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Mast Cell Activation Syndrome: Diagnostic Challenges in Multisystem Involvement

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Abstract

Mast Cell Activation Syndrome (MCAS) is a rare and complex disorder characterized by inappropriate activation of mast cells, resulting in diverse symptoms affecting multiple organ systems. The diagnosis is challenging due to the absence of standardized criteria and significant overlap with other conditions such as Postural Orthostatic Tachycardia Syndrome (POTS) and hypermobile Ehlers-Danlos Syndrome (hEDS). This case report presents a patient with chronic cough and multisystem manifestations who was ultimately diagnosed with MCAS after years of investigation. The patient experienced significant improvement with histamine antagonists and omalizumab. This case highlights the importance of considering MCAS in patients with unexplained multisystem symptoms and provides insight into diagnosis and treatment options.

Keywords: Mast cell activation syndrome; Postural orthostatic tachycardia syndrome

Introduction

Mast Cell Activation Syndrome (MCAS) is an increasingly recognized condition caused by inappropriate mast cell degranulation and release of mediators such as histamine, tryptase, and prostaglandins [1]. These mediators can affect multiple organ systems, leading to dermatological, gastrointestinal, cardiovascular, and neurological symptoms. The clinical presentation can vary widely, ranging from flushing and urticaria to abdominal pain, hypotension, and cognitive disturbances [2].

The overlap of MCAS with other conditions, such as POTS and hEDS, complicates the diagnostic process. Current diagnostic criteria are not universally standardized, and the episodic nature of the disease often results in delayed diagnosis [3]. This report highlights a case of MCAS that underscores the importance of clinical suspicion and a multidisciplinary approach for accurate diagnosis and treatment.

Case Presentation

History and clinical course

A female patient in her 40s presented to the respiratory clinic with a primary complaint of chronic dry cough. Further history revealed progressive multisystem involvement over several years, including gastrointestinal symptoms (bloating, abdominal pain), dermatological manifestations (recurrent erythematous urticarial changes), and cardiovascular symptoms (episodes of flushing, hypotension, and light-headedness). The patient reported 2–3 episodes daily, which significantly impacted her ability to perform daily activities and work responsibilities.

Symptoms often started with burning and paraesthesia, followed by erythematous changes that improved when lying down. The patient described feeling drained of energy during episodes, with stiffness and cognitive impairment ("brain fog").

Examination and investigations

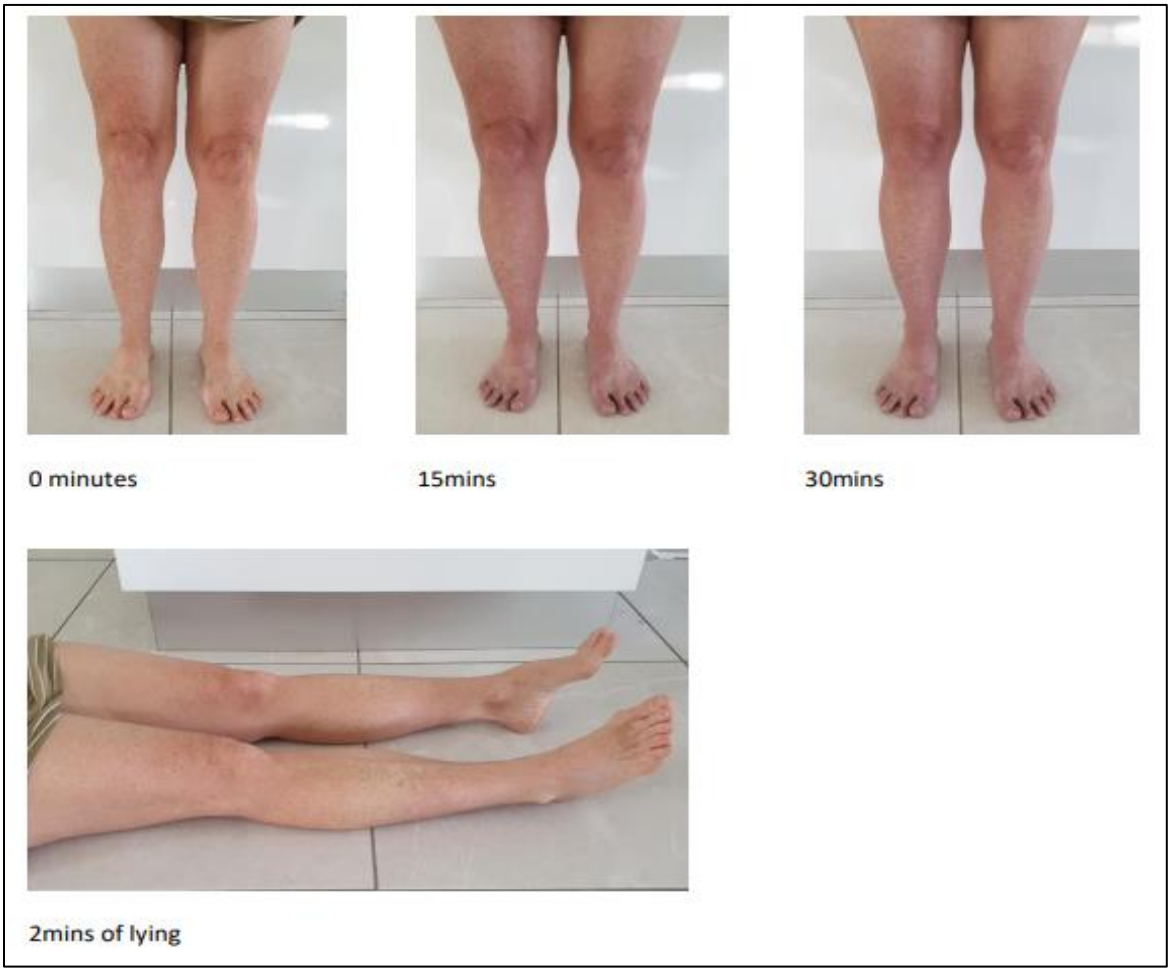
Physical examination revealed erythematous urticarial skin changes during an episode and joint hypermobility. Orthostatic vital signs indicated mild hypotension. Other findings were unremarkable (Figure 1).

Laboratory investigations

- Eosinophils: Up to 0.84 × 10⁹/L (reference: 0.04–0.40 × 10⁹/L)
- IgM: 2.0 g/L (reference: 0.4–1.6 g/L)
- IgE: 1332 kIU/L (reference: 0–100 kIU/L)
- Tryptase: Normal (tested days after symptoms subsided)

Autoimmune screening, gastrointestinal imaging, and endoscopy were unremarkable.

Figure 1: *Erythematous urticarial skin changes during a symptomatic episode, with resolution upon adopting a supine position.*



Differential diagnosis

The patient was initially diagnosed with Postural Orthostatic Tachycardia Syndrome (POTS) and treated with propranolol. However, symptoms worsened, particularly the flushing and hypotension, suggesting a hyperadrenergic form of POTS associated with mast cell activation [4]. The patient also exhibited features of hypermobile Ehlers-Danlos Syndrome (hEDS), including joint hypermobility and chronic fatigue. However, elevated IgE and eosinophilia, along with dermatological manifestations, led to a diagnosis of MCAS.

Management and Outcome

Initial treatment with histamine H1 and H2 antagonists provided partial relief. Sodium cromoglycate eye drops were introduced as a mast cell stabilizer, which improved gastrointestinal symptoms.

Given persistent dermatological symptoms and elevated IgE, a trial of omalizumab (300 mg every four weeks) was initiated. The patient reported significant improvement in symptoms within two months of omalizumab therapy. The frequency and severity of urticarial episodes decreased, and cardiovascular symptoms were better controlled. The patient continues to receive monthly omalizumab injections and reports an improved quality of life.

Discussion

MCAS is a complex disorder that presents with diverse symptoms across multiple organ systems. Its diagnosis is complicated by the absence of standardized criteria and overlap with conditions such as POTS and hEDS. Kohno et al. (2021) observed that 64% of patients with POTS exhibited non-orthostatic symptoms suggestive of mast cell activation [5]. Elevated biomarkers such as tryptase, histamine, and prostaglandins can support the diagnosis, but these markers are often missed due to the episodic nature of the disease [6].

Omalizumab, an anti-IgE monoclonal antibody, has shown significant efficacy in refractory cases of MCAS, particularly in patients with high IgE levels. It reduces mast cell degranulation and mediator release, improving symptoms in chronic spontaneous urticaria and related conditions [7]. This patient's dramatic response to omalizumab highlights its role in managing refractory MCAS.

Learning Points

- Consider MCAS in patients with unexplained multisystem symptoms, especially when involving dermatological, gastrointestinal, and cardiovascular systems.
- Be cautious with beta-blockers in hyperadrenergic POTS, as they may exacerbate symptoms related to mast cell activation.
- Omalizumab is an effective option for refractory MCAS, particularly in patients with elevated IgE levels or chronic spontaneous urticaria.

Patient Perspective

The patient described her experience with MCAS as life-changing, with a prolonged diagnostic journey that significantly affected her professional and personal life. She expressed relief at finally receiving a diagnosis and experiencing substantial improvement with omalizumab. Despite ongoing management, she remains optimistic about her prognosis and grateful for the support provided by her healthcare team.

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