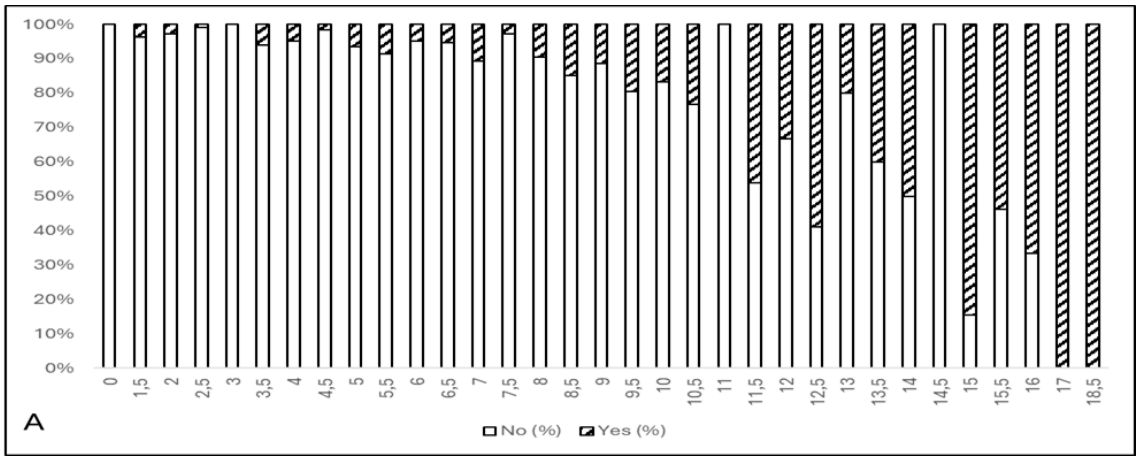
Supplementary Figure 1. Guidance questionnaire for suspected HAE cases (Spanish).

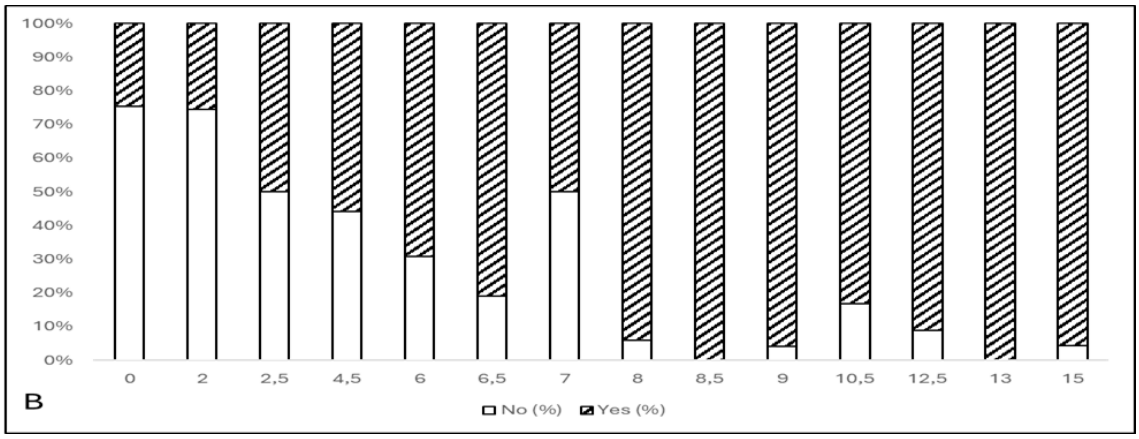
1- Edema recurrente			
Edema pruriginoso	Si		No
Edema en las extremidades	Si		No
Edema facial	Si		No
Persiste ≥24 horas	Si		No
Responde a antihistamínicos y/o corticoides	Si		No
2- Ronchas con picazón	Si		No
3- Dolor abdominal	Si		No
4- Obstrucción intestinal que requirió cirugía	Si		No
5- Vómitos	Si		No
6- Edema de laríngeo	Si		No
7- Eritema sin picazón	Si		No
8- Síntomas causados por	Trauma	Menstruación	Medicación
	Infección	Estrés	Sin causa
9- Edad de inicio de síntomas (años)	0 – 5	5 – 10	10 – 20
	20 – 30	30 – 40	40 – 50
10- Ubicación de los síntomas			
11- Historia familiar de angioedema	Si		No
	Explicación:		

Original questionnaire in Spanish.

Supplementary Figure 2. Stacked column chart showing the percentage of diagnosed and non-diagnosed suspected index cases by each clinical diagnostic score of HAE



Supplementary Figure 3. Stacked column chart showing the percentage of diagnosed and non-diagnosed family cases by each clinical diagnostic score of HAE



Supplementary Table 1. Internal validation in suspected index cases (bootstrapping).

	ß	p value	95% CI of ß	
			Lower	Upper
Age of onset ≤20 years	0,537	0,013	0,124	0,958
Recurrent limb edema	0,894	0,001	0,458	1,380
Abdominal pain	0,635	0,002	0,211	1,069
Family history of angioedema	1,128	0,001	0,690	1,562
Vomiting	1,211	0,001	0,777	1,656
Trauma as a trigger of symptoms	1,262	0,001	0,736	1,765
Absence of wheals	0,927	0,001	0,553	1,364

Supplementary Table 2. Internal validation in family cases (bootstrapping).

	ß	p value	95% CI of ß	
			Lower	Upper
Recurrent limb edema	1,506	0,001	1,017	2,060
Recurrent edema ≥24 hours	1,806	0,001	1,209	2,599
Abdominal pain	0,633	0,007	0,163	1,097
Trauma as a trigger of symptoms	0,921	0,017	0,198	1,842

Supplementary Table 3. Number of events per score in the suspected index cases.

	Confirmed HAE diagnosis		
Score	**No (n, %)**	**Yes (n, %)**	**Total**
0	56 (100%)	0 (0%)	56
1.5	79 (96.3%)	3 (3.7%)	82
2	33 (97.1%)	1 (2.9%)	34
2.5	200 (99%)	2 (1%)	202
3	7 (100%)	0 (0%)	7
3.5	31 (93.9%)	2 (6.1%)	33
4	212 (95.1%)	11 (4.9%)	223
4.5	113 (98.3%)	2 (1.7%)	115
5	86 (93.5%)	6 (6.5%)	92
5.5	32 (91.4%)	3 (8.6%)	35
6	140 (95.2%)	7 (4.8%)	147
6.5	87 (94.6%)	5 (5.4%	92
7	83 (89.2%)	10 (10.8%)	93
7.5	36 (97.3%)	1 (2.7%)	37
8	47 (90.4%)	5 (9.6%)	52
8.5	57 (85.1%)	10 (14.9%)	67
9	23 (88.5%)	3 (11.5%)	26
9.5	62 (80.5%)	15 (19.5%)	77
10	15 (83.3%)	3 (16.7%)	18
10.5	23 (76.7%)	7 (23.3%)	30
11	1 (100%)	0 (0%)	1
11.5	7 (53.8%)	6 (46.2%)	13
12	22 (66.7%)	11 (33.3%)	33
12.5	7 (41.2%)	10 (58.8%)	17
13	8 (80%)	2 (20%)	10
13.5	3 (60%)	2 (40%)	5
14	4 (50%)	4 (50%)	8
14.5	1 (100%)	0 (0%)	1
15	2 (15.4%)	11 (84.6%)	13
15.5	6 (46.2%)	7 (53.8%)	13
16	1 (33.3%)	2 (66.7%)	3
17	0 (0%)	1 (100%)	1
18.5	0 (0%)	6 (100%)	6
Total	**1484 (90.4%)**	**158 (9.6%)**	**1642**

Supplementary Table 4. Number of events per score in the family cases.

	Confirmed HAE diagnosis		
Score	**No (n, %)**	**Yes (n, %)**	**Total**
0	356 (75.2%%)	117 (24.7%)	473
2	41 (74.5%)	14 (25.5%)	55
2.5	1 (50%)	1 (50%)	2
4.5	15 (44.1%)	19 (55.9%)	34
6	4 (30.8%)	9 (69.2%)	13
6.5	9 (19.1%)	38 (80.9%)	47
7	3 (50%)	3 (50%)	6
8	1 (5.9%)	16 (94.1%)	17
8.5	0 (0%)	1 (100%)	1
9	1 (4%)	24 (96%)	25
10.5	4 (16.7%)	20 (83.3%)	24
12.5	3 (8.8%)	31 (91.2%)	34
13	0 (0%)	5 (100%)	5
15	2 (4.4%)	43 (95.6%)	45
Total	**440 (56.3%)**	**341 (43.7%)**	**781**