ONLINE REPOSITORY

CASE REPORT

We report on a 48-year-old female patient suffering from smoldering systemic mastocytosis with a history of multiple (n = 64) episodes of life-threatening anaphylactic reactions. In 1998, therapy with H1- and H2-receptor blockers (desloratadine and ranitidine) was initiated. Since 2001, she also received levocetirizine (see Table E6). Despite this therapy, recurrent life-threatening anaphylactic reactions were recorded. The severity and frequency of these anaphylactic reactions as well as the high MC burden present in this patient (as assessed by bone marrow histology and serum tryptase levels) prompted us to initiate cytoreductive therapy with 2-chlorodeoxyadenosine (cladribine) (2CdA). Between December 2003 and October 2004, 6 subsequent cycles of 2CdA (0.13 mg/kg/d, days 1-5) were given. Treatment resulted in a marked decrease in the serum tryptase level (Figure 3, *A*) and a decrease in the MC burden confirmed by a bone marrow biopsy. In the next 11 months, no further severe symptoms were observed. However, 12 months after the last cycle of 2CdA she again started suffering from recurrent severe anaphylactic reactions. In May 2007, 30 months after the end of the first series of 2CdA cycles, a second series of 3 cycles of therapy with 2CdA (0.13 mg/kg/d; days 1-5) was initiated followed by a period without severe symptoms. In addition, a further decrease in serum tryptase level was observed (Figure 3, *A*). Similar to the first series, recurrence of severe events was observed 20 months after the completion of this series of 2CdA cycles. In 2014, treatment with omalizumab (300 mg subcutaneous every 3-4 weeks) was initiated and resulted in a marked improvement (see Table E6). No life-threatening events were recorded during the last 4 years when the patient received omalizumab. Serial measurements of total serum immunoglobulin (IgE) showed a clear increase following cytoreduction induced by 2CdA (Figure 3, *A*). Serum tryptase remained at relatively low levels for more than 6 years after cytoreductive therapy with 2CdA (despite recurrence of anaphylaxis).

TABLE E1. Characteristics of patients with mastocytosis

Patient no.	Age (y)	Sex	Diagnosis (WHO)	Tryptase (ng/mL)	WBC (cells/μL)	Hemoglobin (g/dL)	Platelets (cells/μL)	Total IgE (kU/L)	History of allergic reactions	Type of allergen(s)	Severity of symptoms
1	35	F	SSM	202	6,800	13.8	216,000	12.10	No	—	—
2	46	F	ISM	938	6,450	13.6	279,000	NA	Yes*	Birch, nuts, food, wasps	Anaphylaxis
3	47	F	ISM	47.9	7,300	14.5	237,000	10.20	No	—	—
4	55	F	SSM	352.5	4,860	13.1	280,000	<2.00	NK	—	—
5	34	F	ISM	45.6	5,910	12.3	288,000	22.40	Yes*	Wasps	Anaphylaxis
6	35	F	MIS	NA	NA	NA	NA	8.44	No	—	—
7	36	M	ISM	34.4	8,400	15.6	341,000	47.80	Yes*	Wasps, bees	Not reported
8	36	F	ISM	23.3	10,880	13.9	329,000	473	Yes	Birch, timothy grass, nuts	Anaphylaxis
9	45	M	ISM	90.6	7,250	12.5	242,000	6.80	No	—	—
10	26	F	ISM	68	3,750	13.3	204,000	10.40	No	—	—
11	37	F	ISM	69.7	7,400	12.7	272,000	33.90	No	—	—
12	37	M	ISM	33.5	7,280	14.8	307,000	336	No	—	—
13	53	M	SM-AHN	204.0	35,490	16.4	287,000	5.54	No	—	—
14	33	F	ISM	15.5	9,220	15	251,000	5.55	No	—	—
15	38	F	CM	13.7	8,660	13.6	378,000	177	No	—	—
16	59	M	ASM	285	6,760	9.6	115,000	15.6	No	—	—
17	33	M	CM	12.4	10,000	15.8	158,000	90.6	No	—	—
18	37	F	ISM	46.5	5,190	13.9	221,000	12.4	No	—	—
19	31	F	ISM	17.9	6,620	13.5	256,000	9.95	No	—	—
20	53	F	ISM	53.7	5,110	12.4	205,000	70.2	No	—	—
21	36	F	CM	17.1	5,760	13.6	264,000	39.1	Yes	Birch, mugwort	Rhinitis, conjunctivitis
22	31	F	MIS	13.5	7,800	14.1	305,000	87.5	NK	—	—
23	58	M	ISM	108	6,100	14.2	307,000	11.3	No	—	—
24	42	M	ISM	14.5	5,450	14.3	265,000	5.52	No	—	—
25	56	M	ISM	34.8	7,960	13.5	320,000	17.5	No	—	—
26	48	F	SSM	1090	5,250	11.2	212,000	17.0	Yes	Timothy grass, mugwort, food	Anaphylaxis
27	64	M	ISM	164	10,480	16.1	206,000	NA	No	—	—
28	72	M	SM-AHN	77.7	2,950	12.2	101,000	16.3	No	—	—
29	21	M	ASM	53.6	5,030	12.9	269,000	29.2	No	—	—
30	62	F	ISM	25.6	5,410	14.8	257,000	46.7	No	—	—
31	47	F	SM-AHN	NA	NA	NA	NA	<2.00	No	—	—
32	50	F	SSM	175	3,820	12.8	193,000	18.3	No	—	—
33	72	M	ASM	1,617	4,370	9.1	25,000	12.6	No	—	—
34	40	M	SSM	937	3,980	12.8	201,000	5.91	No	—	—
35	52	F	SM-AHN	379	7,250	10.2	86,000	16.9	No	—	—
36	56	M	ISM	650	10,480	14.4	329,000	NA	No	—	—

37	53	M	SM-AHN	615	27,950	8.8	54,000	41.9	No	—	—
38	73	M	ISM	49.9	5,130	14.2	265,000	60.1	Yes	Timothy grass	Not reported
39	53	M	ISM	17.1	4,360	15.1	215,000	8.63	No	—	—
40	48	F	ISM	78.5	4,690	13.6	237,000	6.65	Yes	Birch	Not reported
41	45	F	CM	6.1	5,720	13.2	269,000	124	No	—	—
42	33	F	ISM	45.5	8,960	12.1	274,000	4.90	No	—	—

ASM, Aggressive systemic mastocytosis*; CM*, cutaneous mastocytosis; *f*, female; *ISM*, indolent systemic mastocytosis; *m*, male; *MIS*, mastocytosis in the skin; *NA*, not available; *NK*, not known; *SM-AHN*, systemic mastocytosis with an associated hematologic neoplasms; *SSM*, smoldering systemic mastocytosis; *WBC*, white blood cell count; *WHO*, World Health Organization.
*In these patients, hypersensitivity reactions against bee or wasp were recorded. In patient number 5, a previous sting did not result in anaphylaxis but the second exposure resulted in a severe hypersensitivity reaction. In the other 2 patients, no history about previous stings was available.

TABLE E2. List of allergens spotted on the chip used in this study

Allergen source	Allergen
Kiwi fruit	Act d 1
Kiwi fruit	Act d 2
Kiwi fruit	Act d 5
Kiwi fruit	Act d 8
Alder	Aln g 1
Alternaria plant rot fungus	Alt a 1
Alternaria plant rot fungus	Alt a 6
Ragweed	Amb a 1
Cashew	Ana o 1
Cashew	Ana o 2
Cashew	Ana o 3
Herring worm	Ani s 1
Herring worm	Ani s 3
Celery	Api g 1
Honeybee	Api m 1
Honeybee	Api m 2
Honeybee	Api m 4
Peanut	Ara h 1
Peanut	Ara h 2
Peanut	Ara h 3
Peanut	Ara h 6
Peanut	Ara h 8
Peanut	Ara h 9
Mugwort	Art v 1
Mugwort	Art v 3
Common mold	Asp f 1
Common mold	Asp f 3
Common mold	Asp f 6
Brazil nut	Ber e 1
European white birch	Bet v 1
European white birch	Bet v 2
European white birch	Bet v 4
German cockroach	Bla g 1
German cockroach	Bla g 2
German cockroach	Bla g 5
German cockroach	Bla g 7
Storage mite	Blo t 5
Domestic cattle	Bos d 4
Domestic cattle	Bos d 5
Domestic cattle	Bos d 6
Domestic cattle	Bos d 8
Domestic cattle	BSA
Milk	aS1-casein
Milk	aS2-casein
Milk	b-casein
Milk	K-casein
Milk	Lactoferrin
Dog	Can f 1
Dog	Can f 2
Dog	Can f 3
Dog	Can f 4
Dog	Can f 5
Dog	Can f 6
Goosefoot	Che a 1
Fungus of plants	Cla h 8
Hazelnut	Cor a 1.0401
Hazelnut	Cor a 8
Hazelnut	Cor a 9
Sugi	Cry j 1
Bermuda grass	Cyn d 1
Cypress	Cup a 1
American house-dust mite	Der f 1
American house-dust mite	Der f 2
European house-dust mite	Der p 1
European house-dust mite	Der p 2
European house-dust mite	Der p 4
European house-dust mite	Der p 5
European house-dust mite	Der p 7
European house-dust mite	Der p 10
European house-dust mite	Der p 11
European house-dust mite	Der p 14
European house-dust mite	Der p 15
European house-dust mite	Der p 18
European house-dust mite	Der p 21
European house-dust mite	Der p 23
Domestic horse	Equ c 1
Domestic horse	Equ c 3
Common buckwheat	Fag e 2
Cat	Fel d 1
Cat	Fel d 2
Cat	Fel d 4
Baltic cod	Gad c 1
Chicken	Gal d 1
Chicken	Gal d 2
Chicken	Gal d 3
Chicken	Gal d 5
Soybean	Gly m 4
Soybean	Gly m 5
Soybean	Gly m 6
Latex	Hev b 1
Latex	Hev b 3
Latex	Hev b 5
Latex	Hev b 6.01
Latex	Hev b 8
English walnut	Jug r 1
English walnut	Jug r 2
English walnut	Jug r 3
Storage mite	Lep d 2
Apple	Mal d 1
Annual mercury	Mer a 1
Mouse	Mus m 1
Bromelain	MUXF3
Olive	Ole e 1
Olive	Ole e 5
Olive	Ole e 6
Olive	Ole e 7
Olive	Ole e 8
Olive	Ole e 9

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TABLE E2. *(Continued)*

Allergen source	Allergen
Olive	Ole e 10
Timothy grass pollen	Phl p 1
Timothy grass pollen	Phl p 2
Timothy grass pollen	Phl p 4
Timothy grass pollen	Phl p 5
Timothy grass pollen	Phl p 6
Timothy grass pollen	Phl p 7
Timothy grass pollen	Phl p 11
Timothy grass pollen	Phl p 12
Pellitory-of-the-Wall	Par j 2
Black tiger shrimp	Pen m 1
Black tiger shrimp	Pen m 2
Black tiger shrimp	Pen m 4
Pistachio	Pis v 3
London plane tree	Pla a 1
London plane tree	Pla a 2
London plane tree	Pla a 3
London plane tree	Pla l 1
Mediterranean paper wasp	Pol d 5
Peach	Pru p 1
Peach	Pru p 3
Almond	Pru du 3
Almond	Pru du 4
Almond	Pru du 6
Almond	Pru du 6.01
Almond	Pru du 6.02
Sesame	Ses i 1
Wheat	Tri a 14
Wheat	Tri a 19.0101
Wheat	Tri a 36
Yellow jacket	Ves v 1
Yellow jacket	Ves v 5

IUIS, International Union of Immunological Societies.
The sources and names of the allergens according to IUIS are shown.

TABLE E3. Heat map of IgE reactivities detected in patients with mastocytosis as assessed by allergy chip-profiling (only those allergens for which at least 1 patient showed a positive result are shown). A detailed description of allergens is presented in Table E4.

Patient no.	Act d 1	Aln g 1	Amb a 1	Api g 1	Api m 1	Api m 4	Ara h 1	Ara h 8	Art v 1	Bet v 1
1	0	0	0	0	0	0	0	0	0	0
2	0	7.28†	0	0.48*	0	0	0	0.1	0	16.48‡
3	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0
6	0	0.25	0	0	0	0	0	0.17	0	0.91*
7	0	0	0	0	0	0	0	0	0	0
8	0.18	0.15	0	0	0	0	0	0	0	0.71*
9	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0.12	0.35*	0.19	0	0	0
13	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0
15	0.18	0	0	0	0.75*	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0	0	0
21	0	0.32*	6.17†	0	0	0	0	0	0	0.56*
22	0	0	0	0	0	0	0	0	0	0
23	0	0	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0	0	0
25	0	0	0	0	0	0	0	0	0	0
26	0	0	0	0	0	0	0	0	1.22†§	0
27	0	0	0	0	0	0	0	0	0	0
28	0	0	0	0	0	0	0	0	0	0
29	0	0	0	0	0	0	0	0	0	0
30	0	0	0	0	0	0	0	0	0	0
31	0	0	0	0	0	0	0	0	0	0
32	0	0	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0	0	0
34	0	0	0	0	0	0	0	0	0	0
35	0	0	0	0	0	0	0	0	0	0
36	0	0	0	0	0	0	0	0	0	0
37	0	0	0	0	0	0	0	0	0	0
38	0	0	0	0	0	0	0	0	0	0
39	0	0	0	0	0	0	0	0	0	0
40	0	2.14†	0	0	0	0	0	0.19	0	8.15†
41	0	0	0	0	0	0	0	0	0	0
42	0	0	0	0	0	0	0	0	0	0

Patient no.	Can f 3	Cor a 1.0401	Cyn d 1	Cup a 1	Der f 2	Der p 2	Fel d 2	Gal d 1	Lep d 2	Mal d 1
1	0	0	0	0	0	0	0	0	0	0
2	0	5.2†	0	0	0	0	0	0	0	1.73†
3	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0
6	0	0.09	0	0	0	0	0	0	0	0
7	0	0	0	0	0.08	0.11	0	0	0	0
8	0.24	1.18†	0.12	0	0	0	0.26	0	0	0.22
9	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0

(continued)

TABLE E3. *(Continued)*

Patient no.	Can f 3	Cor a 1.0401	Cyn d 1	Cup a 1	Der f 2	Der p 2	Fel d 2	Gal d 1	Lep d 2	Mal d 1
11	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0.12	0	0
16	0	0	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0
19	0	0	0.34*	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0	0	0
21	0	0.2	0	0.11	0	0	0	0	0	0
22	0	0	0	0	0	0	0	0	0	0
23	0	0	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0	0	0
25	0	0	0	0	0	0	0	0	0	0
26	0	0	0.84*§	0	0	0	0	0	0	0
27	0	0	0	0	0	0	0	0	0	0
28	0	0	0	0	0	0	0	0	0	0
29	0	0	0	0	0	0	0	0.08	0	0
30	0	0	0	0	0	0	0	0	0	0
31	0	0	0	0	0	0	0	0	0	0
32	0	0	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0	0	0
34	0	0	0	0	0	0	0	0	0	0
35	0	0	0	0	0	0	0	0	0	0
36	0	0	0	0	0	0	0	0	0	0
37	0	0	0	0	0	0	0	0	0	0
38	0	0	0	0	0	0	0	0	0	0
39	0	0	0	0	0	0	0	0	0	0
40	0	0.75*	0	0	0.21	0.29	0	0	0.34*	0
41	0	0	0	0	0	0	0	0	0	0
42	0	0	0	0	0	0	0	0	0	0

Patient no.	Ole e 1	Phl p 1	Phl p 4	Phl p 5	Pol d 5	Pru p 1	Pru du 3	Ves v 5
1	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0.44*	0	0
3	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0.87*
6	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	2.2†
8	1.01†	0.76*	0	1†	0.27	0.15	0	0.58*
9	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0
12	0	0	0.2	0	0	0	0	0.32*
13	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0.21	0
16	0	0	0.2	0	0	0	0	0.12
17	0	0	0	0	0	0	0	0
18	0	0	0	0	0.09	0	0	1.74†
19	0	0.68*	0	0.67*	0	0	0	0
20	0	0	0.17	0	0	0	0	0.1
21	0	0	0	0	0	0.11	0	0

(continued)

TABLE E3. *(Continued)*

Patient no.	Ole e 1	Phl p 1	Phl p 4	Phl p 5	Pol d 5	Pru p 1	Pru du 3	Ves v 5
22	0	0	0	0	0	0	0	0.1
23	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0
25	0	0	0	0	0	0	0	0
26	1.63†§	0.58*§	0.71*§	0	0.6*§	0	0	1.66†§
27	0	0	0	0	0	0	0	0
28	0	0	0	0	0	0	0	0
29	0	0	0	0	0	0	0	0
30	0	0	0	0	0	0	0	0
31	0	0	0	0	0	0	0	0
32	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0
34	0	0	0	0	0	0	0	0
35	0	0	0	0	0	0	0	0
36	0	0	0	0	0	0	0	0
37	0	0	0.11	0	1.37†	0.08	0	1.88†
38	0	0	0	0.56*	0	0	0	0
39	0	0.31*	0	0	0	0	0	0
40	0.32*	0	0	0	0	0	0	0
41	0	0	0	0	0	0	0	0
42	0	0	0	0	0	0	0	0

Sera obtained from 42 patients with mastocytosis were analyzed using microarrayed allergens. Levels of specific IgE were semi-quantified by Microarray Image Analyzer v3.1.2 software and expressed by ISU. For positivity, a cutoff of 0.3 ISU was used. Chip scoring system: <0.3 ISU below cutoff. A detailed description of allergens is presented in the Table E4.

*Class 1: ≥0.3 to <1, ISU low.

†Class 2: ≥1 to ≤10 ISU, moderate to high.

‡Class 3: >10 ISU, very high.

§In this patient, allergen-chip detected sensitization against various allergens after treatment-induced reduction of the MC burden.

TABLE E4. Description of allergens shown in Figure E3

No.	Allergen source	Name/function of the protein	Allergen
1	Kiwi fruit	Thaumatin-like protein	Act d 2
2	Alder	PR-10, Bet v 1 family member	Aln g 1
3	Alternaria plant rot fungus	Acidic glycoprotein	Alt a 1
4	Ragweed	Pectate lyase	Amb a 1
5	Celery	PR-10, Bet v 1 family member	Api g 1
6	Honeybee	Phospholipase A2	Api m 1
7	Honeybee	Hyaluronidase	Api m 4
8	Peanut	PR-10, Bet v 1 family member	Ara h 8
9	Mugwort	Defensin-like protein	Art v 1
10	European white birch	PR-10, Bet v 1 family member	Bet v 1
11	European white birch	Profilin	Bet v 2
12	European white birch	Polcalcin	Bet v 4
13	Dog	Lipocalin	Can f 1
14	Goosefoot	Ole e 1–related protein (trypsin inhibitor)	Che a 1
15	Hazelnut	PR-10, Bet v 1 family member	Cor a 1.0401
16	Japanese cedar	Pectate lyase	Cry j 1
17	Cypress	Cypress	Cup a 1
18	Bermuda grass	Beta-expansin	Cyn d 1
19	American house-dust mite	NPC2 family	Der f 2
20	European house-dust mite	NPC2 family	Der p 2
21	Cat	Uteroglobin	Fel d 1
22	Latex	Profilin	Hev b 8
23	English walnut	Vicilin seed storage protein	Jug r 2
24	Storage mite	NPC2 family	Lep d 2
25	Apple	PR-10, Bet v 1 family member	Mal d 1
26	Annual mercury	Profilin	Mer a 1
27	Olive	Ole e 1–related protein (trypsin inhibitor)	Ole e 1
28	Timothy grass pollen	Beta-expansin	Phl p 1
29	Timothy grass pollen	Grass group 2/3	Phl p 2
30	Timothy grass pollen	Grass group 4 (Berberine bridge enzyme)	Phl p 4
31	Timothy grass pollen	Grass group 5	Phl p 5
32	Timothy grass pollen	Grass group 5/6	Phl p 6
33	Timothy grass pollen	Polcalcin	Phl p 7
34	Timothy grass pollen	Ole e 1–related protein (trypsin inhibitor)	Phl p 11
35	Timothy grass pollen	Profilin	Phl p 12
36	London plane tree	Polygalacturonase	Pla a 2
37	English plantain	Ole e 1–related protein (Pectate lyase)	Pla l 1
38	Mediterranean paper wasp	Antigen 5	Pol d 5
39	Peach	PR-10, Bet v 1 family member	Pru p 1
40	Almond	Profilin	Pru du 4
41	Yellow jacket	Antigen 5	Ves v 5

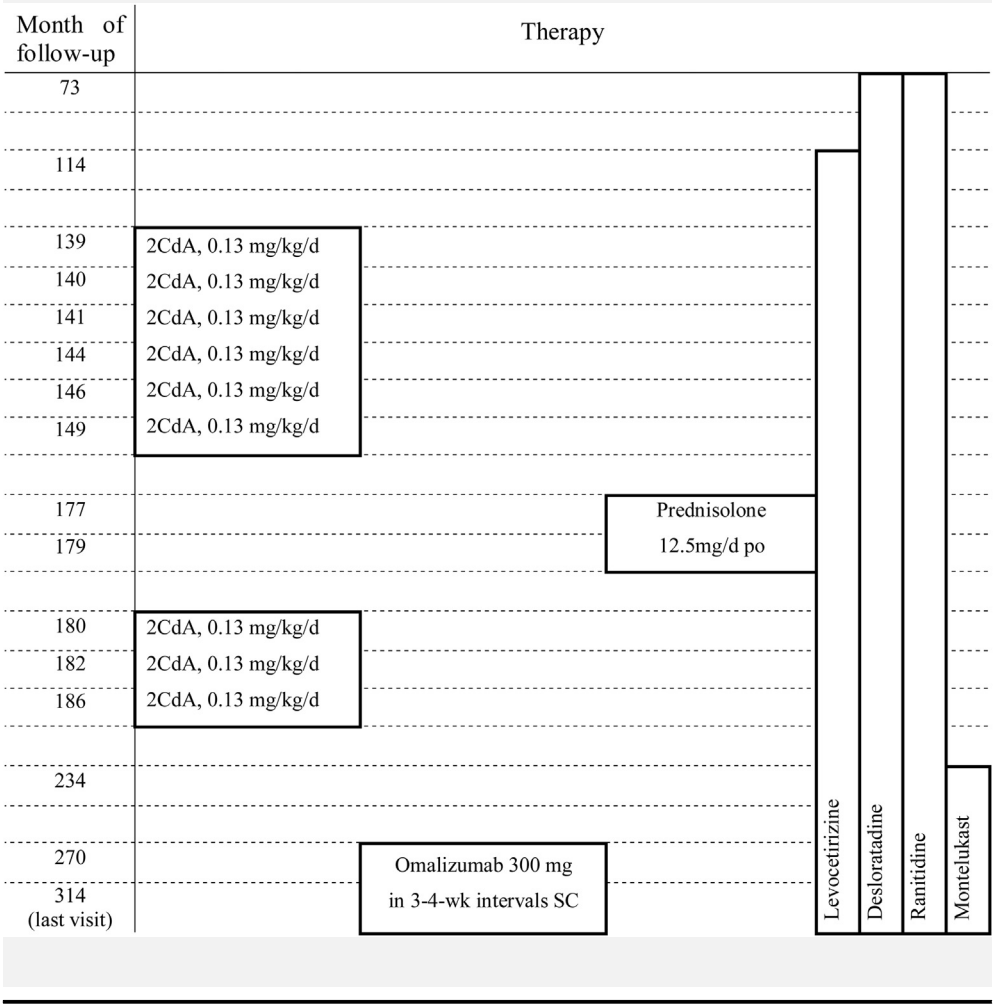
IUIS, International Union of Immunological Societies; *PR-10*, pathogenesis-related protein 10.
The sources and names of the allergens according to IUIS are shown.

TABLE E5. Evaluation of allergen-microarray in various cohorts

Study population	Allergic individuals among all patients, n (%)	Positive IgE reactivity by allergen-microarray testing in patients, n (%)	Mediator-induced symptoms of patients with allergies (previous studies) or mastocytosis (this study)	Reference
BAMSE	546/786 (69.5%)*	409/786 (52%)*	Asthma, rhinitis, asthma and/or rhinitis	Wickman et al[E1]
BAMSE	122/686 (17.8%)*	173/686 (25.2%)*	Rhinitis	Westman et al[E2]
EGEA	197/340 (57.9%)†	166/340 (48.8%)	Asthma, rhinitis	Siroux et al[E3]
ECA	83/132 (62.9%)*	132/265 (49.8%)*	Asthma	Skrindo et al[E4]
	109/132 (83.1%)*	132/265 (49.8%)*	Rhinitis	
Mastocytosis	9/42 (21%)‡	15/42 (35.7%)	Mediator-related symptoms§	Smiljkovic et al (this study)

BAMSE, Barn/Children, Allergy, Milieu, Stockholm, Epidemiological study; *ECA*, environment and childhood asthma; *EGEA*, asthma, bronchial hyperresponsiveness and atopy.
*Samples tested at age 16 y and allergic status confirmed with asthma, rhinitis, asthma, and/or rhinitis at age 16 y.
†Allergic sensitization determined on the basis of ≥1 positive skin prick test result among the 11 allergen sources.
‡Based on reported allergy in patient history.
§Mediator-related symptoms: flush, vascular instability, anaphylaxis, rhinitis, headache, diarrhea.

TABLE E6. Therapy of the patient during follow-up



po, *Per os* (by mouth).
2CdA was given intravenously 0.13 mg/kg/d for 5 d per cycle. Orally administered medication was ranitidine 300 mg twice daily, desloratadine 5 mg once daily, montelukast 10 mg once daily, and levozetirizine 5 mg once daily. Omalizumab 300 mg was given subcutaneously (SC) in 3-4-wk intervals.

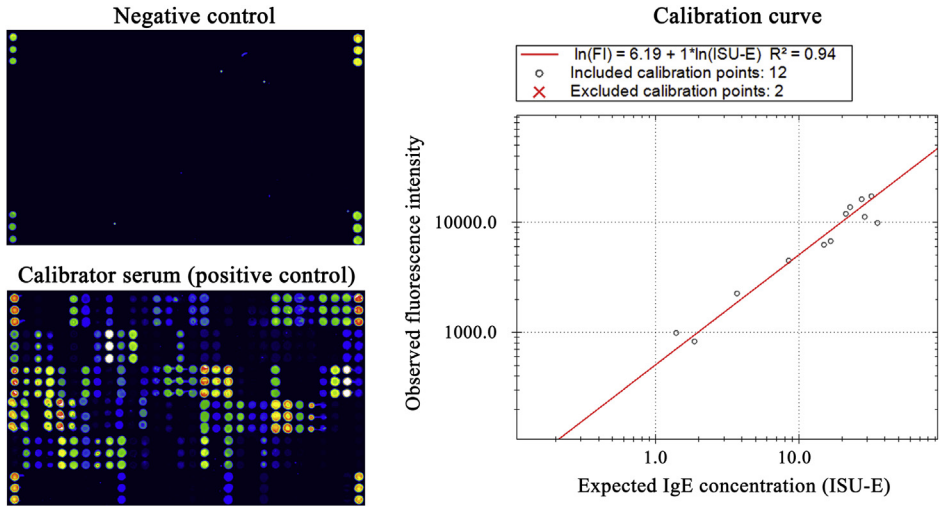


FIGURE E1. Calibration curve plus positive and negative controls for microarray analyses. Fluorescence signal intensities of the dots are encoded, with red dots representing high levels of allergen-specific IgE and blue color corresponding to low IgE levels as measured by a confocal laser-scanner. Levels of specific IgE were semi-quantified by Microarray Image Analyzer v3.1.2 software and expressed by ImmunoCAP Solid-phase Allergen-Chip standardized units for IgE. *FI*, fluorescence.

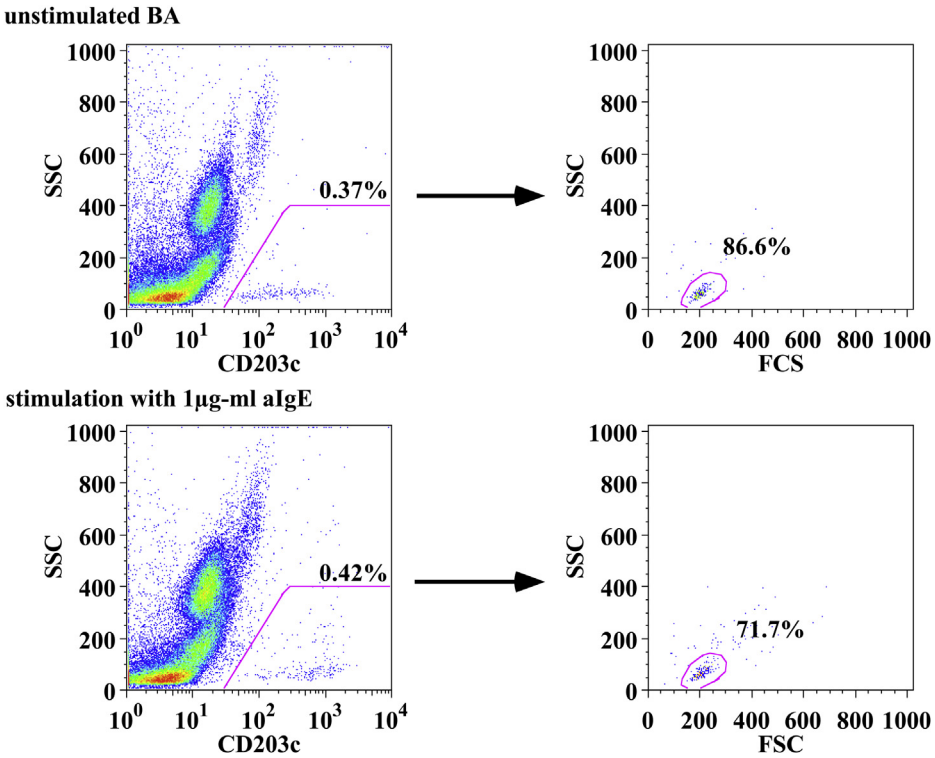


FIGURE E2. Gating strategy for basophils in the basophil CD203c activation test. Allergen-induced upregulation of CD203c was determined by multicolor flow cytometry on a FACS Calibur. For these experiments, cells were stained with the phycoerythrin -labeled CD203c antibody 97A6. Basophils were detected on the basis of their SSC and FSC characteristics and expression of CD203c (purple line). *BA*, Basophils; *FSC*, forward scatter; *SSC*, side scatter.

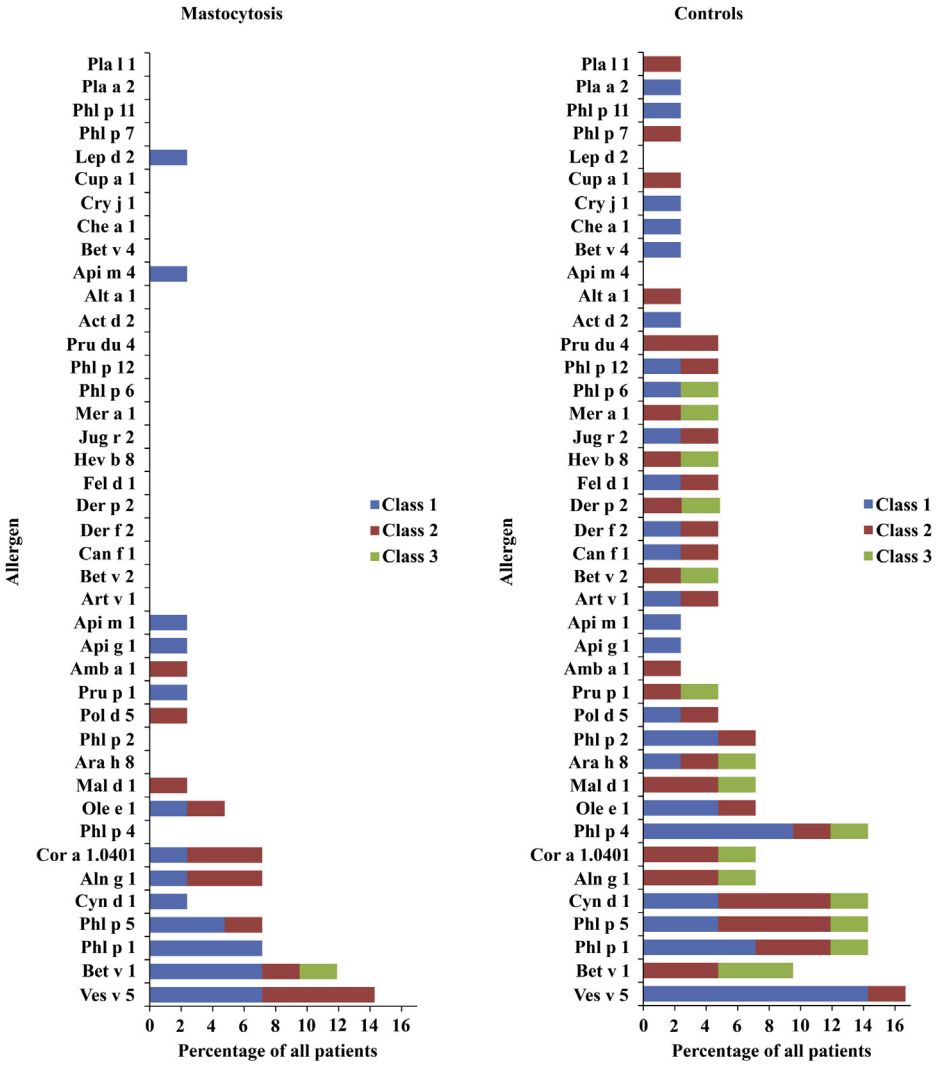


FIGURE E3. Profiling of specific IgE reactivities for allergens detected in the sera of patients with mastocytosis compared with age-matched controls. Sera obtained from 42 patients with mastocytosis and 42 age- and sex-matched controls without mastocytosis were analyzed by chip-profiling. Results are expressed as a percentage of patients with mastocytosis or percentage of controls testing positive in the chip assay. Levels of specific IgE are shown as: class 1: $\geq$0.3-$<$1 ISU, class 2: $\geq$1-$\leq$10 ISU, and class 3: $>$10 ISU. A detailed description of allergens is presented in Table E4.

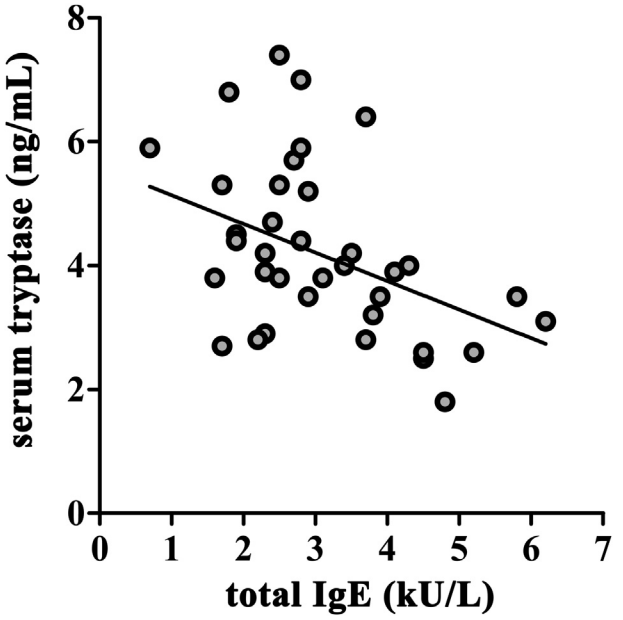


FIGURE E4. Correlation between serum tryptase levels and total IgE in patients with mastocytosis. Serum tryptase levels and total serum IgE levels were measured in 37 patients with mastocytosis in whom both markers were determined. Results are expressed in natural log units. A significant negative correlation between serum tryptase levels and total IgE levels was found (Pearson correlation coefficient: $r = 0.41$; $P < .05$).

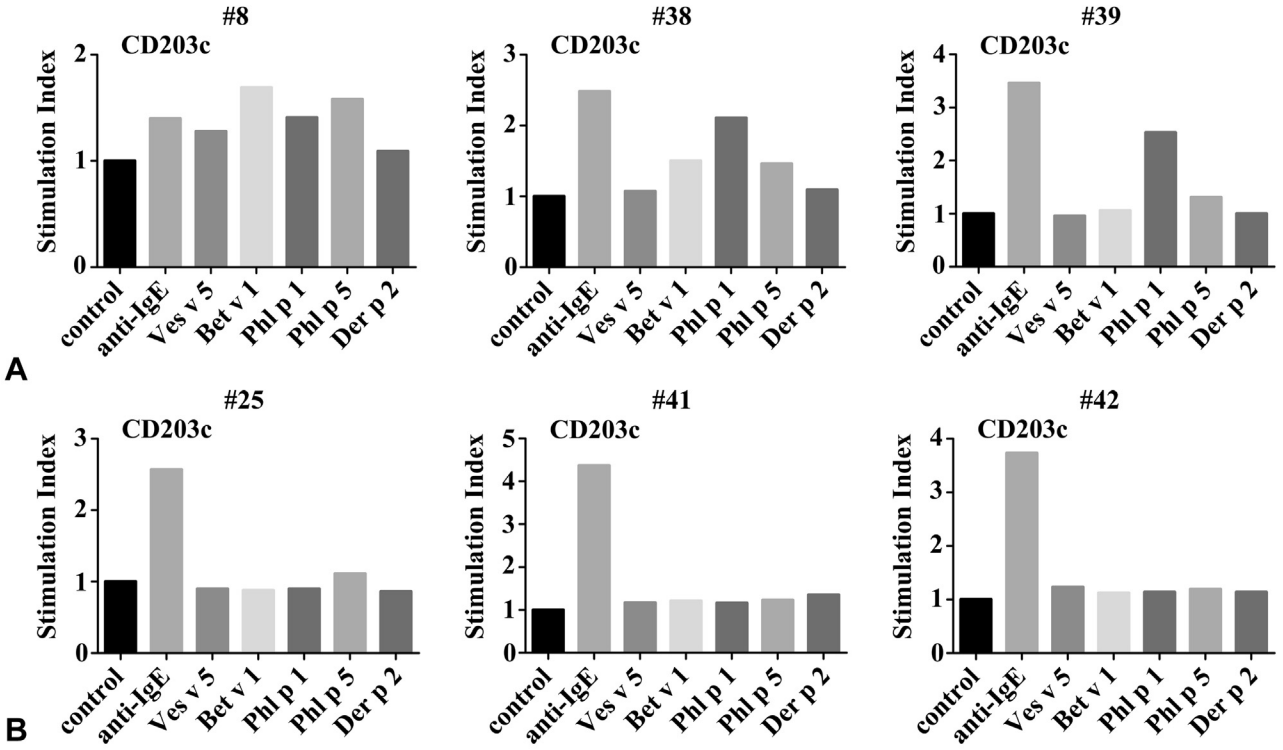


FIGURE E5. Basophil CD203c activation test with some of the most frequent allergens performed in our patients with mastocytosis. Patients with mastocytosis with (**A**) or without (**B**) specific IgE by allergen-chip-profiling were analyzed: patient number 8 had IgE against Bet v 1, Phl p 1, Phl p 5, and Ves v 5, number 38 IgE against Phl p 5, and number 39 IgE against Phl p 1. Blood cells were incubated with allergens (1 μg/mL), anti-IgE (1 μg/mL), or control buffer for 15 minutes (37°C). Allergen-induced upregulation of CD203c was determined as described in the text.

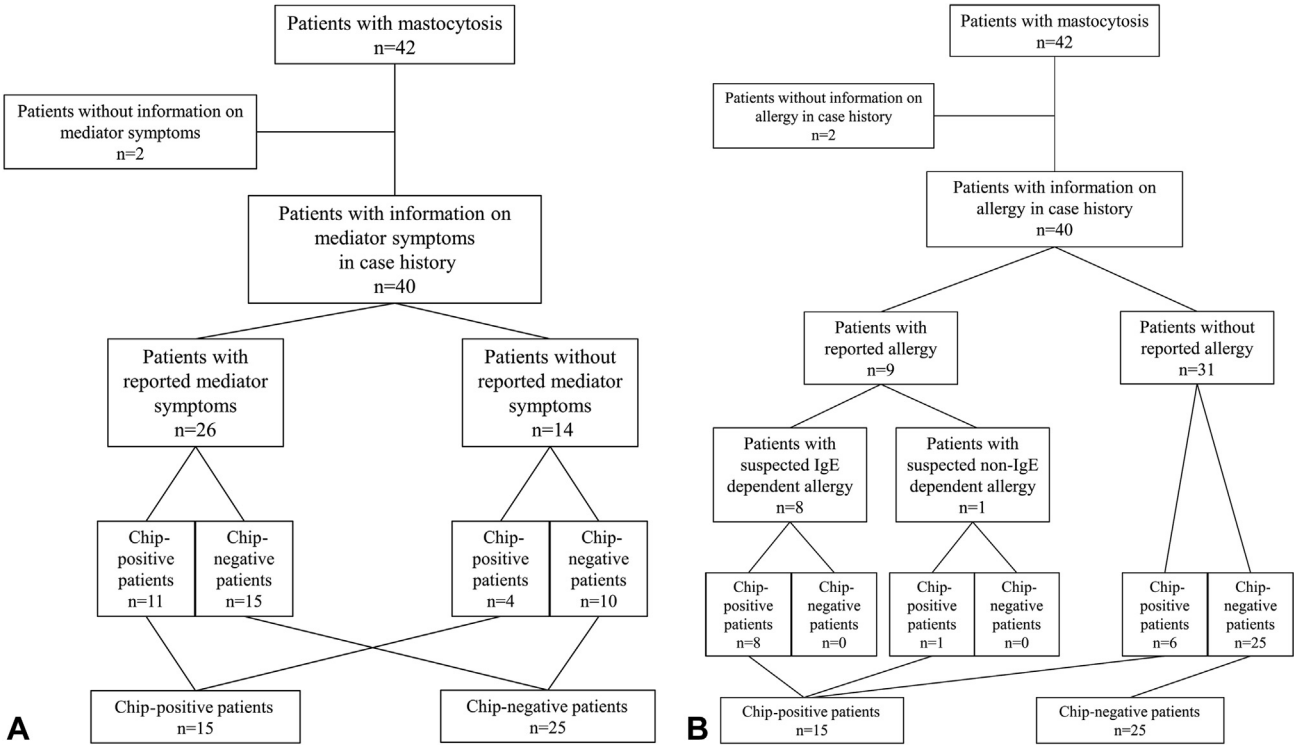


FIGURE E6. Flowchart diagram of patients included in the study. Forty-two patients with mastocytosis were included. In 2 patients no information about mediator-related symptoms (**A**) and no information on allergies in the case history (**B**) were available. Positive results in the allergen-chip were found in 15 patients, whereas in 25 patients the allergen-chip showed negative results.

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