Case Report

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Mistaken administration of a repeat loading dose of Degarelix leading to acute psychosis

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Summary

Advanced and metastatic prostate cancer is often managed with hormonal blockage. Luteinising hormone-releasing hormone antagonists achieve rapid testosterone suppression and are used for the treatment of advanced or metastatic prostate cancer. Degarelix is a luteinising hormone-releasing hormone antagonist and is given as a loading dose, followed by a monthly maintenance dose. We report a case where a patient was inadvertently given a second loading dose of Degarelix that resulted in acute psychosis in the form of panic attacks, delusions, suicidal thoughts, insomnia and some visual hallucinations, which are not reported as side-effects of Degarelix.

Keywords

clinical, drugs, psychiatry, oncology, prostate cancer, psychiatry, psychotic disorders (incl schizophrenia)

Background

Hormonal blockage is widely used for the management of advanced or metastatic androgen-dependent prostate cancer. Medical androgen deprivation therapy is in the form of luteinising hormone-releasing hormone analogues and androgen blockade with anti-androgens.[1,2]

Luteinising hormone-releasing hormone antagonists are used in the treatment of advanced prostate cancer. They block the pituitary luteinising hormone-releasing hormone receptor and directly suppress the release of gonadotrophins and testosterone.[3,4] Consequently, castrate serum testosterone levels are achieved much quicker and the risk of tumor flare, seen with luteinising hormone-releasing hormone agonists, is avoided. Degarelix is a luteinising hormone-releasing hormone-antagonist that rapidly achieves androgen deprivation.[5]

Case presentation

A 62-year-old patient presented to Accident and Emergency feeling unwell, shivery and short of breath. He had recently returned from a holiday in Spain. He had a productive cough and reported 1 kg in weight loss over the last two months. On arrival he was pyrexial at 38°C. He had no significant past medical history. His initial blood tests revealed an elevated serum alkaline phosphatase of 276 IU/L (44–147 IU/L) and C-reactive protein of 81 mg/L (<10). All other blood results were within normal range. A chest X-ray showed right middle lobe consolidation and he was commenced on intravenous antibiotics for a lower respiratory tract infection.

In view of his history of weight loss, a computerised tomography scan of the chest, abdomen and pelvis was organised to investigate malignancy. This revealed pathological nodal enlargement above and below the diaphragm with extensive retroperitoneal and pelvic lymphadenopathy. There were multifocal areas of sclerosis within the bones and vertebrae with multilevel crush fractures.

The patient was referred to the urology team as the sclerotic areas on computerised tomography raised a suspicion of prostate cancer. A digital rectal examination revealed a clinical stage T3 prostate cancer. An initial prostate specific antigen was significantly elevated at 1440 ng/mL and a bone scan performed confirmed metastatic prostate cancer. Magnetic resonance imaging spine was performed, which excluded cord compression and further confirmed widespread bony metastasis. We relied on the clinical diagnosis of prostate cancer in this patient by using digital rectal examination, prostate specific antigen reading and radiological imaging. Despite this prostate cancer cannot be fully diagnosed without a histological diagnosis but in some cases clinical diagnosis is acceptable with no tissue diagnosis.

Following multi-disciplinary team discussion and review of images, he was started on Degarelix (luteinising hormone-releasing hormone antagonist) and dexamethasone. He received a loading dose of 240 mg of Degarelix in the hospital.

He was subsequently discharged on dexamethasone and monthly injection of Degarelix, which was to be continued in primary care.

The discharge note to the general practitioner (GP) mentioned to be on Degarelix 240 mg stat dose and then to have it 80 mg monthly by subcutaneous injection, it was not mentioned clearly to the GP this patient already had his first dose and should be on the 80 mg dose. To improve this now all the GPs in our local area has a leaflet about the dosing and regimes of hormonal treatment of prostate cancer.

One month later, the patient presented to Accident and Emergency with an acute agitation, suicidal thoughts, panic attacks, insomnia, delusions and visual hallucinations. He had no previous history of mental health illness. The patient did not report any other side-effects from Degarelix. His symptoms started one week following his second loading dose.

A computerised tomography head excluded brain metastasis. His alkaline phosphatase had risen to 620 IU/L while prostate specific antigen had dropped to 751 ng/mL. There was no clear explanation for the raised alkaline phosphatase. All other routine blood tests including electrolytes and thyroid function tests were within normal limits. His serum testosterone had reached castrate levels (<0.4 ng/dL) confirming he was responding to hormone therapy.

His psychosis and attempts at self-harm worsened initially during the admission and he was then treated by the psychiatric liaison team with anti-psychotic medication as medical causes had been excluded. He was discharged from the psychiatric ward on haloperidol, mirtazapine, lorazepam, quetiapine and diazepam.

On review of his paper work during his urology clinic visit few weeks following discharge, it transpired that the patient's symptoms commenced after the second dose of Degarelix was administered and instead of a reduced 80 mg maintenance dose, a further 240 mg loading dose was given in the community. As this was discovered prior to the third dose, a decision was made to stop Degarelix and the patient was started on bicalutamide, which is an anti-androgen hormonal treatment for the management of hormone-sensitive prostate cancer. The patient's psychological state improved drastically and his antipsychotics medications were stopped gradually.

His steroids were gradually stopped by the oncologist six months following the initial start at diagnosis.

It was very unlikely that his symptoms were related to testosterone as directly after stopping Degarelix his symptoms resolved and there was no change in his psychiatric symptoms with different levels of testosterone during the treatment period.

Initially, prostate specific antigen continued to decline and reached a nadir of 30.2 ng/mL. Subsequent to this a rise was noted and a luteinising hormone-releasing hormone analogue Zoladex 10.8 mg was added to achieve maximum androgen blockade. He showed no further signs of acute psychosis. His prostate cancer continued to progress despite maximum androgen blockade and reached a level of 1109 ng/mL. He was started on Enzalutamide, a more potent anti-androgen as well as given bisphosphonate infusions. The patient died two months following the start of Enzalutamide. His disease progression from the day of diagnosis to the day he passed away was 14 months.

Discussion

Degarelix is a third-generation selective antagonist of luteinising hormone-releasing hormone. It acts directly on the luteinising hormone-releasing hormone receptors on the pituitary gland and achieves rapid testosterone suppression.[5,6] It is therefore preferable to luteinising hormone-releasing hormone analogues use in advanced disease with widespread metastasis as the risk of 'tumor flare' is prevented and the use of concomitant anti-androgen flare protection is not required.[6] According to the British National Formulary it should be given as a subcutaneous injection of 240 mg loading dose, followed by 80 mg every 28 days. As the dose increases, so does the half-life.[7] Therefore, in our case it took over two months for the patient's symptoms to resolve.

In this case, incorrect dosing of the drug lead to serious consequences for the patient. Psychosis is not a recognised side-effect of the drug and, consequently, other diagnoses were explored and treated prior to discovering the root cause of his reversible psychosis and suicidal ideation.

This case teaches us a valuable lesson of the importance of accurate discharge summaries and dosing of drugs.

There are two published case reports of acute mania and psychiatric symptoms following the use of leuprolide acetate injection in patients with no previous psychiatric history.[8] Leuprolide acetate injection treatment was administered in a 65-year-old male with a history of metastatic prostate cancer. Two months after the first injection, the patient showed the following peculiarities: extreme agitation, shouting of profanities, decreased sleep, an increasingly talkative nature, and pressured speech.[8] The other case was a 62-year-old male with metastatic prostate cancer, who developed acute manic and psychiatric symptoms two months after subcutaneous leuprolide acetate injection.[8] These symptoms were relieved after administration of neuroleptic drugs, such as risperidone. Administration of leuprolide acetate was eventually stopped. Anxiety and

depression have been suggested as a potential side-effect of Degarelix.[6] Some uncommon side-effects also include cognitive impairment and depression. Our case suggests that in higher doses Degarelix may cause psychotic side-effects.

On the European Database of suspected adverse drug reaction reports we found two cases of Degarelix-related anger and aggression, one case was Degarelix-related depression and one case of Degarelix-related cognitive impairment, despite that none of these cases were mentioned to have a second loading dose of Degarelix.[9]

To our knowledge, this is the first case of an acute psychosis to happen following a second high dose of Degarelix.

Declarations

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Guarantor: SM

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