlying mechanism remain unclear.

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