Palliative and Supportive Care

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Facial edema as an adverse drug reaction to olanzapine in a patient with cancer receiving palliative care

Miguel Julião, M.D., M.SC., PH.D[1], Maria Ana Sobral, M.D.[1], Tiago Ferreira, M.D.[2], Patrícia Calaveiras, R.N., M.SC.[1], Elisabeth Costa, R.N.[1], Ana Sara Daniel, R.N.[1], Mafalda Lemos-Caldas, M.D., M.SC.[3] and Eduardo Bruera, M.D., F.A.A.H.P.M., F.A.C.P.[4]

[1]Equipa Comunitária de Suporte em Cuidados Paliativos de Sintra, Sintra, Portugal; [2]Departamento de Saúde Mental, Hospital Prof. Doutor Fernando da Fonseca EPE, Amadora, Portugal; [3]ACeS Loures-Odivelas, USF Travessa da Saúde, Lisboa, Portugal and [4]Department of Palliative, Rehabilitation and Integrative Medicine, University of Texas MD Anderson Cancer Center, Houston, TX

Case Report

Cite this article: Julião M, Sobral MA, Ferreira T, Calaveiras P, Costa E, Daniel AS, Lemos-Caldas M, Bruera E (2022). Facial edema as an adverse drug reaction to olanzapine in a patient with cancer receiving palliative care. *Palliative and Supportive Care* **20**, 752–753. https://doi.org/10.1017/S1478951522000037

Received: 25 November 2021
Revised: 13 December 2021
Accepted: 2 January 2022

Key words:
Cancer; Case report; Facial edema; Olanzapine; Palliative care; Terminally ill

Author for correspondence:
Miguel Julião,
Equipa Comunitária de Suporte em Cuidados Paliativos de Sintra 2635-364 Rio de Mouro, Sintra, Portugal.
E-mail: migueljuliao@gmail.com

Abstract

Objective. Atypical neuroleptics such as olanzapine are indicated for the treatment of various psychiatric disorders and have been used in the palliative care setting also for several clinical indications. Peripheral and facial edema are a rare side effect of the treatment with olanzapine. We report a case of an advanced cancer patient cared receiving palliative care who developed severe facial edema after initiating a low dose of olanzapine in monotherapy.
Method. A patient with advanced cancer who presented with severe facial edema after initiating olanzapine for the treatment of her opioid use disorder.
Results. After excluding other differential diagnosis for facial edema, olanzapine was discontinued with complete resolution of the edema.
Significance of results. To the best of our knowledge, this is the first case reporting facial edema due to olanzapine treatment in a patient with advanced cancer. Our report will help clinicians recognize the possible role of olanzapine in cases of rapid onset of facial edema, allowing its rapid resolution.

Introduction

Olanzapine is an atypical neuroleptic indicated for various psychiatric disorders. Additionally, olanzapine has found to be useful in opioid-dependent patients with cancer and it has been used in the palliative care setting, reducing craving and overall opioid misuse (Go et al., 2018; Julião et al., 2021).

Peripheral edema can occur in approximately 3% of patients receiving olanzapine (Ng et al., 2003), and there have been only a few case reports of facial edema published in the literature (Durst et al., 2000; Deshauer et al., 2006; Yalug et al., 2007; Zinh et al., 2007; Nayak et al., 2009; Akin et al., 2013; Malhotra and Shrivastava, 2013; Korkmaz et al., 2015; Han Almiş and Çeli, 2017; Williams, 2019). The mechanism responsible for olanzapine-induced edema has not yet been clarified and some hypotheses include vasodilatation due to blockage in alpha-1 and 5-HT2 receptors, and the disturbance in renal regulation of fluid and electrolyte balance (Zinh et al., 2007). Clinical factors such as dose, age or frailty might be contributing factors (Han Almiş and Çeli, 2017).

We present a woman in her 60s with advanced cancer who developed severe facial edema after initiating a monotherapy with 5 mg olanzapine daily.

Case presentation

A woman in her 60 s with advanced metastatic tongue cancer and no indication for further chemo or radiotherapy due to her locally and metastatic disease progression was referred to our home-based palliative care. Her past medical history revealed no significant medical or psychiatric problems. Due to her severe and disruptive opioid use disorder, she was treated with olanzapine 5 mg daily, resulting in marked reduction of anxiety and craving behaviors and improved well-being, motivation, and pleasure in daily activities. The improvement in her non-medical opioid use behavior treated with olanzapine has been reported elsewhere (Julião et al., 2021).

After day 7 of her treatment with olanzapine at a low dose of 5 mg, she developed a severe non-pruritic facial edema and swelling, and it continued to worsen and widespread to her chin, lips, nose, and forehead, particularly severe on the eyelids, impairing her vision, function, and motivation to perform house chores and participate in leisurely activities. Although the

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patient's facial edema did not increase her pain, it caused additional psychosocial distress, mainly anxiety, irritability, and sadness. She presented no lower extremities edema, airway compromise, or systemic signs such as fever. No new drugs or foods were introduced prior to or during the appearance of the facial edema, and a dermatologist was consulted excluding allergy reaction due to dietary intake or insect sting skin reaction. Based on her physical examination, differential diagnoses contributing to face swelling and edema such as local infection, cancer-related edema/lymphangitis, and angioedema were also excluded. Her cutaneous fistula located at her left chin maintained a normal and serous exudate, without increasing local pain, bleeding, odor, or necrotic tissue detachment, as well as no neck vessels enlargement. Due to the patient's low-performance status and frail condition, the palliative care team decided not to order any imaging exams.

At this point, laboratory tests were conducted to exclude any possible organic factors, and the patient's complete blood count, liver, kidney function, and electrolytes were all within normal limits, except for an asymptomatic hyponatremia. A probability score for this adverse drug reaction was calculated using the Naranjo algorithm (Naranjo et al., 1981), which described it as a probable drug reaction to olanzapine. After consulting a psychiatrist who concurred with the possible diagnosis of facial edema due to olanzapine, the drug was interrupted. The team and the family caregiver set a close monitoring follow-up of her facial edema and swelling during the following days and seven days after cessation of olanzapine, facial edema disappeared completely.

Discussion

The pathophysiology and underlying clinical factors associated with peripheral edema due to olanzapine warrant further research. Evidence in the literature where olanzapine use resulted in the development of peripheral edema is scarce, and the majority of it relates to lower extremity edema and is rarely localized to a facial region (Durst et al., 2000; Deshauer et al., 2006; Yalug et al., 2007; Zinh et al., 2007; Nayak et al., 2009; Akin et al., 2013; Malhotra and Shrivastava, 2013; Korkmaz et al., 2015; Han Almiş and Çeli, 2017; Williams, 2019).

To the best of our knowledge, this is the first case report of severe facial edema after olanzapine treatment in an advanced cancer patient receiving palliative care.

Our report shows the appearance of facial edema in a frail and elderly patient with metastatic cancer receiving a low dose of olanzapine daily. This case is similar to other reports, suggesting that this rare adverse effect might not be dose-dependent, but rather related to clinical factors such as age, advanced disease, and frailty.

Although the team decided not to undertake any imaging exams of the patient's face and neck, the probability score for a possible adverse effect of olanzapine, along with the clinical examination and the lab results, helped to exclude the main differential diagnoses of facial edema. It is possible that impairment in venous and lymphatic drainage due to the location of the tumor and previous oncological treatments might have contributed in some degree to the local vulnerability of her face tissues, along with the olanzapine pathophysiologic mechanisms.

Hyponatremia is a rare, yet potential complication of antipsychotics such as olanzapine (Meulendijks et al., 2010). Our patient presented mild asymptomatic hyponatremia and we think that her laboratory findings might also be an olanzapine-induced effect, although its clinical and psychiatric expression did not warrant any need for acute medical treatment.

Clinicians aware of facial edema as a rare but serious complication of olanzapine can discontinue this drug and observe the clinical improvement, thereby helping patients regain their quality of life, comfort, autonomy, and self-esteem. Facial edema resulted in severe emotional distress that affected the patient's quality of life well beyond the purely physical evidence of local swelling, and it is a completely reversible source of emotional distress.

Future case series reporting the adverse effects of olanzapine and other antipsychotics are needed. Such studies should report on drug doses, treatment duration, patients' characteristics, the clinical manifestations, response to the drug interruption, switching, and remission. Altogether, this information can help further understanding of the multidimensional causes of olanzapine-induced edema.

Acknowledgments. A deep word of gratitude to C. and her son.

Funding. The authors received no financial support for this report.

Conflict of interest. The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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https://doi.org/10.1017/S1478951522000037 Published online by Cambridge University Press