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Omeprazole-induced hallucinations. Not as rare as you might think[☆]



Alucinaciones por omeprazol. No tan raras como se cree

In an attempt to find information on a rare adverse reaction associated with omeprazole use, the onset of auditory hallucinations, I consulted a magnificent review published recently in *Gastroenterology* on potential risks associated with long-term use of proton pump inhibitors (PPIs),¹ but did not find any relevant information. I did not manage to find anything in another recent review in Spanish either.² I continued searching on PubMed and finally found a few references to hallucinations associated with omeprazole use.^{3–5} It therefore seems that this is an uncommon adverse reaction, reported very rarely in literature, especially in Spanish.

Omeprazole, which has been marketed since 1989, is a safe and effective drug with few side effects, the most common of which appears to be diarrhoea, followed by nausea/vomiting, abdominal pain and headache.⁶ In rare cases, acute psychotic symptoms, in the form of delirium⁷ and visual^{3,4} and auditory⁵ perception disturbances (i.e. hallucinations), may appear. In all published cases, illusions or hallucinations have appeared in elderly patients, aged between 77 and 92.^{3–5}

The case in question is that of a 36-year-old male patient with a history of hiatus hernia and peptic oesophagitis and no history of psychiatric disorders or hearing problems. He was experiencing symptoms of gastro-oesophageal reflux disease (GORD) and was therefore prescribed 40 mg omeprazole/day. Within 48 h of commencing treatment, the patient reported experiencing auditory hallucinations in the form of insults and malicious phrases from his wife and closest friends, with whom he got angry and showed strange, aggressive behaviour. The hallucinations appeared intermittently and the patient continued with this treatment for about 6 weeks, after which time he discontinued therapy after suspecting that this was an adverse effect. Within 4 days,

all hallucinations disappeared completely. As an alternative therapy, he was prescribed esomeprazole, which provided very good control of his reflux symptoms with no new hallucinations to date.

Apparently, besides the adverse effect itself, the case is considered rare because of the patient's young age at which hallucinations appeared, compared to other reports, and the duration of the adverse effect, which lasted until the patient stopped taking omeprazole.

However, things were not as they seemed. Having contacted a well-known medical editor, Dr Marta Pulido, who I would like to thank for her help and insight, she recommended that I consult the on-line tool eHealthMe.com (<http://www.ehealthme.com>), which can be used to check the adverse reactions of more than 45,000 drugs and supplements reported by patients experiencing such effects to the US Food and Drug Administration (FDA) since 1977.

On checking this source of information,⁸ up until 4 May 2017, 168,361 patients had reported having had a side effect when taking omeprazole, with 981 (0.58%) of these being hallucinations and 0.09% auditory (appearing most commonly during the first month of treatment [49.12%] and at the age of 60 or older [61.09%]).

According to this same source, the most common side effects associated with omeprazole use were: 10,097 cases of nausea, 7968 cases of fatigue, 9131 cases of difficulty breathing, 9089 cases of diarrhoea, 7968 cases of weakness, 7322 cases of nausea and vomiting, 7196 cases of pain, 7107 cases of dizziness and 6633 cases of fever. In fact, hallucinations associated with other PPIs, including esomeprazole magnesium (0.48% with 0.05% auditory hallucinations), appeared with a similar frequency, with lansoprazole appearing to be associated with the highest number of cases of hallucinations (0.71% with 0.15% auditory hallucinations).

In addition to the above, the aforementioned online FDA application allows us to check interactions reported between different drugs and the diseases associated with such interactions over time. For example, a few years ago, interactions were reported between omeprazole and the anti-platelet effect of clopidogrel (which is reduced), with the resulting risk of coronary heart disease and myocardial infarction.⁹ According to this source, up until 26 April 2017, 2765 patients who were taking both drugs reported some kind of side effect, with 119 (4.78%) reporting myocardial infarction and 65 (2.61%) reporting gastrointestinal bleeding, both within the first month of treatment.

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As a result, I recommend checking this magnificent online FDA tool when documenting or reporting possible adverse effects with drugs or drug interactions.

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Gastrointestinal bleeding caused by neurofibroma of the ileum[☆]



Hemorragia digestiva por neurofibromas en íleon

Neurofibromatosis type 1 (NF1), or von Recklinghausen disease, is an autosomal dominant-inherited disease caused by mutations in the NF1 gene located at chromosome 17q11.2.¹ Its incidence is approximately 1/3000 newborns and it occurs in all races and ethnic groups and in both genders. The mutation is “de novo” and not inherited in 50% of cases.

For diagnosis, 2 or more of the following criteria must be met: 6 or more café-au-lait spots larger than 5 mm in prepubertal patients and larger than 15 mm in postpubertal patients; 2 or more neurofibromas of any type or 1 plexiform neurofibroma; axillary or inguinal freckling (Crowe’s sign); optic nerve gliomas; 2 or more benign iris hamartomas (Lisch nodules); distinctive osseous lesions (sphenoid dysplasia, thinning of the long bone cortex with or without pseudoarthrosis); first-degree relative (parent or sibling) with NF1.²

There is relatively common association between neurofibromatosis and gastrointestinal tumours, which may appear in 3 different ways: (a) stromal tumours (neurofibromas or leiomyomas), which is the most common form of presentation, located in the stomach or small intestine and

more rarely in the colon³; (b) neuronal hyperplasia and ganglioneuromatosis; (c) endocrine tumours in the duodenum and peri-ampullary region.^{4–6}

Our case study is a 69-year-old male patient diagnosed with NF1 who was admitted with asthenia and severe anaemia (haemoglobin 6.4 g/dl) together with self-limiting episodes of rectorrhagia. A gastroscopy and colonoscopy was performed with no relevant findings. Computed tomography (CT) scans of the chest and abdomen, magnetic resonance imaging (MRI) scans of the intestines and a capsule endoscopy were done, showing tumours in the middle portion of the ileum consistent with his underlying disease (Fig. 1A–C). It was decided to schedule surgery (segmental resection of the ileum with end-to-end anastomosis (Fig. 2A).

The patient’s initial progress was favourable and he was discharged 5 days after surgery. However, 16 days after surgery, the patient was re-admitted due to acute abdominal pain and, as a result, an abdominal CT scan was performed, showing fluid collection near the anastomosis. The patient underwent emergency surgery and localised purulent peritonitis was found that was probably due to anastomatic leakage, which was treated with parenteral nutrition and catheter drainage of the leak. A control CT scan was performed, which showed improvement of the fluid collection, and the patient was discharged. During outpatient follow-up, the patient was asymptomatic with no recurrent bleeding.

The results of the pathology analyses performed on the surgical specimen showed multiple nodular lesions with diffuse proliferation of mesenchymal stromal (stem) cells of neural lineage and chronic inflammation of the basal lamina propria with distortion and displacement of adjacent glandular epithelium (Fig. 2B). They also showed dehiscence of the mucosal muscle fibres and overgrowth of adipose tissue into the submucosal layer with congested vessels and

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