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Letter

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A UK Survey Examining the Experience of Adults With Mastocytosis Receiving COVID-19 Vaccination

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Mastocytosis is a group of heterogeneous conditions characterized by clonal proliferation of abnormal mast cells in the skin and/or other organs. There are 3 major subforms: cutaneous mastocytosis (CM), in which there is cutaneous but no systemic involvement; systemic mastocytosis (SM), in which there is presence of abnormal mast cells in extracutaneous organs, with or without skin involvement; and mast cell sarcoma. SM can be further subclassified into 5 types, with or without skin involvement: indolent (ISM), smoldering, and aggressive forms; SM with an associated hematological neoplasm (SM-AHN); and mast cell leukemia.[1] The clinical presentation is extremely variable, and symptoms can occur due to release of mast cell mediators (such as histamine, tryptase, eicosanoids, and cytokines) or through infiltration of the skin or extracutaneous organs. Acute release of mast cell mediators through degranulation can cause anaphylaxis, a serious and potentially life-threatening systemic hypersensitivity reaction.

The lifetime risk of anaphylaxis in adult patients with mastocytosis is 49%, and up to 56% in those with systemic forms, and the predominant trigger is Hymenoptera stings.[2] Regarding vaccine reactions, a previous study found that among 42 adults with mastocytosis receiving a total of 57 vaccine doses, none had any adverse reaction.[3] However, the same study suggested that vaccination itself is a potential cause of mediator release particularly in children.

Vaccines against the coronavirus disease 2019 (COVID-19) have emerged at a rapid pace, and there were early reports of anaphylaxis following vaccination with the BNT162b2 Pfizer/BioNTech RNA vaccine.[4] Anecdotally from patients contacting The UK Mastocytosis Support Group (UK Masto), this resulted in increased anxiety and hesitancy about receiving the vaccine for patients with mastocytosis. However, small case series have found that 2 healthcare workers with mastocytosis received the Pfizer/BioNTech vaccine without major adverse reactions,[5] and a larger series of 18 patients by Kaakati et al[6] found that all tolerated COVID-19 vaccination (13 Pfizer/BioNTech; 4 Moderna; 1 Janssen) without adverse reaction. There are no existing data on this from the United Kingdom.

UK Masto therefore developed an anonymous patient survey to collect data regarding reactions after the first dose of the COVID-19 vaccine in adults. The survey was distributed on the UK Masto website, social media, and support forums and data collected between January 26, 2021, and May 21, 2021. As a noninterventional survey of charity members, no ethical approval was required. Respondents were asked about their diagnosis including subtype, and whether it was confirmed/suspected. Where more than 1 subtype was selected, the more advanced form was used in analysis (eg, for patients who selected CM and ISM, the latter diagnosis was used). Responses reporting suspected (rather than confirmed) mastocytosis and mast cell disorders other than mastocytosis were excluded from this analysis.

Patients were asked about the brand of vaccine received, premedication with antihistamines, and whether or not they had experienced anaphylaxis requiring adrenaline in the 12 months prior to vaccination. With regard to adverse effects, they were asked about development of urticaria, flushing, lip swelling, shortness of breath, palpitations, and presyncope, and timing of onset after vaccination. An optional free-text box was provided for further details.

A total of 227 responses were received from patients reporting a variety of clonal and nonclonal mast cell disorders. The responses were assessed by a consultant allergist (A.F.W.) independently, blinded to the underlying diagnosis and subtype, according to World Allergy Organization criteria: acute onset (we defined as <1 hour) mucocutaneous features and at least one of (1) respiratory, (2) cardiovascular, and/or (3) gastrointestinal symptoms/signs.[7] Reactions were classified as Grade 1–5 (Grades 3–5 constitute anaphylaxis, with Grade 5 involving respiratory failure and/or hypotension/collapse).

Following this assessment of the 227 responses, patients with confirmed mastocytosis were extracted for further analysis. This consisted of 130 adults with mastocytosis; 23 (17.7%) had CM (potentially including some without formal systemic evaluation through biopsy of bone marrow or other extracutaneous organs) and the remainder (82.3%) had SM. The majority of patients were female (106; 82%), and the age spectrum of respondents varied between mastocytosis subtype (Figure 1). Eighty-two (63%) received the Oxford/AstraZeneca (Oxford) vaccine, 45 (35%) the Pfizer/BioNTech vaccine (Pfizer), 1 (0.8%) the Moderna vaccine, and 2 (1.5%) were unsure.

Only 2 patients (1.5%), both female, reported symptoms consistent with anaphylaxis by World Health Organization criteria (Figure 2). One was aged 46–55 years; 15–30 minutes after receiving the Pfizer/BioNTech vaccine, she developed urticaria, flushing, shortness of breath, palpitations, and presyncope, and a "feeling of doom," consistent with a Grade 4 reaction.

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HemaSphere (2021) 5:11(e650).
http://dx.doi.org/10.1097/HS9.0000000000000650.
Received: 9 August 2021 / Accepted: 11 September 2021

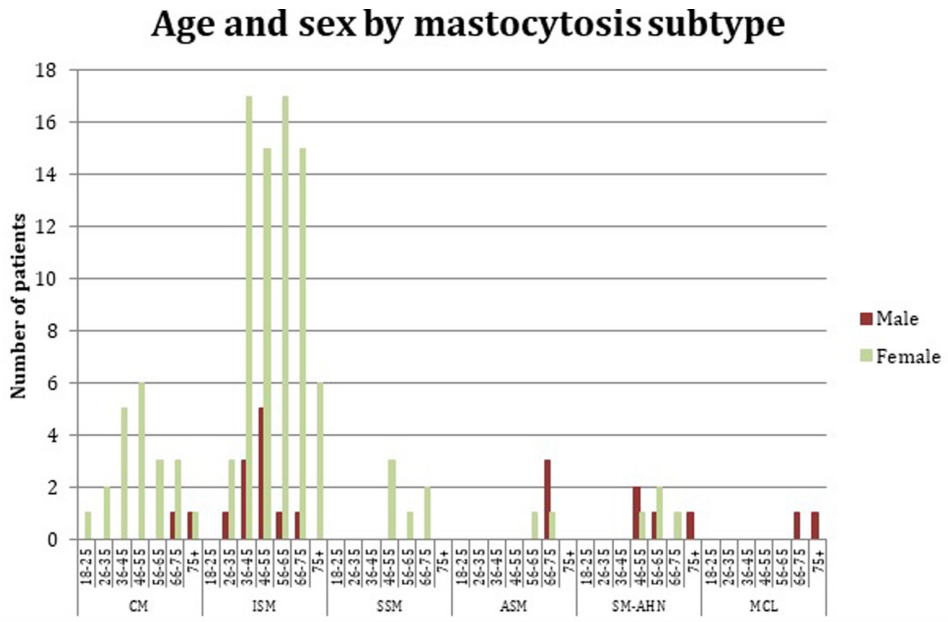

Figure 1. Baseline demographics for patients with mastocytosis recorded in survey. ASM = aggressive systemic mastocytosis; CM = cutaneous mastocytosis; ISM = indolent systemic mastocytosis; MCL = mast cell leukemia; SM-AHN = systemic mastocytosis with an associated hematological neoplasm; SSM = smoldering systemic mastocytosis.

She had not experienced anaphylaxis requiring adrenaline in the 12 months prior to the dose. The second patient was aged 36–45 years, and within 15 minutes of receiving the Oxford/AstraZeneca vaccine, she developed flushing, pruritus, presyncope, and vocal hoarseness, consistent with a Grade 3 reaction. She reported having 1–2 episodes of anaphylaxis requiring adrenaline in the preceding 12 months.

An additional 8 patients (6.2%) reported allergic reactions, none of which had experienced anaphylaxis in the preceding 12 months (Figure 2). Three had CM; of these, 2 (both female, aged 36–55; 1 received the Oxford/AZ vaccine and 1 was not sure) had Grade 1 reactions consisting of urticaria or flushing within 15 minutes of the dose, with no other symptoms. The third was a female aged 56–65 years who received the Oxford/AstraZeneca vaccine and reported flushing and slight presyncope within 15 minutes of the dose.

Five patients with SM also reported nonanaphylaxis allergic reactions (Figure 2). Four of these had ISM and 1 had SM-AHN. Three patients with ISM (2 males aged 26–55 receiving the Oxford vaccine, and 1 female aged 46–55 receiving the Pfizer) had flushing or urticaria within 30 minutes of the dose but no other symptoms. A fourth patient with ISM (female, aged 46–55 receiving the Oxford vaccine) had urticaria, flushing, presyncope, and dysgeusia within 15 minutes consistent with a Grade

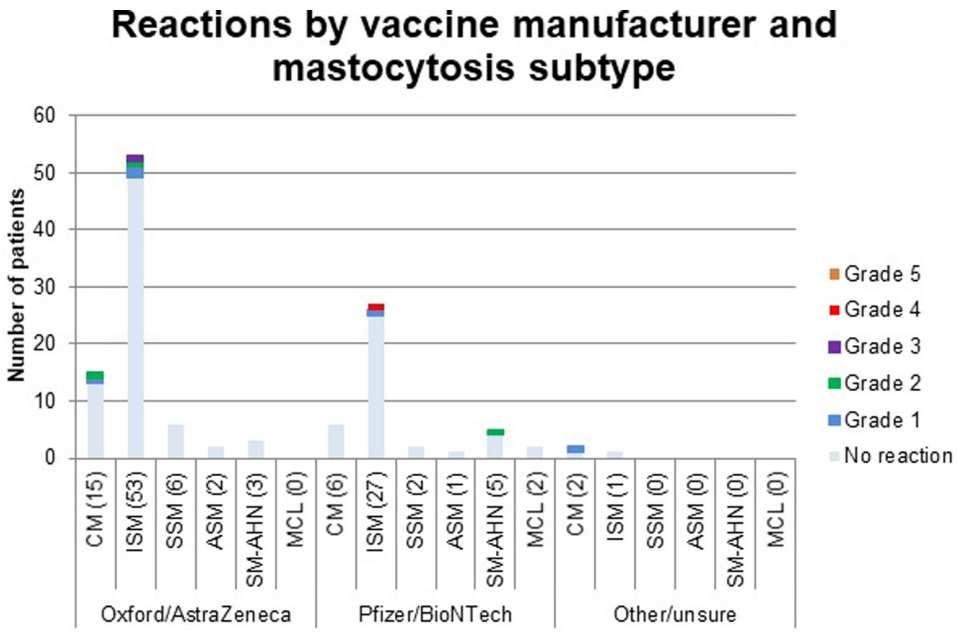

Figure 2. Reactions subdivided by vaccine manufacturer against mastocytosis subtype. All reactions were graded according to WAO criteria.[7] ASM = aggressive systemic mastocytosis; CM = cutaneous mastocytosis; ISM = indolent systemic mastocytosis; MCL = mast cell leukemia; SM-AHN = systemic mastocytosis with an associated hematological neoplasm; SSM = smoldering systemic mastocytosis; WAO = World Allergy Organization.

2 reaction. The patient with SM-AHN was female aged 46–55 and received the Pfizer vaccine, and within 30 minutes had flushing and presyncope, consistent with a Grade 2 reaction.

Overall, most patients (73; 56%) premedicated with antihistamines. Of the 10 who reacted, both with anaphylaxis had taken antihistamine premedication, and 2 of 8 with nonanaphylaxis reactions had premedicated. Seven patients (5.4%) reported at least 1 prior episode of anaphylaxis requiring adrenaline in the last 12 months; only 1 of these had a reaction to the vaccine (Grade 3).

This study has several limitations. Most importantly, the data relies on self-reported diagnosis and self-reported symptoms following vaccination, which is less robust than medically confirmed diagnosis and observed symptoms. However, in the absence of a UK registry and either direct observation of dosing or access to patients' medical records, this is difficult to avoid. Secondly, the distribution of the survey through a patient support group is more likely to have responses from patients actively interested and engaged in their condition. The demographic of the UK Masto membership is predominantly female, consistent with the majority of responses being from females, but less representative of the epidemiology of mastocytosis in the population, which includes more male patients.

Despite these limitations, and until prospective data emerges, our study provides support for the overall safety of COVID-19 vaccination in patients with mastocytosis. We have found a low rate of anaphylaxis (1.5% of patients), which must be balanced against the risk of infection and complications of COVID-19 itself. Nonanaphylaxis reactions including flushing and urticaria are more common (6.2%). Patients should be aware of this and carry an emergency plan to follow in case of reactions, and consideration should be given to longer observation times (up to 30–60 minutes) in patients with mastocytosis.

Acknowledgments

We would like to thank Dr Clive Grattan for his advice and input, as well as Luka Pivovarsky for his help with analyzing the data.

Disclosures

The authors have no conflicts of interest to disclose.

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