Case Report

ANNALS OF MEDICINE & SURGERY

OPEN

Indolent systemic mastocytosis (ISM) without skin lesions as a recurrent anaphylaxis: a case report study

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Introduction and importance: Mastocytosis encompasses a diverse range of disorders characterized by the clonal accumulation of mast cells in various tissues, including the skin, bone marrow, and gastrointestinal tract.

Case presentation: This case report describes a 32-year-old male patient who presented with a history of recurrent anaphylactic attacks and elevated serum tryptase levels without apparent skin involvement. The diagnostic process and clinical implications of non-cutaneous mastocytosis are discussed in the context of existing WHO criteria.

Clinical discussion: Mastocytosis, although a rare disease, carries the potential for severe complications and can present with atypical symptoms, thereby complicating its diagnosis and management. Consequently, the development of a reliable diagnostic and therapeutic strategy is of paramount importance.

Conclusion: There is a pressing need to delve deeper into the investigation of the potential impacts and manifestations of mastocytosis to further our understanding and enhance patient care.

Keywords: anaphylaxis, case reports, mastocytosis

Introduction

Mastocytosis is a heterogeneous group of disorders characterized by the accumulation of mast cells in various tissues of the body such as skin, bone marrow (BM), and gastrointestinal tract by clonal mast cells[1].

This accumulation is caused by clonal mast cells resulting from gain-of-function mutations in the tyrosine kinase domain of the KIT gene. The most prevalent mutation in adult systemic mastocytosis (SM) is KIT D816V. The disease can be categorized into cutaneous mastocytosis (CM), SM, and a rare aggressive form known as mast cell sarcoma (MCS). SM can be further divided into different subtypes, including indolent SM (ISM), bone marrow mastocytosis (BMM), smoldering SM (SSM), SM with an associated hematologic neoplasm (SM-AHN), aggressive SM (ASM), and mast cell leukemia (MCL). In over 90% of adult patients with typical ISM, SSM, or ISM-AHN, neoplastic mast cells carry the KIT D816V mutation[2].

HIGHLIGHTS

- Mastocytosis, although a rare disease, carries the potential for severe complications and can present with atypical symptoms, thereby complicating its diagnosis and management.
- Consequently, the development of a reliable diagnostic and therapeutic strategy is of paramount importance.
- Moreover, there is a pressing need to delve deeper into the investigation of the potential impacts and manifestations of mastocytosis to further our understanding and enhance patient care.

The prevalence of mastocytosis is estimated to be 10 cases per 100 000 individuals (0.010%) overall and 97 cases per 100 000 individuals (0.097%) among those with *Hymenoptera* venom allergy (HVA). The disease affects both men and women equally[3]. Manifestations of mastocytosis in adults can vary, ranging from characteristic symptoms such as typical skin lesions known as urticaria pigmentosa (UP) and flushing to less specific symptoms like osteoporosis, diarrhea, and anaphylaxis, particularly following insect stings[4]. The diagnosis of systemic mastocytosis is based on the criteria established by the World Health Organization (WHO). To confirm the diagnosis, the presence of the major criterion and at least one minor criterion, or more than two minor criteria, is required. These criteria are outlined in Table 1 of the WHO classification[5].

Some individuals with SM and severe symptoms may also have bee or wasp venom allergy. In these cases, lifelong administration of specific immunotherapy is advised to provide adequate protection. If immunotherapy proves ineffective, alternative

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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Annals of Medicine & Surgery (2024) 86:6179–6181

Received 3 April 2024; Accepted 1 August 2024

Published online 14 August 2024

http://dx.doi.org/10.1097/MS9.0000000000002472

approaches such as IgE-depleting treatment with omalizumab or other experimental therapies should be considered[6]. In this article, we report a 32-year-old male with a history of recurrent anaphylactic attacks with a high level of serum tryptase level without skin involvement. The work has been reported in line with the CARE criteria[7].

Case presentation

This case study presents the detailed medical history, clinical manifestations, and diagnostic workup of a 32-year-old male patient referred to a tertiary immunology department at Taleghani Hospital in Gorgan City, Iran, due to recurrent anaphylaxis. Notably, the patient had also experienced three episodes of spontaneous loss of consciousness and seizures in the past year, unrelated to insect bites. According to the case presentation, some episodes of insect bites have occurred in the last years, but there is no information data about the exact time of insect bite. Laboratory results of a child are recorded in Table 2.

Despite multiple visits to various general practitioners, the patient's symptoms were only temporarily alleviated but not fully resolved. Furthermore, no comprehensive diagnostic workup had been conducted before the referral.

The patient provided a detailed medical history, emphasizing recurrent anaphylaxis episodes triggered by various factors, including insect stings. He had a childhood history of rhinitis, wheezing, and skin lesions. Notably, the patient had sought treatment from different general practitioners, with only temporary symptom relief. The patient belonged to a high-risk group due to smoking, history of consumption of opium, and frequent anaphylaxis attacks. Also, the history of the metabolic assessment, EEG and MRI is normal.

The patient experienced symptoms such as coughing, flushing, severe dyspnea, hypotension, and abdominal pain, which closely resembled anaphylaxis, following insect stings. Additionally, three episodes of spontaneous loss of consciousness and seizures occurred in the absence of any known trigger. A comprehensive physical examination did not reveal any remarkable findings. Nasal and oropharyngeal inspection, cardiopulmonary auscultation, and abdominal examination yielded normal results.

Complete blood counts, liver function tests, thyroid function tests, and HIV antibody tests were performed, all of which showed no significant abnormalities. Oral food allergy tests were negative. However, the serum basal tryptase level was elevated at 28 ng/ml, raising suspicion of mastocytosis.

To confirm the diagnosis, bone marrow aspiration was conducted, revealing a normocellular sample with an increased number of mast cells. Immunohistochemistry markers, particularly CD117, were positive in scattered mast cells.

Table 1

Criteria of WHO for diagnosis of systemic mastocytosis.

Major criteria	Multifocal, compact infiltrates of MCs > 15% in BM biopsy and/or other extracutaneous organ
Minor criteria	More than 25% of spindle-shaped MCs in BM smears
	Aberrant expression of CD25 and/or CD2 by BMMCs
	Detection of D816V KIT mutation in BM
	Serum tryptase levels exceeding 20 ng/ml (does not count in patients who have clonal hematological non-MCs lineage disease

Table 2

Routine blood examination performed.

	Count	Reference	Unit
WBC	5970	4000–10 000	$10^3/\mu l$
Neutrophil	2567 (43%)	2500–7000	$10^3/\mu l$
Lymphocyte	2881 (47%)	1000–4800	$10^3/\mu l$
Eosinophil	179 (3%)	30–350	$10^3/\mu l$
Monocyte	6%	2–8%	$10^3/\mu l$
Platelets	195 000	140 000–400 000	$10^3/\mu l$
BUN	16	6–24	mg/dl
Cr	1.4	0.7–1.4	mg/dl
SGOT	34	8–45	U/l
SGPT	59	7–56	U/l
ALP	173	44–147	IU/l
Serum Ig A	131	87–352	mg/dl
HIV 1,2	Neg	–	–
HCV Ab	Neg	–	–
HBS-Ag	Neg	–	–
Beta Tryptase (ECL.Method)	28	1–15	ng/ml

ALP, alkaline phosphatase; BUN, blood urea nitrogen; Cr, creatinine; HBS-Ag, hepatitis B surface antigen; HCV, hepatitis C virus; HIV, human immunodeficiency virus; SGOT, serum glutamic-oxaloacetic transaminase; SGPT, serum glutamic-pyruvic transaminase; WBC, white blood cell.

Trephine bone biopsy included in the section shows bony terabecula interspaced with marrow tissue with about 60% cellularity composed of all hematopoietic cells in different stages of maturation and an increased number of mast cells (Table 3). Considering the patient's recurrent anaphylaxis and the possibility of mastocytosis, an action plan for anaphylaxis management and mastocytosis control was developed. Additionally, the patient provided consent for the design of a bee venom immunotherapy program.

Discussion

In this manuscript, we detail an instance of SM punctuated by recurrent anaphylaxis. The early identification of this condition carries substantial significance, as available pharmacological interventions can effectively manage it, thereby reducing the risk of associated complications. The lapse in time prior to accurate diagnosis assumes particular importance for cases lacking cutaneous manifestations, notably when the disease exhibits a more aggressive course. Complications that can be circumvented by prompt diagnosis and appropriate therapeutic strategies include organ dysfunction and mortality in the context of disease progression, potentially fatal anaphylactic reactions, and pathological bone fractures resulting from severe osteoporosis[8].

In the process of diagnosing systemic involvement, patients presenting with recurring symptoms or indications of organ

Table 3

Bone marrow aspiration.

Diff count					
Blast	1	Promyelocyte	2	Myelocyte	11
Metamyelocyte	2	Segment	8	Band	14
Plasma cell	4	Eosinophil	14	Lymphocyte	8
Erythroid	36	M/E	52/36 = 1.4	Iron stain	4+
Erythroid Series	Matured as order	Myeloid Series	Matured as order	Megacaryocyte	Adequate

involvement – such as anemia, leucopenia, thrombocytopenia, hematochezia, melena, or severe bone pain – undergo comprehensive diagnostic evaluations. These evaluations commonly encompass a bone marrow biopsy, abdominal ultrasound, and gastrointestinal procedures like endoscopy and colonoscopy. In the patient discussed in this case report, a bone marrow biopsy revealed a positive result for CD117. It is notable that elevated tryptase levels have been found to correlate with the quantity of mast cells present in the skin.

Conclusion

Mastocytosis, although a rare disease, carries the potential for severe complications and can present with atypical symptoms, thereby complicating its diagnosis and management. Consequently, the development of a reliable diagnostic and therapeutic strategy is of paramount importance. Moreover, there is a pressing need to delve deeper into the investigation of the potential impacts and manifestations of mastocytosis to further our understanding and enhance patient care.

Ethical approval

This study adhered to the principles of the Declaration of Helsinki and received approval from the Research Ethics Committees of the Medical University of Golestan under the reference number IR.GUMS. REC.1403.082.

Consent

Written informed consent was obtained from the patient's parents/legal guardian for publication and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request. The whole research was done under the permission of the Ethics committee of Golestan University of Medical Sciences.

Source of funding

None.

Author contribution

S.A.A.: diagnosed and managed this patient and interpretation; S.D. and E.G.: writing the first manuscript draft; M.G.-G. and S. A.A.: revised the manuscript and finalized the draft..

Conflicts of interest disclosure

The authors declare no conflict of interest.

Research registration unique identifying number (UIN)

To register for research, one needs to pay a charge. We are under international sanction, so unable to pay or transfer the registration fee.

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Data availability statement

The datasets are available from the corresponding author on reasonable request.

Provenance and peer review

Not commissioned, externally peer-reviewed, Journal Pre-proof.

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