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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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Anaphylaxis in the Emergency Department Unit: Before and during COVID-19

To the Editor,

After the declaration of coronavirus disease 2019 (COVID-19) as a global health emergency, healthcare systems have faced unprecedented challenges worldwide.[1] During the same period, emergency departments have reported a significant drop in the average number of daily accident and emergency (A&E) visits and admissions.[2]

We undertook a retrospective audit (registration number: 10952)and enrolled patients attending our Emergency Department Unit (EDU) to investigate how this pandemic has affected the lives of patients experiencing systemic allergic reactions requiring A&E admission.[3] We compared adult patients attending with clinical findings of a systemic allergic reaction and mast cell tryptase elevation in the first half of 2019 from January until the end June with the same period in 2020. This period was chosen as the first cases of COVID-19 in the UK were diagnosed in January 2020.[4]

Demographics, severity of reaction according to the Brown classification being mild, moderate or severe,[5] existence of a possible trigger for anaphylaxis according to the EDU discharge letter, tryptase values during the acute reaction, management and follow-up strategies in the EDU have been evaluated.

There was a significant reduction from 62 to 10 in the number of patients attending EDU with systemic allergic reactions between 2019 and 2020, respectively (Table 1). There were no differences in age or gender between the two groups. The majority of patients in 2019 (52%) experienced mild symptoms and presented with skin and/or mucosal involvement. In 2020, 80% of attendances were with moderate reactions affecting multiple systems. The difference between these two rates was significant suggesting a reduction in the number of EDU attendances of patients with likely milder spontaneous reactions.

Existence of an obvious allergic trigger was lower in 2019 at 54%. However, in 2020 according to EDU discharge letters, 8 of the 10 patients had exposure to a possible culprit trigger shortly before the reaction. Among the reactions occurring in 2020, 60% were likely drug related and followed administration of amoxicillin in four cases. Nitrofurantoin and ibuprofen were identified in single cases. Suspected food triggers in 2020 were walnut and celery each associated with a single case. Adrenaline was used in 80% of cases in 2020 and patients have all been referred to the Allergy Service.

TABLE 1 Comparison of two groups

	Pre-COVID (2019)	During COVID (2020)	*p* value
Number of adult patients attended A&E (*n*)	87545	64230	**<.0001**
Number of adult patients attended A&E with symptoms of systemic allergic reaction and elevated tryptase value (*n*)	62	10	
Age (mean, SD, in years)	51 ± 17	45 ± 18	.7
% female	45	40	.7
Mast cell tryptase value (mean, SD, in µg/L)	19.1 ± 8	20.8 ± 12	.1
Brown classification (%)			
• Mild	52	10	**.007**
• Moderate	40	80	
• Severe	8	10	
Possible culprit trigger (%)			
• Food	9	20	.2
• Drug	40	60	
• Venom	5	0	
• Not indicated	46	20	
Adrenaline usage in EDU (%)	50	80	.09
Referral to Allergy Service (%)	60	100	**.03**

Note: Data are summarized as number, percentage or mean ± standard deviation (SD).
Continuous variables were analysed using Student's *t* test and "*N*-1" chi-squared test. Comparisons of the qualitative data were performed with chi-square test.
Bold values indicate $p < .05$.

Unlike some other countries, outdoor physical activities were encouraged in the UK and increased alcohol intake has been recorded during the lockdown.[6] Although these are considered as potential cofactors for anaphylaxis, no typical cofactor induced reaction was noted according to discharge summaries.

In summary, we believe that despite its limitations such as being an observational, retrospective, monocentric study which has possibly left out certain number of cases with normal tryptase value, this small cohort has helped us to understand what is happening in real life to patients with systemic reactions during the pandemic.

As speculated in previous reviews written about COVID-19 and anaphylaxis, a significant decrease in the number of episodes has been observed. This may be related to the closure of restaurants, reducing the number of food-related anaphylaxis.[3] It is possible that media reports raising concerns about ibuprofen and ACE inhibitors, reduced their use and consequently drug-related skin or mucosal problems. Conversely, we may also deduce from the reduction in the number of patients and the increase in the severity of reactions a fear of virus exposure and reluctance to attend emergency services unless absolutely necessary. Therefore, we believe that we must continue discussing ways to increase accessibility to healthcare, to provide better prevention strategies and to work to reduce unfavourable outcomes of this pandemic on patients with allergic conditions.

KEYWORDS

anaphylaxis, COVID, epidemiology, prevention

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CONFLICT OF INTEREST

The authors declare that they have no relevant conflicts of interest.

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Characterization of the major allergen, Que ac 1, from sawtooth oak pollen

To the Editor,

Oak is the most commonly found tree in Korea, occupying about 40% of the forest area, while the birch population is sparse. Recently, strong IgE reactivity to Bet v 1 was reported due to sensitization to oak in birch-free region.[1] Comparison of allergenicity of birch and oak pollen extracts revealed that sawtooth oak is the main cause of tree pollinosis in Korea.[2] Nevertheless, diagnosis and immunotherapy for pollinosis are performed with products prepared from species (*Q. alba*) that are not native to Korea.[3] We are now reporting the full characterization of Que ac 1, a 17 kDa allergen, which was detected by IgE immunoblotting in a previous study.[2]

Native (n) Que ac 1 was purified in three chromatography steps: anion exchange chromatography, hydrophobic interaction chromatography, and gel filtration (Figure 1A). Edman degradation of this protein resulted in multiple amino acid sequences, indicating the polymorphism of Que ac 1: Gly(Asp)Val(Glu/Pro/Ile)Phe(Tyr/Ile)Thr(Glu)His(Val)Glu(Lys)Ser(Asn)Thr(Ala)SerValIleProProAlaArg(Ala)LeuPheLys. Purified protein was separated into 12 isoforms by 2D gel electrophoresis, and most of these were confirmed to be PR-10 proteins by LC ESI MS/MS and Edman degradation (Figure 1D) (Table S1). Furthermore, Que ac 1 is highly polymorphic as homologous allergens,[4] and 22 isoforms were identified by RT-PCR (Figure S1A). At least 3 isoallergens (1.0101, 10201, 10301) are present, and isoallergen Que ac 1.0101 was deposited in GenBank under accession No.MN201198, Que ac 1.0201 under MN201199, and Que ac 1.0301 under MN201200. Que ac 1.01 accounts for 88.0% of Que ac 1, while 1.02 for 9.3% and 1.03 for 2.7%, respectively (Figure S1A). Furthermore, many of the substitutions found in 1.02 and 1.03 are present in individual 1.01 variants. A predominant isoallergen Que ac 1.0101, officially listed in the WHO/international union of immunological societies allergen nomenclature subcommittee according to the guideline,[5] showed 58.1 to 83.0% sequence identity to homologous allergens (Figure S1B). Notably, it shares a homology of 58.1% to Bet v 1 and only 73.1% to Que a 1, which are the most commonly used molecules for diagnosis of allergy to Fagales pollen.

Recombinant (r) Que ac 1.0101 showed a protein band at about 20 kDa, whereas nQue ac 1 manifests as a 17 kDa protein (Figure 1B). The calculated molecular mass of nQue ac 1 was 17.309 kDa (pI 5.4) and that of its recombinant counterpart was 20.164 kDa (pI 5.53) including 26 amino acids (MGHNHNHNHNHNHNAAGDDDDKASVD-) at the N-terminus. In CD analyses, similar spectra of both native and recombinant Que ac 1 were recorded (Figure 1C), although native protein contained multiple isoforms (Figure 1D). Both native and recombinant Que ac 1 were recognized by IgE antibodies from 91.3% of the oak pollinosis patients' sera. IgE reactivity to rQue ac 1 and nQue ac 1 showed a strong correlation with reactivity to sawtooth pollen extract (Pearson's correlation coefficient = 0.96 and 0.93), while IgE reactivity to nQue ac 1 correlated strongly with rQue ac 1 (Pearson's correlation coefficient = 0.91) (Figure 2A-C). rQue ac 1 was able to inhibit 67.2% of IgE reaction to the whole pollen extract, while 57.6% was inhibited by rBet v 1, 88.7% by nQue ac 1, and 94.7% by the pollen extract at 10 μg of inhibitor concentrations, respectively