

CPD

Aquagenic pruritus successfully treated with omalizumab

B. Murphy,¹ M. Duffin¹ and J. Tolland¹¹Department of Dermatology, Ulster Hospital, Upper Newtownards Road, Dundonald, Belfast, UK

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Aquagenic pruritus (AP) is a rare condition characterized by intense itch without discernible skin lesions, evoked by contact with water. The itch is transient, but can be debilitating. AP is most commonly associated with haematological disorders such as polycythaemia rubra vera, but it can be idiopathic. Its pathogenesis is poorly understood, and response to standard antipruritic medication such as antihistamines is often unsatisfactory, suggesting that there are additional contributing aetiological factors. We report an idiopathic case of aquagenic pruritus resistant to conventional therapies treated successfully with the anti-IgE antibody drug omalizumab, and discuss potential mechanisms of action for this treatment.

A 61-year-old man presented with a 10-year history of intense itch affecting his whole body following contact with water. The symptoms lasted 30–60 min after showering or bathing; rain was not a trigger because his body was clothed when outdoors. He reported having no weals or systemic features. Comorbidities included type 2 diabetes mellitus and hyperlipidaemia; any medications for these had been started after the onset of pruritus. He had no history of haematological disorder.

At initial review, the patient's dermatology quality of life score (Dermatology Life Quality Index; DLQI) was 21, and the urticaria activity score for the previous 7 days (UAS7) was also 21 because of the lack of weals.

Screening blood tests revealed a normal full blood picture, including haematocrit, renal and liver function. Antinuclear antibody, immunoglobulins and C1-esterase inhibitor levels were normal. Chest radiography scan was clear.

A skin biopsy was taken after 15 min of exposure to ice, but this was nondiagnostic without inflammatory infiltrate.

Treatment with the H1-receptor antagonist antihistamines cetirizine and rupatadin, then the H2-receptor antagonist ranitidine (all at maximum dose), failed to provide adequate relief, as did addition of 10 mg daily montelukast. An 8-week course of ciclosporin 2.5 mg/kg/day also produced no improvement. We performed a literature review of treatments for refractory aquagenic pruritus, and the patient consented to receive anti-IgE antibody therapy (six subcutaneous 300 mg doses at 4-weekly intervals). No allergic reactions were noted after dosing in clinic. This resulted in complete symptomatic remission; DLQI and UAS7 were 0 at the 3-month review. Antihistamine therapies were stopped, and the patient was able to shower several times per week without pruritus or urticaria development. After 6 months, he had a mild relapse with a UAS7 score of 7, but this was controlled with cetirizine.

AP is a rare disorder associated with severe itch following contact with water of any temperature, but with no visible skin lesions differentiating it from aquagenic urticaria where skin lesions are present. Its pathogenesis is poorly understood. It is unclear why some patients develop skin lesions and others not when exposed to water, however, AP responds poorly to standard antihistamines compared with aquagenic urticaria,¹ therefore suggesting different disease mechanisms.

AP can be idiopathic or associated with polycythaemia rubra vera (PRV), drugs and other haematological disorders.² Some authors suggest that true AP differs from PRV water-induced itch in that the temperature of the water is not important,³ as in our case. Common treatments for AP include H1-receptor antagonist antihistamines, with or without H2-receptor antagonists, and phototherapy; all have had variable success. Examples of other trialled agents include aspirin³ and ciclosporin.⁴

The anti-IgE antibody drug omalizumab is used to treat chronic spontaneous urticaria and asthma; our

Correspondence: Dr Bryan Murphy, Department of Dermatology, Ulster Hospital, Upper Newtownards Road, Dundonald, Belfast, Northern Ireland, BT16 1RH, UK
Email: bryan.murphy@hscni.net

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literature review found only two reports describing its use in AP.^{4,5} Omalizumab suppresses circulating IgE levels, which in turn reduces basophil activation and mast cell degranulation, and thus reduces release of histamine and triggers for itch. IgE binds to and activates high-affinity FcεRI receptors⁶ on the aforementioned inflammatory effector cells, so it is likely that omalizumab reduces this FcεRI-receptor mediated inflammatory activation. Kaplan *et al.*⁶ further proposed suppression of autoimmune IgG antibodies against IgE and/or FcεRI receptors. IgE antibodies against an unknown antigen possibly contribute to omalizumab's mode of action; however, an interplay in various mechanisms is likely and requires further study.

We present our case as an example of successful and safe use of omalizumab, which achieved prolonged remission in a case of severe and refractory AP. Although our patient had a later relapse, we consider his improved quality of life, fewer clinic appointments and reduced employment absence as indicators of success. Multiple courses of omalizumab are used safely in patients with asthma, so we plan to consider further treatment for our patient if his UAS7 reaches ≥ 14 , given his lack of weals. Alongside better understanding of the disease pathogenesis, further research is required to ascertain the mechanism(s) of action for omalizumab therapy in AP.

References

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- 4 O'Connor R, McCarthy S, Bourke J *et al.* Omalizumab: a new therapeutic option for aquagenic pruritus. Poster 09, presented at the Irish Association of Dermatologists Autumn Meeting, 2016.
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CPD questions

Learning objective

To demonstrate knowledge of aquagenic pruritus and potential treatments.

Question 1

Aquagenic pruritus may be associated with which of the following haematological disorders?

- (a) Haemophilia.
- (b) Polycythaemia rubra vera.
- (c) Chronic lymphocytic leukaemia.
- (d) Acute myeloid leukaemia.
- (e) Thalassaemia.

Question 2

Omalizumab antagonizes the action of which human immunoglobulin?

- (a) IgA.
- (b) IgD.
- (c) IgE.
- (d) IgG.
- (e) IgM.

Instructions for answering questions

This learning activity is freely available online at <http://www.wileyhealthlearning.com/ced>

Users are encouraged to

- Read the article in print or online, paying particular attention to the learning points and any author conflict of interest disclosures
- Reflect on the article
- Register or login online at <http://www.wileyhealthlearning.com/ced> and answer the CPD questions
- Complete the required evaluation component of the activity

Once the test is passed, you will receive a certificate and the learning activity can be added to your RCP CPD diary as a self-certified entry.

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