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Eosinophilia highly probable induced by carbapenems: A case report

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Eosinofilia probablemente inducida por carbapenems: Reporte de un caso

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ABSTRACT
Eosinophilia is a challenge to our everyday clinical practice. There are multiple causes to consider when diagnosing eosinophilia, and drug hypersensitivity must be taken into account. It is especially difficult to manage it in hospitalized patients with multiple complications and infections. Allergy tests are not always as helpful as we would like, so we rely on clinical observation and laboratory analysis to establish our diagnosis. We present a unique clinical case because the same patient presented two clinical episodes of eosinophilia after the administration of Carbapenems in the context of abdominal infection.
Keywords: *Anti-Bacterial Agents; Beta Lactam Antibiotics; Carbapenems; Eosinophilia; Hypersensitivity.*

RESUMEN
La eosinofilia es un reto en nuestra práctica clínica diaria. Existen múltiples causas que hay que tener en cuenta a la hora de diagnosticar la eosinofilia, y entre esos factores, se debe considerar la hipersensibilidad a fármacos. Es especialmente difícil manejarla en pacientes hospitalizados con múltiples complicaciones e infecciones. Las pruebas de alergia no siempre son tan útiles como quisiéramos, por lo que nos basamos en la observación clínica y los análisis de laboratorio para establecer nuestro diagnóstico. Presentamos un caso clínico único, donde el mismo paciente presentó dos episodios clínicos de eosinofilia tras la administración de carbapenemes en contexto de infección abdominal.

This study has been presented in poster form at The European Academy of Allergy and Clinical Immunology (EAACI) Congress 2018, celebrated in Munich, Germany from May 26-30. The poster had the abstract number 1129.

Abbreviations/Acronyms:
DRESS: Drug rash with eosinophilia and systemic symptoms
ID: Intradermoreaction
BPO-PPL: bencilpeniciloil
MDM: minor determinant mixture

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Palabras clave: *Antibacterianos; Antibióticos Betalactámicos; Carbapenémicos; Eosinofilia; Hipersensibilidad.*

Eosinophilia represents an increased number of eosinophils in the tissues and/or blood. Absolute eosinophil counts exceeding 450 to 550 cells/μL or percentages generally above 5%, depending on laboratory standards, are reported as elevated[1]. The eosinophilia and its management can be challenging for the clinical practice, especially to identify the culprit agent in patients having different clinical processes and taking multiple drugs at the same time. The induction of eosinophilia by drugs may occur with or without other clinical symptoms.

There are only a few report cases of eosinophilia due to carbapenems, a class of beta-lactam antibiotics[2], but there is always at least one organ affected as a common fact. While DRESS syndrome is every day better known, eosinophilia and rash as unique symptom remains uncharted. We present the first case of eosinophilia and rash cutaneous without other organs affected, induced by a carbapenem in a patient with proven tolerance to other beta-lactams.

A 45-year-old Caucasian man, without a personal or familial history of atopy, presented hypertension and a cholangiocarcinoma that required Roux-en-Y Gastric Bypass, with recurrent infections. As basic pharmacotherapy, the patient was only taking Enalapril 5 mg daily. Ex-smoker of 20 cig/day for 12 years, and subsequent occasional irregular consumption. Left inguinal herniorrhaphy in youth. I.Q.: Internal meniscus of the knee (2011). Discopathy L5-S1 (2016). Due to an ulterior infection, he was treated with Meropenem (1 gram IV every 8 hours), showing in less than 8 hours after the initial infusion, a generalized light exanthema and progressive eosinophilia (1.010 cells/μL absolute count or 14%). There were no other symptoms or organs affected, as analytic controls shown. After the suspension of the antibiotic, symptoms disappeared in less than 24 hours without any specific treatment.

The patient had previously tolerated Meropenem (1 gram IV every 8 hours for seven continuous days). Therefore, Meropenem was substituted by Piperacillin-Tazobactam (4 gram IV every 8 hours) and other non-beta-lactams (cephalosporins) which the patient tolerated, resulting in a positive evolution. the evolution of the case can be followed visually in figure 1.

Two weeks later, due to a new abdominal infection, he was prescribed imipenem (500 mg IV every 6 hours), showing a generalized cutaneous exanthema and higher eosinophilia (up to 2020 cells/μL absolute count or 22.1%). After the interruption of the treatment, he experienced a full recovery in the next two days. Afterward, he tolerated cephalosporin (Ceftriaxone 2 grams every 24 hours).

Methods

A complete physical examination was performed, followed by a blood analysis including liver parameters, kidney function test, and consecutive tryptase determination. Three weeks later, an allergy testing was performed including cutaneous test and tolerance test by an oral drug challenge test.

Physical exploration revealed a very light generalized papular-erythematosus and confluent lesions, more severe on chest and back. Blood analysis showed a progressive increase of the eosinophilia figures starting with 1.010 cells/μL absolute count or 14%.1% at the first episode related with Meropenem. No pathologic findings were found in liver and kidney functions. Tryptase was consecutively within normal limits. Cutaneous test performed with beta-lactams was negative both by prick and intradermoreaction (ID) tests to bencilpeniciloil (BPO-PPL), minor determinant mixture (MDM), Penicillin G-Na, Ampicillin and Amoxicillin, 2 mg/ml and 20 mg/ml, respectively. Prick and ID test to Cefazoline, Cefotaxime, Ceftazidime, Piperacillin-Tazobactam (all doses: 200 mg/ml), Imipenem and Meropenem (doses: 10 mg/ml) and ID 20 mg/ml. No clinical or analytical changes were observed during oral challenge with a therapeutic dose of Amoxicillin, confirming tolerance to this antibiotic. No challenge was performed with carbapenems due to a very suggestive history of allergy and the risk of the test.

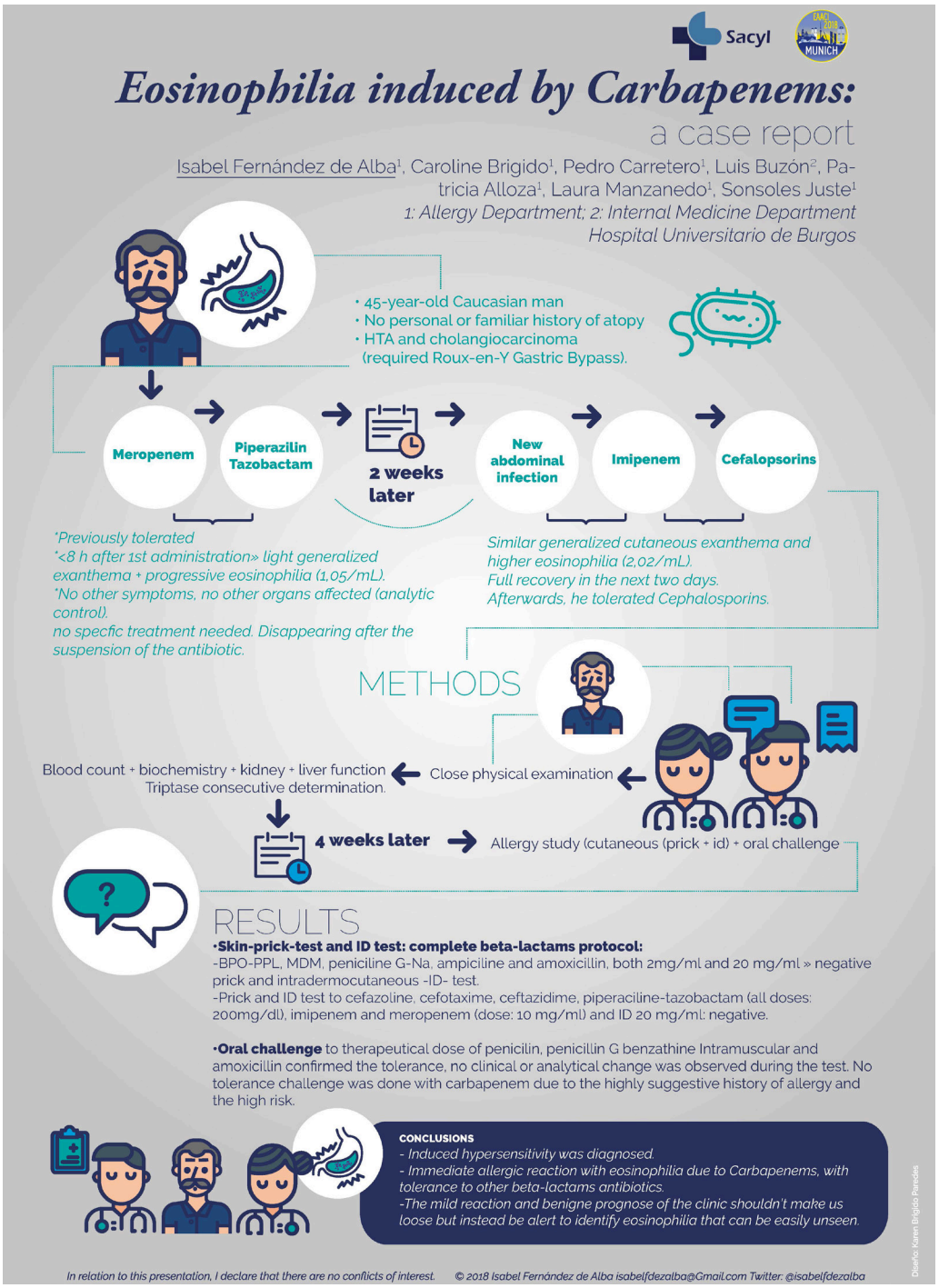

Figure 1: *It represents in a visual way all the information related to the case: The clinical evolution, the treatment regimen administered, the allergological study performed and the results.*

Discussion

As previously described, antibiotics is one of the main agents accepted to cause eosinophilia by a hypersensitivity reaction type I or IV, affecting 25% of patients receiving parenteral antibiotics[3]. Usually, the occurrence of eosinophilia is after the administration of the drug implied. The prognosis is typically benign after the interruption of the administration of the carbapenem, typically the clinic is solved without the need of medication, but in determined circumstances of difficult cutaneous or systemic pathology, a short cycle of corticoids is advisable. Despite the assumption that a drug reaction is Il-5 mediated, there are many aspects of the process that remain unclear[2]. Patients with eosinophilia are four times as likely to have rash and twice as likely to have renal injury as patients without eosinophilia[1]. There is also a possible correlation between the high figures of eosinophilia and the intensification of the clinical rash[3,4], as observed in the case described. The prognosis is usually benign and both eosinophilia and the rash disappear with the suspension of the carbapenem. The patient had previously tolerated meropenem without issues, which is puzzling considering the later negative reaction. This situation shows that people's reactions to drugs can change over time. The skin tests for carbapenems were negative, but these tests aren't always perfect in predicting what will happen when the drug is given in real-life situations[5]. This case teaches us to be cautious when interpreting skin test results and to consider the patient's full medical history and symptoms. It's important to look at the whole picture, combining test results with the patient's past experiences, to make the best decisions about their treatment and avoid unwanted reactions.

Conclusion

To sum up, the patient showed an immediate allergic reaction very probably induced by Carbapenems with eosinophilia and rash as the unique clinical feature, and tolerance to other beta-lactam antibiotics. In conclusion, this case demonstrates that Carbapenems are highly suggestive to induce eosinophilia without systemic damage on organs or tissues other than cutaneous rash. In conclusion, this case highlights the complexity of diagnosing and managing drug-induced eosinophilia. Notably, the skin tests for carbapenems returned negative, indicating no hypersensitivity, yet the patient exhibited a systemic reaction upon administration of the drugs. This underscores the essential understanding that negative skin test results do not always predict the absence of systemic allergic reactions. Such findings emphasize the importance of integrating clinical history and observational data alongside diagnostic test results to make informed decisions regarding patient care and medication management.

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