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CASE AND RESEARCH LETTER

[Translated article] Acquired Nonfamilial Vibratory Angioedema

Angioedema vibratorio adquirido (no familiar)

To the Editor:

Vibratory angioedema is defined as a pruriginous inflammatory reaction that occurs a few minutes after exposure to vibration.[1] An autosomal dominant variant, hereditary type of vibratory angioedema has been reported, manifesting as prolonged angioedema (hours to days) resulting from exposure to a vibratory stimulus.[2] The more frequent sporadic form, acquired (nonfamilial) vibratory angioedema, is characterized by similar symptoms.[3–13] Boyden et al.[14,15] reported another autosomal dominant variant, which is characterized by mutations in adhesion G protein-coupled receptor E2 (ADGRE-2) and wheals instead of angioedema. This form is known as ADGRE-2-linked hereditary vibratory urticaria.[2,16]

Diagnosis is based on the clinical history and the vortex provocation test (Fig. 1). Dermographism should be ruled out. Elevated serum histamine and mast cell degranulation mediators have been reported during episodes.[3–5,14,17,18] Treatment involves avoiding exposure to vibratory stimuli or, if this is not feasible (e.g., owing to occupational settings), administration of antihistamines (anti-H1) (level of evidence C).[1]

We performed a literature review on acquired (nonfamilial) vibratory angioedema in September 2020. The search terms applied were ''vibratory'' or ''vibrational'' or ''vibration-induced'' and ''angioedema'' or ''urticaria''. We searched for articles in English, French, and Spanish, without time restrictions, in MEDLINE, Cochrane Central Register of Controlled Trials, and Web of Science.

We identified 21 articles between 1982 and 2016. Ten were ruled out owing to insufficient information and/or hereditary cases. We recorded 12 cases of acquired disease (Table 1), including 7 males (58%), and 6 occupational cases (50%). The mean age at diagnosis was 35 (16–70) years,

Figure 1 The volar surface of the forearm should be exposed to the vibration for 5 minutes. This should be induced by a laboratory vortex mixer (780–1380 rpm), with readings taken at 10 minutes once the stimulus has stopped. The result is considered positive when inflammation resulting the vibratory stimulus induced by the movement of the vortex. According to recommendations from consensus guidelines (EAACI/GA(2)LEN/EDF/UNEV), inflammation can be quantified by measuring the circumference of the forearm at 3 points (cubital fossa, wrist, and midpoint between the two). This measurement should be made with a measuring tape before application of the vibratory stimulus and 5 minutes afterwards.

and the mean age at onset of symptoms was 31 years. The latency period between onset of symptoms and consultation ranged from 3 months to 20 years.

The most frequent triggers were lawnmowers[3,6,10] and musical instruments.[8,10,11] All of the affected patients had localized lesions, although none had generalized wheals. One patient reported chronic spontaneous urticaria[5] and another, carpal tunnel syndrome caused by severe edema of the wrist after occupational exposure to vibration.[4] Three patients (25%) had systemic symptoms (flushing, chest tightness, generalized heat, dizziness, tachycardia, and hypertension), and 1 fulfilled the criteria for anaphylaxis.[6,9,13]

The vortex test was used in 9/12 cases (75%), with the type and frequency (rpm) reported in 5/9. The frequency recommended in guidelines (780–1380 rpm) was applied in 3 cases.[5,6] The forearm circumference (before and after testing) was specified in only 2 patients (increases of 4 and

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Table 1 Review of the Literature on Acquired Vibratory Angioedema.

Author/year of publication	Sex/age, y	Triggers: findings, symptoms, and duration	Systemic symptoms	Vortex test performed/ oscillation frequency	Measurement of forearm circumfer- ence/results	Symptoms and latency (time to onset after initiation of the vortex test)	Diagnostic tests for other CIndU/results	Treatment
Alpern et al.[13]/2016	F/53	Massage bed: onset in the form of anaphylaxis; 2 additional episodes of edema affecting hands and feet, pruritus, and mild dizziness. No further episodes of anaphylaxis in the following 3 y	Anaphylaxis (generalized pruritus, flushing, nausea, vomiting, hypotension, presyncope)	No	–	–	No	Avoidance of vibratory stimulus
Kalathoor[12]/2015	F/70	Snoring: lingual and pharyngeal edema with difficulty swallowing (every 3 mo for 3 y); driving; some episodes of pruritus and hand edema	No	No	–	–	No	CPAP
Guarneri et al.[11]/2014	M/20	Horn: labial angioedema (for 5 months, although he had been playing it for 6 y)	No	No	–	–	No	–
Sarmast et al.[10]/2014	M/38	Trumpet: pain, edema, and erythema affecting the upper lip (3 y); lawnmower: hand edema	No	Yes/NS	NS	Burning sensation, edema, erythema, and mild pain in forearm (5 min after test)	Negative (DPU)	Prednisone
Pressler et al.[9]/2012	F/36	Exercise (running, walking quickly, cycling over rough ground, skiing): angioedema (20 y with worsening of systemic symptoms during recent months)	Dizziness, tachycardia, and hypotension	Yes/2400 rpm	NS	Angioedema affecting the area of contact (5–10 min after test)	Negative (heat, cold, DPU, SD)	Ketotifen
Patruno et al.[8]/2009	M/28	Saxophone: lower lip edema (6 mo)	No	Yes/NS	NS	Angioedema (5 min after test)	Negative (heat, cold, DPU, CholU, SD)	Prednisone
Mathelier-Fusade et al.[7]/2001	F/34	Mountain bike for 10 min: forearm edema (4 y)	No	Yes/NS	NS	Erythema, pruritus, and circumferential edema (5 min after test)	Negative (DPU, CholU, SD)	

Table 1 (*Continued*)

Author/year of publication	Sex/age, y	Triggers: findings, symptoms, and duration	Systemic symptoms	Vortex test performed/ oscillation frequency	Measurement of forearm circumfer-ence/results	Symptoms and latency (time to onset after initiation of the vortex test)	Diagnostic tests for other CIndU/results	Treatment
Lawlor et al.[6]/1989	F/28	Applauding for 5 min, and/or electric lawnmower or garden shears: tingling, pruritus, and erythema on wrists and forearms lasting minutes; walking for < 10 min: pruritus followed by erythema on the anterior aspect of the thighs (10 y)	Facial flushing, chest tightness, and generalized sensation of heat	Yes/780 rpm	Yes/4-mm increase in circumfer-ence at the mid forearm	Tingling (2 min after test) and pruritus (4 min after test)	Positive (DPU, SD) Negative (CholU, cold)	Terfenadine
Keahey[5]/1987	M/37	Machinist (pressure and/or friction): pruriginous and painful lesions (3 y)	No	Yes/1380 rpm	NS	Pruritus and erythema (immediate); localized angioedema (4 to 6 h after the test)	Negative (SD, DPU: several occasions)	
	M/28	Carpenter (pressure and/or friction): pruriginous and painful lesions (5 y)	No	Yes/1380 rpm	NS	Urticarial reaction (minutes after the test); localized angioedema (4 to 6 h after test)	Negative (SD, DPU: several occasions) SCU	
Wener[4]/1983	M/32	Grinding machine: erythema and edema affecting the left hand, and wrist affected by secondary carpal tunnel syndrome (1 y)	No	Yes/NS	Yes/12-mm increase in wrist cir-cumference	Edema, pruritus, paresthesia, and pain affecting the wrist, hand, forearm, and arm (1 min after test); inability to flex fingers (4 min after test); slowed nerve conduction velocity (5 min after test)	Negative (cold, SD)	Surgery (carpal tunnel release)
Ting[3]/1982	M/16	Motorcycle or lawnmower: hand edema (3 mo)	No	Yes/6000 rpm		Prolonged angioedema at various sites (arm, leg, and trunk) lasting 12 h (onset seconds after test)	Negative (SD)	Desensitization to vibration

Abbreviations: CPAP, continuous positive airway pressure; CIndU, chronic inducible urticaria; CholU, cholinergic urticaria; DPU, delayed pressure urticaria; F, female; M, male; NS, not specified; SCU, spontaneous chronic urticaria; SD, symptomatic dermographism.

12 mm, respectively).[4,6] Symptoms triggered by the vortex appeared between 0.5 and 10 minutes once the oscillation had stopped. Only 1 patient developed wheals with the vortex (i.e., the patient with concomitant spontaneous urticaria). Median nerve conduction velocity slowed after the vortex was applied in the patient with carpal tunnel syndrome.[4]

Controls were included in 6 articles. Ting et al.[3] studied 17 controls; of these, 4/7 relatives of the patient with acquired vibratory angioedema and 5/10 healthy volunteers developed edema that extended beyond the area in contact with the vortex.

Provocation tests for other types of inducible urticaria were carried out in 9 patients. These were positive in only 1 patient, who had delayed pressure urticaria and dermographism.[6]

There have also been 2 reports of acquired vibratory urticaria secondary to identifiable causes: a patient with *Candida glabrata* infection who experienced urticaria on the fingers when using a typewriter,[19] and another with anaphylaxis after using a sewing machine 17 hours after being stung by a wasp.[20] These cases were not included in the present review owing to the fact that the clinical findings differed from those of acquired angioedema (wheals and no angioedema), the need for a previous condition that triggered symptoms when co-occurring with the vibration, and the subacute course that resolved after control of the previous condition.

The factors involved in acquired vibratory angioedema are unclear. While serum levels of histamine and other mast cell degranulation mediators are elevated during episodes, we do not know why patients present with angioedema and no wheals, generally no systemic symptoms, and no association with spontaneous urticaria.

Similarly, there is considerable heterogeneity in the practice, methodology, and interpretation of the vortex test, thus making it difficult to define response patterns or ranges of intensity and revealing the need for the method to be standardized.

A high percentage of the general population experiences symptoms when exposed to a vibratory stimulus (7%–41.3%),[18,21] thus suggesting that some cases could involve physiological responses. In order to distinguish between physiological and pathological responses, it would be interesting to set a threshold, as is the case in other types of inducible urticaria (e.g., simple dermographism and symptomatic dermographism). In our opinion, considering this phenomenon as pathological should also be based on functional compromise and on impairment of quality of life owing to the individual's obligation to be exposed to vibratory stimuli in both professional and nonprofessional settings.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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M.A. Pastor-Nieto[a,b,*], L. Vergara-de-la-Campa[c], M.E. Gatica-Ortega[c], A. Giménez-Arnau[d]

[a] *Servicio de Dermatología, Hospital Universitario de Guadalajara, Guadalajara, Spain*
[b] *Departamento de Medicina y Especialidades Médicas, Facultad de Medicina y Ciencias de la Salud, Universidad de Alcalá, Alcalá de Henares, Madrid, Spain*
[c] *Servicio de Dermatología, Complejo Hospitalario de Toledo, Toledo, Spain*
[d] *Servicio de Dermatología, Hospital del Mar, IMIM, Universitat Autònoma, Barcelona, Spain*

[*] Corresponding author.
E-mail address: mapastornieto@gmail.com
(M.A. Pastor-Nieto).