

# Cholinergic Urticaria Due To Acquired Generalized Anhidrosis in a Young Male Nigerian

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## ABSTRACT

**Introduction:** Cholinergic urticaria (CU) is a rare condition, even in Nigeria, which is sometimes associated with hypohidrosis/anhidrosis and pulse steroid therapy is recommended as first line therapy. We report this 18years old male Nigerian with CU due to acquired generalized anhidrosis.

**Case Report:** Mr CH, an 18years old student, seen with 3 months of recurrent generalized urticarial rashes in response to increased environmental temperature or on mild exertion which commenced on arrival to Nigeria after spending 1 year in Europe. He had been on various antihistamines, montelukast/levocetirizine and low dose prednisolone without improvement.

On consultation, he volunteered that he doesn't sweat, which equally started at time of onset of urticaria. Blood count showed eosinophilia (12.4% of total white cell count), and elevated IgE level. A diagnosis of CU due to acquired generalized anhidrosis was made and he was commenced on tab dexamethasone 100mg daily for three (3) days every month (to have a total of six cycles). He started sweating after the first cycle and urticaria severity reduced markedly.

**Conclusion:** A diagnosis of CU due to anhidrosis requires a high index of suspicion. A multidisciplinary approach and appropriate literature search is essential in achieving desirable treatment.

**Keywords:** cholinergic urticaria, anhidrosis, generalized, Nigerian

## INTRODUCTION

Cholinergic urticaria (CU) can be described as a condition characterized by pruritus and wheals usually associated with physical exercise, hot showers, sweating, anxiety, or other conditions that causes an increase in the body's core temperature presenting in a localized or generalized fashion.<sup>1</sup>

Magerl et al in a consensus panel stated that this CU should be differentiated from exercise-induced anaphylaxis which involves no passive warming and should be considered a differential diagnosis.<sup>1</sup> Cholinergic urticaria is a chronic urticaria which may also be precipitated by a warm bath while exercise-induced anaphylaxis follows exercise.<sup>2</sup> Cholinergic urticaria can be conveniently divided into the following subtypes<sup>3</sup>: Cholinergic urticaria with poral occlusion, Cholinergic urticaria with acquired, generalized hypohidrosis, Cholinergic urticaria with sweat allergy and, Idiopathic cholinergic urticaria.

The exact mechanism(s) of urticaria formation in CU has been unclear but it is thought to be due to a strong sweat-hypersensitivity to autologous sweat, which can be non-follicular with development of satellite wheals and a lack of positive autologous serum skin tests (ASSTs) or, a follicular type wheal with positive ASST but no hypersensitivity to

autologous sweat or satellite wheals.<sup>2</sup> In the first instance, patients are hypersensitive to unknown substances in their sweats and develop urticaria in response to sweat substance leaking from the syringeal ducts to the dermis possibly by obstruction of the ducts.<sup>4</sup> Acetylcholine is thought to play a role in development of CU in a dose-dependent fashion and occasionally accompanied by anhidrosis or hypohidrosis.<sup>5</sup> Serum histamine, considered to be the principal mediator, increases in concentration with induced exercise, along with eosinophil and neutrophil chemotactic factors and tryptase.<sup>6</sup> Also, a reduction in the alpha1-antichymotrypsin level, similarly seen in some other forms of urticaria, is present. Patients with atopic dermatitis and cholinergic urticaria are thought to develop skin reactions and histamine release of basophils in response to autologous sweat.<sup>6</sup>

Also, CU associated with acquired generalized hypohidrosis is thought to be due to leakage of sweat antigen into the surrounding dermis after occlusion of the intraepidermal sweat ducts, leading to mast cell activation by binding of surface IgE molecules to sweat antigen.<sup>4</sup> Most reported cases of patients with acquired generalized hypohidrosis/anhidrosis were also observed to have had episodes of cholinergic urticaria.<sup>7</sup>

Anhidrosis or hypohidrosis have been reported to be due to absence of sweat glands, dysfunctional sweat glands, occlusion of the pores or dysfunction of sympathetic nerves in neuropathies.<sup>7</sup> Cholinergic urticaria usually presents with itching, burning, tingling, warmth, or irritation which precedes the onset of numerous small (1-4mm in diameter), pruritic wheals with large, surrounding flare appearing anywhere on the body, except on the palms or the soles and rarely in the axillae. In more severe cases, patients may experience systemic symptoms, like: fainting, abdominal cramps, diarrhea, excessive salivation or headaches. Hepatocellular injury, angioedema, asthma, and even anaphylactic reactions have been reported in literature.

There are various treatments for CU that have been tried. Omalizumab, an anti-IgE antibody, is effective in severe CU<sup>8</sup> suggesting that an IgE mediated response is involved in the pathogenesis of CU. Anti-histamines used alone are thought

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to have a limited effect but combining H<sub>1</sub> and H<sub>2</sub> antagonists was observed to be more effective in complete control of cholinergic urticaria with lower rates of relapse.<sup>9</sup> In CU with anhidrosis and or hypohidrosis pulse therapy with a high dose of corticosteroid is considered a first line option.<sup>5</sup> This decreases the lymphocytic infiltrate around the sweat glands and allow acetylcholine receptor to re-express, resulting in the improvement of sweating and CU. Methylprednisolone or dexamethasone may be used for steroid pulse therapy at 20-30mg/kg (500-1000 mg/m<sup>2</sup>) and 4-5 mg/kg (100-200 mg) per pulse respectively.<sup>10</sup>

In this report we present a case of an 18 years old Nigerian male who complained of features in keeping with anhidrosis with cholinergic urticaria.

## CASE REPORT

Mr CH is an 18 years old university student who left Nigeria fifteen (15) months prior to presentation to us for Europe, for the first time, to commence his university academic education. Shortly after returning for holidays three (3) months prior to presentation, he began to experience intermittent but frequent episodes of generalized pruritic maculo-papular wheals. This he experienced two or three times each day lasting sometimes from a few minutes to up to three (3) hours. Rashes are precipitated by increased environmental temperature or increased body heat from physical exertion like exercise. He sometimes has to take cold showers several times in the day or use a wet towel to wipe his body to relieve the symptoms. He could not tolerate a warm environment and had to wear very light clothing and sometimes no shirts at all while at home over a two (2) month period prior to presentation. He had had various prescriptions for antihistamines like chlorpheniramine and loratidine as well as a combination of montelukast/levocetirizine (10/5mg daily) including a low dose of prednisolone (5mg daily for a week) with short lasting or sometimes little relief. He was then referred to our service.

On consultation, additional history revealed he had generalized anhidrosis of equal duration (3 months) similar with the urticarial rashes. He had no respiratory or ocular symptoms, or history of allergies. There was no prior ill-health or previous hospital admission, use of recreational drugs or exposure to radiation. He was not on any medication(s) prior to the onset of anhidrosis or urticaria rashes. On examination, he appeared normal generally with normal vital signs (pulse and blood pressure) except that his whole body remained dry, including his palms and soles, even after a few minutes of exercise. He had normal mentation and no signs of neurological deficit.

Investigations done include: total white cell count 3.29x 10<sup>9</sup>/L (neutrophils 23.8%, lymphocytes 58.4%, eosinophils 12.4%, monocytes 4.2%, basophils 1.2%); hemoglobin 13.8g/dl (packed cell volume 42%); with normal mean corpuscular volume and mean corpuscular hemoglobin; platelets 165 x 10<sup>9</sup>/L; erythrocyte sedimentation rate 3mm in 1<sup>st</sup> hour (Westergreen method); serum IgE was markedly elevated (1465 IU/ml); a random blood sugar was 92mg/dl. A urinalysis and, stool microscopy and culture did not reveal any abnormalities.

A diagnosis of cholinergic urticaria due to a possible acquired idiopathic generalized anhidrosis was made. He was commenced on a trial of high dose dexamethasone 100mg daily for three (3) days every month (to have a total of six cycles).

After the first cycle, anhidrosis resolved and he started sweating on exertion or with increased environmental temperature, a situation he described as normal for him. Urticarial rash intensity and frequency also markedly reduced. He occasionally now (about twice a week) has urticarial rashes on sweating after a vigorous exercise. He was prescribed tab loratidine 10mg daily in between cycles.

## DISCUSSION

Urticaria is a common but benign skin condition. However, cholinergic urticaria is uncommon especially among Nigerians as no documented case is yet to be reported. It can very easily be missed or misdiagnosed as was the case in our patient. In addition, he also had generalized anhidrosis. Anhidrosis/hypohidrosis has been associated with development of CU.<sup>4,5,7</sup> A cause of the generalized anhidrosis was not readily known to us as his history of possible cause and physical examination was unremarkable. Perhaps the change of environment from Nigeria to Europe may have contributed. However, he had similar clinical presentation; with lack of sweating which was generalized, rash precipitated by exertion and a need to shower several times daily, as other reported cases of CU due to acquired idiopathic generalized anhidrosis.<sup>4,5,7</sup> CU is commonly associated with bronchial hyper-responsiveness which is unrelated to gender, disease duration, intolerance to NSAID, positive autologous serum skin test or respiratory allergy in addition to urticarial rashes<sup>10</sup>, but our patient showed no evidence of this.

The markedly elevated eosinophil count and IgE levels observed in our patient suggests an allergic response which involves activation of mast cells.<sup>4</sup> Mast cell activation by binding of circulating IgE in response to sweat antigens is associated with CU due to anhidrosis/hypohidrosis.<sup>4</sup>

CU due to other causes respond well to combinations of H<sub>1</sub> and H<sub>2</sub> antihistamines, scopolamine<sup>8</sup> and danazol<sup>9</sup>, but pulse steroid therapy is first line treatment for CU due to anhidrosis/hypohidrosis.<sup>5</sup> It is therefore not surprising that our patient did not respond appropriately to initial treatment with antihistamines like chlorpheniramine, loratidine; and a combination of montelukast/levocetirizine. Only after he was commenced on high dose dexamethasone did we observe a positive response to the symptoms.

## CONCLUSION

A diagnosis of CU due to anhidrosis/hypohidrosis is rare among Nigerians and requires a high index of suspicion. With a multidisciplinary approach and appropriate literature search, achieving a desirable treatment outcome is possible.

## REFERENCES

1. Magerl M, Borzova E, Giménez-Arnau A, Grattan CEH, Lawlor F, Mathelier-Fusade P, Metz M, Mlynek A, Maurer M. The definition and diagnostic testing of physical and cholinergic urticarias—EAACI/GA2LEN/EDF/UNEV consensus panel recommendations. *Aller-*

- gy. 2009;64:1715-1721.
2. Horikawa T, Fukunaga A, Nishigori C. New concepts of hive formation in cholinergic urticaria. *Curr Allergy Asthma Rep.* 2009;9:273-279.
  3. Nakamizo S, Egawa G, Miyachi Y, Kabashima K. Cholinergic urticaria: pathogenesis-based categorization and its treatment options. *J Eur Acad Dermatol Venereol.* 2012;26:114-6.
  4. Kobayashi H, Aiba S, Yamagishi T, Tanita M, Hara M, Saito H, Tagami H. Cholinergic urticaria, a new pathogenic concept: hypohidrosis due to interference with the delivery of sweat to the skin. *Dermatology* 2002;204:173-178.
  5. Sawada Y, Nakamura M, Bito T, Fukamachi S, Kabashima R, Sugita K, Hino R, Tokura Y. Cholinergic urticaria: studies on the muscarinic cholinergic receptor M3 in anhidrotic and hypohidrotic skin. *J Invest Dermatol.* 2010;130:2683-2686.
  6. Takahagi S, Tanaka T, Ishii K, et al. Sweat antigen induces histamine release from basophils of patients with cholinergic urticaria associated with atopic diathesis. *Br J Dermatol.* 2009;160:426-8.
  7. Itakura E 1, Urabe K, Yasumoto S, Nakayama J, Furue M. Cholinergic urticaria associated with acquired generalized hypohidrosis: report of a case and review of the literature. *Br J Dermatol.* 2000;143:1064-6.
  8. Metz M, Bergmann P, Zuberbier T, Maurer M. Successful treatment of cholinergic urticaria with anti-immunoglobulin E therapy. *Allergy.* 2008;63:247-249.
  9. Alsamarai AM, Hasan AA, Alobaidi AH. Evaluation of Different Combined Regimens in the Treatment of Cholinergic Urticaria. *World Allergy Organ J.* 2012;5: 88-93.
  10. Sinha A, Bagga A. Pulse steroid therapy. *Indian J Pediatr.* 2008;75:1057-1066.

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