THE MASTOCYTOSIS SOCIETY SURVEY ON MAST CELL DISORDERS: Part 2-Clinical Experiences, Co-Morbidities, Diet, Families and Opinions

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ABSTRACT

Rationale: Mast cell diseases such as mastocytosis and mast cell activation syndromes involve abnormal proliferation or activation of these cells leading to many potentially debilitating symptoms. In order to determine the characteristics and experiences of people known or suspected to have a mast cell disorder, The Mastocytosis Society (TMS), a U.S. based patient advocacy, research and education organization, conducted a survey of patients.

Methods: This web-based survey was publicized through specialty clinics and the Society's newsletter, Web site and online blogs. Both online and paper copies of the questionnaire were provided together with required statements of consent.

Results: The first set of results from this survey of 420 respondents has been previously published[1]; the second set is now presented. These results include source(s) of diagnosis, clinical and laboratory tests performed, co-morbid conditions, dietary practices, possible familial occurrence of mast cell diseases, and perceptions concerning mast cell related medical care in the United States.

Conclusions: These patient survey results are provided to assist medical professionals in defining clinical approaches and research goals and to give patients with mast cell disorders the opportunity to review the experiences of similar patients.

BACKGROUND

Mature mast cells (MC) are found around blood vessels in all tissues, and also where the body interacts with its surroundings, well-positioned for quick reaction to environmental threats. MC disorders (MCD) include diseases involving abnormal proliferation and/or activation of these cells. Patients may have a primary MCD or non-clonal IgE mediated or non-IgE mediated MC activation including MC activation syndrome (MCAS)[2-5]. People with MCD may be at risk for anaphylaxis and chronic and debilitating symptoms.

Clonal MC carrying D816V or other KIT tyrosine kinase mutations have been identified in patients with primary MCD, including mastocytosis and (mono)clonal MCAS.[2-5] Cutaneous mastocytosis (CM) usually occurs in children, while systemic mastocytosis (SM), involving internal organs, is generally diagnosed in adults.

MC activation occurs by both IgE-dependent and independent mechanisms, causing MC to release mediators including histamine, tryptase, arachidonic acid metabolites, such as prostaglandins and leukotrienes, cytokines and chemokines, which initiate or exacerbate symptoms.

METHODS

- Confidential cross-sectional survey questionnaire
- Eligible participants were patients with MCD of all ages, or caregivers, living in or outside the U.S.
- Publicized through TMS (*The Mastocytosis Chronicles*), clinic notices of physicians working with TMS support groups, TMS website and online MCD-related blogs.
- Posted online through TMS website link, April 15 - May 24, 2010.
- Valid responders defined as answering at least some questions beyond opening section, "Demographics and Diagnosis".

Demographics

- Responders 530, Valid 420
- Ages (of 416 subjects providing birth years)
  Average 44.8, Median 48, Range 1 - 80
- Gender:
  Female 62.6%
  Male 22.1%
- Ethnicity
  White 93.6% Native American, Hispanic or Other/mixed 6.0%
- Residence (not collected due to confidentiality concerns)
  Care in U.S. received by 84.3%

RESULTS:

Table I. "Who diagnosed your mast cell disorder?"

Physician Type(s) Recalled as Source(s) of Diagnosis	Total Respondents No. (% of 420)	Recalled Single Physician Type No. (% of 252)
Dermatologist	196 (46.7)	103 (40.9)
Allergist/immunologist	130 (31.0)	61 (24.2)
Hematologist/oncologist	111 (26.4)	38 (15.1)
Primary Care Physician	57 (13.6)	6 (2.4)
Gastroenterologist	49 (11.7)	18 (7.1)
Other*	26 (6.2)	9 (3.6)
Unspecified no./type (eg. "doctor", hospital name)	21 (5.0)	

*Other includes endocrinologist (13), internist-internal medicine specialist (5), pediatrician (4), rheumatologist (3), and others reported by 2 or less.

TABLE II. Clinical Exams and Laboratory Tests reported by 389 respondents

Exams/Tests	Total* Respondents No. (%)†	Frequency‡ Annual or More	Not Routine
Clinical Exams			
History & physical	323 (83.0)	183 (56.7)	113 (35.0)
Visual skin	321 (82.5)	185 (57.6)	101 (31.5)
Photographic skin	100 (25.7)	26 (26.0)	52 (52.0)
Diagnostic Tests			
Complete Blood (CBC)	337 (86.6)	263 (78.0)	62 (18.4)
Serum chemistries	147 (37.8)	105 (71.4)	36 (24.5)
Serum ferritin	76 (19.5)	41 (53.9)	30 (39.5)
Skin biopsy	237 (60.9)	Not queried	
Bone marrow biopsy	221 (56.8)	36 (16.3)	154 (69.7)
Diagnostic Markers			
Serum tryptase	300 (77.1)	175 (58.3)	105 (35.0)
24hr urine histamine	198 (50.9)	51 (25.8)	128 (64.6)
24hr urine prostaglandins	84 (21.6)	29 (34.5)	44 (52.4)
C-kit - other genetic	123 (31.6)	Not queried	

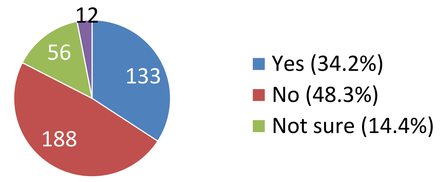
*Total of "yes" (test ever performed) plus those with no answer, but selected or noted a frequency.
†Percent of 389 respondents. ‡Percent of total for each test.

Tests Continued, Radiographic

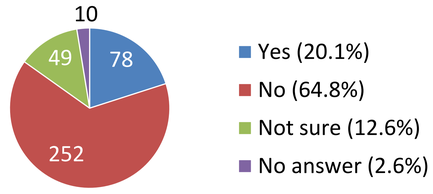
Type	Total	Annual or more	Not routine
Bone scan	132 (33.9)	31 (23.5)	83 (62.9)
Bone density*	213 (54.8)	61 (28.6)	109 (51.2)
Scans: X-ray, CT	239 (61.4)	52 (21.8)	148 (61.9)

***Bone density test, gender**
Female 142 (66.7%) Male 32 (15.0%) No answer 39 (18.3%)

Tryptase measured, baseline



Tryptase measured, acute symptoms/anaphylaxis



Positive genetic tests (389 respondents)

C-Kit D816V mutation
Yes 47 (24.4%) No 61 (15.7%) Not sure 85 (21.9%)
Not tested 191 (49.1%)

Other genetic mutation
Yes 15 (3.9%) No 73 (18.8%) Not sure 98 (25.2%)
Not tested 193 (49.6%)

Cells express CD2 and/or CD25
Yes 24 (6.2%) No 13 (3.3%) Not sure 185 (47.6%)
Not tested 162 (41.6%)

Co-morbid conditions
Osteopenia or Osteoporosis 120 (31.4%)
High blood pressure 88 (23.0%)
Hypercholesterolemia 82 (21.5%)
Cancer 53 (13.9%)
skin 32 (8.4%) other 27 (7.1%)
Coronary artery disease 11 (2.9%)
Heart attack 10 (2.6%)

Family occurrence of MCD (376 respondents) 86 (22.9%) reported one or more relative(s) with either suspected or confirmed MCD.

Diet and nutrition 382 respondents (91.0%)
Professional recommendations

-Physician referred to dietitian 41 (10.7%)
-Physician recommended Low Histamine Diet 46 (12.0%)
-Dietitian recommended Low Histamine Diet 22 (5.8%)

Perceptions of 94 who followed a Low Histamine Diet

- Symptoms improved?
  Yes 48 (51.1%)
  No 17 (18.1%)
  Not sure or no answer 27 (28.7%)
- Nutrition adequate?
  Yes 48 (51.1%) (same 48 as above)
  No 32 (34.0%)
  Not sure 14 (14.9%)

Medical care for MCD in U.S 317 respondents (84.3%)

- Number of centers sufficient 51 (16.1 %)
- Being treated by MCD specialist 124 (39.1%)
- Physician said could not treat them 118 (37.2%)
- Comfortable if local & MCD specialist 263 (83.0%)
- Well Informed by physician 208 (65.6%)

SUMMARY AND CONCLUSIONS

- Survey respondents recalled a wide variety of diagnostic physician types and tests, but many were unsure what was performed or its purpose.
- Up to 30% of respondents had co-morbid condition(s).
- Dietary approaches have been tried with success for some, but others believed that their symptoms had not improved and that their nutrition was not adequate.
- A fifth of respondents indicated relative(s) with a MCD.
- Medical care for MCD in the U.S. is limited, but most patients felt they were well informed and would adapt to their physician collaborating with a MCD specialist.

References

1. Jennings S, Russell N, Jennings B, Slee V, Sterling L, Castells M, Valent P, Akin C. The Mastocytosis Society Survey on Mast Cell Disorders: Patient Experiences and Perceptions. J Allergy Clin Immunol Pract. 2014;2(1)70-6.
2. Valent P, Akin C, Escribano L, Fodinger M, Hartmann K, Brockow K, et al. Standards and standardization in mastocytosis: consensus statements on diagnostics, treatment recommendations and response criteria. Eur J Clin Invest. 2007 Jun;37(6):435-53.
3. Valent P, Akin C, Arock M, Brockow K, Butterfield JH, Carter MC, et al. Definitions, criteria and global classification of mast cell disorders with special reference to mast cell activation syndromes: a consensus proposal. Int Arch Allergy Immunol. 2012;157(3):215-25.
4. Alvarez-Twose I, Gonzalez de Olano D, Sanchez-Munoz L, Matito A, Esteban-Lopez MI, Vega A, et al. Clinical, biological, and molecular characteristics of clonal mast cell disorders presenting with systemic mast cell activation symptoms. J Allergy Clin Immunol. 2010 Jun;125(6):1269-78 e2.
5. Akin C, Valent P, Metcalfe DD. Mast cell activation syndrome: Proposed diagnostic criteria. J Allergy Clin Immunol. 2010 Dec; 126 (6): 1099-104.e4.
6. Rothman KJ, Greenland S. Precision and validity in epidemiologic studies. Modern Epidemiology. 2nd ed. Philadelphia (PA): Raven Publishers; 1998. p. 115-34.

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