CASE REPORT

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Orbital Cellulitis Accompanied by a Non-Symptomatic Drug Interaction That Promptly Responded to Drug Modification

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ABSTRACT We report a drug interaction case that might have been progressed to a serious outcome, arrhythmia, due to an electrolyte imbalance that accompanied an acute case of orbital cellulitis. Patients' orbital cellulites was successfully controlled with a broad-spectrum antibiotic and debridement. An increase of serum potassium was observed in patients' routine lab work-up that did not show any of the expected clinical symptoms. This increase was thought to be a result of an interaction between candesartan and aspirin, two drugs the patient had been using chronically. Indeed, changing the patients' antihypertensive with a calcium channel blocker quickly decreased serum potassium to normal range. This study shows that major drug interactions with serious outcomes might be clinically asympthomathic and that even a slight modification in drug selection may be the sufficient to provide intended outcomes both in treatment and in eliminating adverse effects.

Keywords: Orbital cellulitis; drug interacitons; hyperkalemia

Orbital cellulitis is an infectious disease that may progress aggressively in all age groups and in both high- and low-risk populations. Proper antibiotic treatment and surgical interventions -although not conventional- may be able to control the rather aggressive progress of the disease.[1-3]

Extensive research and accumulating evidence raised awareness in current medical practice to drug interactions and their possible outcomes. Especially in those patients with co-morbidities treated with multiple drugs, a detailed interrogation of possible drug interactions must be acknowledged as a priority.[4]

CASE REPORT

Two days ago, a sixty-nine year-old male patient was admitted to Infectious Diseases Clinic at Ankara University with a rapidly progressing bilateral periorbital edema that deteriorated his vision. In his physical examination, purulent discharge, erythema, and an increased temperature were observed that affected both eyes (Figure 1). In addition, the patient reported chills and shivering that accompany fever. His medical history included hypertension, hyperlipidemia, hypothyroidism and vertigo. For these, the patient

FIGURE 1: Significant edema on both eyes. Scaly lesions with purulent discharge accompanied by necrotic patches.

is on aspirin 100 mg, candesartan 8 mg and levothyroxine 75 µg daily.

Prior his admittance at this clinic, a work-up was performed for this sudden clinical representation that included a paranasal tomography. A bilateral diffuse thickening with an infraorbital origin and a recumbence to supraorbital area -more so on the left- and accompanied by contrast retention by dermis-epidermis that supported the diagnosis of cellulitis. Although hospitalized and started with antibiotics at that clinic, the patient decided to discharge at own risk.

When the patient was admitted at our clinic, he was immediately started with meropenem 3x1 g/day and vancomycin 2x1 g/day. His temperature was ≥ 38.3°C at his admittance and 5 days thereafter. No alterations in treatment protocol was considered despite the gradual decrease in his temperature over the course of 10 days due to the mucormucosis identified in tomography. The patient's case was consulted daily with the specialists in Ophthalmology and their suggestions for topical treatment were applied (bacitracin/neomycin and teardrops). Following the debridement of necrotic tissue on day 7 by the specialists, his symptoms lessened more rapidly and his body temperature regressed to 37°C (Figure 2).

After a careful follow-up in Infectious Diseases Clinic, C-Reactive Protein (CRP) dropped from 393 to 8.4 mg/L (normal range: 0.0-5.0mg/L) and his body temperature was stable around 36.5 to 37°C. A 21-day treatment plan was initially scheduled for the patient. Routine biochemical work-up revealed hyperkalemia which -after a retrospective analysis- was confirmed by a slight but steady increase since he was first admitted into the clinic (Figure 3). Immediately after the detection of hyperkalemia, an electrocardiogram (ECG) was scheduled immediately and possible cardiac complications were evaluated by consulting with relevant specialists. The patient had no clinical symptoms and his ECG was normal. Since the hyperkalemia was persistent despite his diet was ordered to restrict potassium intake, the patients' drugs were evaluated for possible drug interactions. This was performed by utilizing 3 different web-based databases. Two of those,-Lexicomp® and drugs- did not report an interaction between candesartan and aspirin. On the other hand, Medscape indicated a major interaction between these two drugs that leads to hyperkalemia. Hyperkalemia is a possible outcome of the inhibition of renin-angiotensin-aldosterone system.[5] Similarly, a reduction in prostaglandin synthesis by aspirin as well as other inhibitors of cylooxygenase may deteriorate renal function which may result in hyperkalemia,

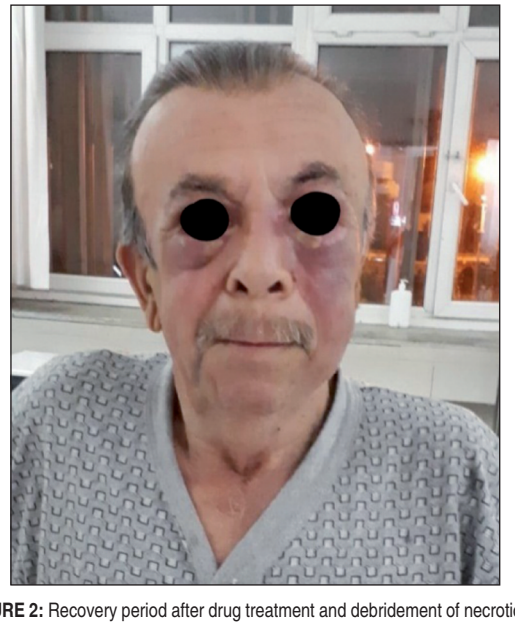

FIGURE 2: Recovery period after drug treatment and debridement of necrotic tissue. Clearance of purulent discharge.

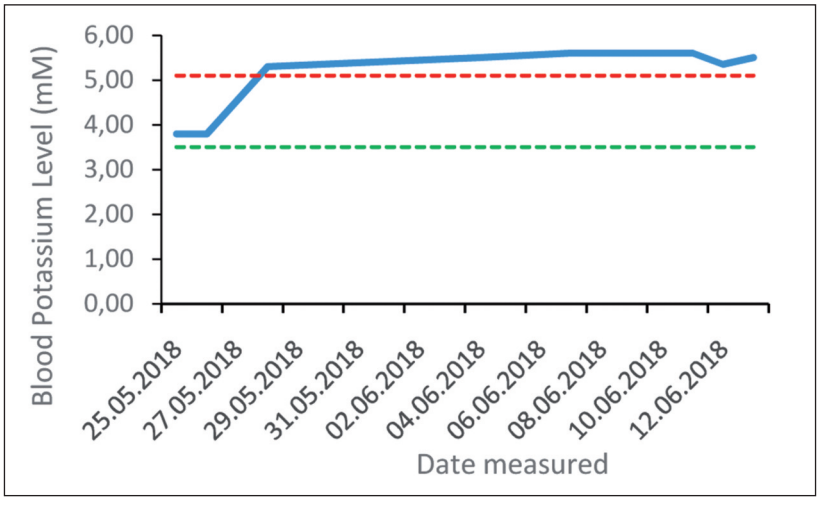

FIGURE 3: Potassium levels and the dates they were measured. Dashed lines indicate lower (3.5mM) and upper limits (5.1mM) of potassium levels.

hyponatremia and edema, particularly in volume-depleted patients.[6] It was therefore thought that hyperkalemia was an outcome of an interaction between aspirin and candesartan. After consulting with the specialists in cardiology, a consensus was reached to change the patient's antihypertensive medication to amlodipine, a calcium channel blocker (5 mg/day). Forty-eight hours after stopping candesartan, potassium levels recessed to normal range without an unfavorable alteration in blood pressure. Symptoms of infection were gradually diminished after a 21-day treatment and his symptoms stabilized. The patient was discharged once his potassium levels were normalized.

DISCUSSION

This was a clinical case where the infection was successfully controlled with a broad-spectrum antibiotic and debridement. While clinical progress was attained with proper treatment, an increase in serum potassium was critically important although no detectable symptoms were observed while the patient was under medical supervision. As is known, a risk for sudden cardiac arrest persists even in patients with no clinical finding or alterations in ECG.[5-8] Since the patient was on these drugs for his chronic conditions, one can assume that hyperkalemia was a result of additive adverse effects of the drugs that are commonly used together and was most probably overlooked in laboratory work-ups, primarily because it did not cause any clinical symptoms. Indeed, when one of the drugs with a potential to induce hyperkalemia (candesartan) was switched for another antihypertensive without this effect, hyperkalemia quickly resolved, an evidence which strongly supports this assumption. In most patients with cardiovascular risk factors, antihypertensive drugs and aspirin are prescribed together. Similarly, in all patients on multiple drugs, especially when alterations in treatment schedules are due, evaluation of possible drug interactions is a rational strategy to successfully manage the treatment and to minimize the outcomes that are reflected in clinic or simply overlooked.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Kemal Osman Memikoğlu, İrem Akdemir Kalkan;* ***Design:*** *Kemal Osman Memikoğlu, İrem Akdemir Kalkan, Büşra Akyol;* ***Control/Supervision:*** *Kemal Osman Memikoğlu, İrem Akdemir Kalkan, Fırat Yılmaz;* ***Data Collection and/or Processing:*** *İrem Akdemir Kalkan, Büşra Akyol, Fırat Yılmaz;* ***Analysis and/or Interpretation:*** *Kemal Osman Memikoğlu, İrem Akdemir Kalkan, Arzu Onay Beşikci;* ***Literature Review:*** *Kemal Osman Memikoğlu, İrem Akdemir Kalkan, Arzu Onay Beşikci, Büşra Akyol, Fırat Yılmaz;* ***Writing the Article:*** *İrem Akdemir Kalkan, Arzu Onay Beşikci;* ***Critical Review:*** *Kemal Osman Memikoğlu, İrem Akdemir Kalkan, Arzu Onay Beşikci;* ***References and Fundings:*** *Kemal Osman Memikoğlu, İrem Akdemir Kalkan;* ***Materials:*** *Kemal Osman Memikoğlu, İrem Akdemir Kalkan, Fırat Yılmaz.*

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