ARQUIVOS DE ASMA, ALERGIA E IMUNOLOGIA

Should a patient with systemic mastocytosis be vaccinated against COVID-19?

Deve um doente com mastocitose sistêmica ser vacinado contra a COVID-19?

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ABSTRACT

A 26-year-old woman was referred to the allergy department for two episodes of anaphylaxis after intake of non-steroidal anti-inflammatory drugs. In both episodes she was evaluated at the emergency department, and her levels of tryptase were 141 ug/L and 117 ug/L, respectively. Baseline tryptase was 92 ug/L. Bone marrow biopsy, myelogram, and immunophenotypic study were performed, confirming systemic mastocytosis. In patients with mast cell disorders, the risk of anaphylaxis after mRNA vaccine against COVID-19 has been under debate. Considering the occupational risk of COVID-19, the risk of anaphylaxis upon exposure to the vaccine was discussed with the patient and, after consent, Pfizer/BioNTech® BNT162B2 was administered under allergist supervision. No premedication was administered and both vaccine inoculations occurred without eliciting mast cell symptoms.

Keywords: Systemic mastocytosis, vaccination, coronavirus infections.

RESUMO

Mulher de 26 anos enviada à consulta de imunoalergologia após dois episódios de anafilaxia no contexto de ingestão de anti-inflamatórios. Em ambos os episódios foi observada no Serviço de Urgência. Os valores de triptase nos episódios foram 141 ug/L e 117 ug/L, respetivamente. A triptase basal 92 ug/L. Realizou biópsia de medula óssea, mielograma e estudo imunofenotípico que confirmaram mastocitose sistêmica. Nos doentes com doença mastocitária, o risco de anafilaxia após administração de vacinas mRNA contra a COVID-19 tem sido debatido. Considerando o risco de exposição à COVID-19, o risco de anafilaxia após administração da vacina foi discutido com a doente e, após consentimento, a vacina Pfizer/BioNTech® BNT162B2 foi administrada sob vigilância de um alergologista. Não foi administrada pré-medicação, e a doente recebeu as duas doses da vacina sem evidenciar sintomatologia relacionada com ativação mastocitária.

Descritores: Mastocitose sistêmica, vacinação, infecções por coronavírus.

Introduction

The diagnosis and management of mast cell disorders are challenging. The COVID-19 pandemic and consequent massive vaccination for its prevention is an extensively discussed topic when considering patients with mastocytosis. In systemic mastocytosis (SM), there is a production of clonal mast cells and an overabundance of these activated cells in hematopoietic and extra-hematopoietic organs, leading to a highly variable disease phenotype.[1-3] In patients with this disease, proinflammatory mediators (histamine, tryptase, prostaglandin D2, leukotriene C4) may be released from mastocytes without a specific trigger or upon exposure to allergens, such as drugs (including vaccines), foods or venom, inducing symptoms that may range from urticaria or gastrointestinal complaints to potentially life-threatening anaphylaxis.[4] Previous

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studies have demonstrated that vaccines are potential elicitors of mast cell symptoms and anaphylaxis.[5,6] Unless the patient has a history of allergic reactions to any of the vaccine components, there is no absolute contraindication for the currently approved COVID-19 vaccines; nonetheless, in patients with mast cell disorders, vaccine administration should be performed in a hospital setting and a longer observation period is advisable.[7,8]

Case report

A 26-year-old female, internal medicine resident, was referred to the allergy department after two episodes of maculopapular rash on the face, trunk, and upper limbs), dyspnea, throat tightness, conjunctivitis, and tachycardia after intake of non-steroidal anti-inflammatory drugs (NSAIDs). The first episode occurred after intake of oral ibuprofen (400 mg) for upper airway infection, and the second after intravenous administration of diclofenac (50 mg) for a backache. In both episodes, the symptoms developed within a few hours after medication intake, and she was evaluated at the emergency department and treated with intravenous antihistamines and corticosteroids. Serum tryptase was 141 ug/L in the first reaction, and 117 u/L in the second. At the allergy department, skin prick test with inhalants, cereals, and peach non-specific lipid transfer protein (in order to exclude cofactor enhanced food allergy) were negative. Total IgE was 7.78 kU/L, and baseline serum tryptase was 92 ug/L (1.0 -15 ug/L). Considering the elevated serum tryptase, she was evaluated by the hematology department; bone marrow biopsy revealed infiltrates of >15 atypical mast cells, with CD25 positivity on the immunophenotypic study, confirming SM; c-kit D816V mutation was negative. There was no evidence of disease-related organ dysfunction, so it was defined as a case of indolent/smoldering SM. NSAIDs eviction was advised and the patient was prescribed ketotifen 1 mg/once daily and bilastine 20 mg/once daily. No other episodes of anaphylaxis were reported since.

Considering the occupational risk of SARS-CoV-2 infection, the risk of anaphylaxis upon exposure to COVID-19 vaccine was discussed with the patient and, after consent, Pfizer/BioNTech® BNT162B2 was administered under allergist supervision for 1 hour. She maintained her regular treatment with ketotifen and bilastine and the authors decided not to premedicate her with antihistamine and/or corticosteroids, considering these drugs could mask early signs and symptoms of anaphylaxis. Administration of the first and second doses of the vaccine, given 21 days apart, elicited no symptoms.

Discussion

Administration of vaccines against COVID-19 in patients with mastocytosis is controversial, considering that these patients have a higher predisposition for mast cell degranulation and anaphylaxis when exposed to a trigger, including vaccines.[5,6] Beyond anaphylaxis, in patients with mastocytosis, vaccines can induce/exacerbate symptoms like flushing, pruritus, urticaria/angioedema, bullous lesions, or gastrointestinal symptoms. The physiopathology underlying unspecific mast cell activation is not clearly understood, but mechanisms including IgE mediated reactions, Toll like receptors activation, or vaccine components acting as superallergens have been hypothesized.[9,10]

The first approved vaccines against COVID-19 were mRNA vaccines developed by Pfizer-BioNTech® and Moderna®. To date, these vaccines have been described as safe, with minor side effects such as inflammatory signs at the injection site, fatigue, headache, myalgia, chills, arthralgia, and fever, most commonly reported.[11,12] After two episodes of anaphylaxis were reported after Pfizer-BioNTech® vaccines (BNT162b2) in two women who had known food and drug allergies and were carrying auto-injectable epinephrine, it was suggested that caution and vigilance should be reinforced in patients with a history of severe allergy to foods and drugs, including vaccines.[12] Systemic allergic reactions to vaccine components are rare, within a range of 1-5 cases per million applications. Risk factors for inducing or potentially aggravating allergic reactions, such as previous severe anaphylactic episodes, uncontrolled asthma, mastocytosis, and other mast cell disorders, have been described and should be clarified when taking the patient's medical history. For the Pfizer/BioNTech® BNT162B2 COVID-19 vaccine, 11.1 cases of allergic reactions (including anaphylaxis) occurred per 1 million doses.[7,8]

The use of premedication is questionable. A recent Portuguese letter to editor reports two cases of heath care workers with cutaneous and systemic mastocytosis who received the first doses of Pfizer/BioNTech® BNT162B2 COVID-19 vaccine under premedication with H1 and H2 antihistamines and

montelukast, with no side effects.[13] In our patient, premedication or regular treatment increment was not performed due to the risk of masking the early signs of a possible anaphylactic reaction, considering that early recognition of anaphylaxis symptoms and immediate treatment improves its prognosis. This case highlights that the Pfizer/BioNTech® BNT162B2 COVID-19 vaccine is safe in patients with mast cell disorders, and the potential benefits should be pondered even in high-risk patients. Nevertheless, considering the risk of reaction and that prompt recognition and treatment is fundamental to a positive outcome in case of anaphylaxis, the authors suggest that, whenever possible, COVID-19 vaccination should be performed under allergist supervision and in a hospital setting with prompt medical equipment for timely anaphylaxis treatment, and patients should remain in observation for a longer period (at least 1 hour).

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