The level of serum tryptase observed in testing did not appear to correlate with the severity of Prolonged anaphylaxis or anaphylaxis with loss of consciousness may be a stronger indicator. Grade ≥3 anaphylactic reactions were suggestive of proliferating disease even in the absence of Serum tryptase during anaphylaxis was recorded in a minority of patients.

Rationale

- Indicated systemic mastocytosis (ISM) is a clonal mast cell disease primarily driven by the KIT D816V mutation.1
- Systemic mastocytosis (SM) is estimated to affect 1 in 10,000 adults.2
- The phenotypic presentation of ISM is highly individualized and non-specific, with many patients experiencing chronic debilitating symptoms across multiple organ systems. Accumulation and activation of abnormal mast cells can lead to symptoms including mucosal or extracutaneous lesions with blanche sign, flushing, hypotension, anaphylactic, diarrhea, nauaeousness, and brain fog. Among others.3 These symptoms commonly result in polydysautonomia and a poor quality of life.4
- In a real-world allergy community setting, distinguishing ISM, a clonal mast cell disease from non-clonal mast cell activation (NMCAS) remains challenging. Patients with ISM, are often underdiagnosed due to the generalised presentation, prolonging diagnosis, and treatment.3 Diagnosis is further complicated by patients often presenting to a diverse range of healthcare specialists, the necessity for bone marrow biopsy, and limited availability of molecular testing.5
- The current World Health Organization (WHO) diagnostic criteria may not fully characterize the total phenotypic spectrum of ISM.6
- Here we describe the observable objective findings readily accessible in the community practice setting SM criteria that were retrospectively collected and analyzed to develop a scoring system with the purpose of existing clinical decision-making to determine SM diagnosis in the community allergy practice setting.

Methods

- Data from electronic medical records (EMR), including total immunoglobulin E (IgE) and serum tryptase, from 4 Consortium of Independent Immunology Clinics (CIIC) community allergy sites were retrospectively collected and analyzed (Figure 4).7–9
- The study population comprised 20 patients with ISM
- Data from electronic medical records (EMR), including total immunoglobulin E (IgE) and serum tryptase, from 4 Consortium of Independent Immunology Clinics (CIIC) community allergy sites were retrospectively collected and analyzed (Figure 4).7–9
- The study population comprised 20 patients with ISM
- Patient data were trended against frequently co-existing conditions, and a weighted scoring system with the purpose of assisting clinical decision-making to determine ISM diagnosis

Results

Patient demographics (n=20) are shown in Figure 3. Twenty patients had severe, but also frequent symptoms of allergic reactions. These symptoms commonly result in polydysautonomia and a poor quality of life.10
- Since March 2022, 11 patients were previously undiagnosed and have been correctly diagnosed with ISM based on positive KIT D816V detection in blood (Figure 4).11
- In 20 cases, no abnormal mast cell morphology was noted outside the bone marrow

Conclusions

* Due to the heterogeneity and wide-ranging clinical presentation of ISM, it remains challenging to separate clonal from non-clonal activation symptoms
* Since the WHO criteria for confirming ISM require tests which may not be readily accessible in the real-world practice setting, relying on pathology of skin, gut, and bone marrow biopsies
* In this patient population, median-driven symptoms outside of anaphylaxis did not correspond to all WHO criteria
* The level of serum tryptase observed in testing did not appear to correlate with the severity of symptoms and corresponding burden on quality of life

ISM minor criteria include serum tryptase >20 ng/mL, but no bone marrow mast cell burden

** Patient vignettes for 2 patients are shown in Figure 5. Study period began March 2022 and completed October 2022

Figure 3. Patient demographics (n=20)

Figure 4. Identified ISM patient phenotypes

References