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Research Article

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Management of Adult Chronic Urticaria: Practical Approach

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Abstract

Chronic urticaria is an itchy inflammatory skin condition, also known as hives, weal's, welts or nettle rash. The main symptom is raised blotchy rash which can be intensely itchy. Its cause is unknown, although it can be triggered by an allergen, physical triggers, underlying health conditions or drugs. Several serious conditions can lead to anaphylaxis which is a medical emergency. Chronic urticaria can be difficult to manage hence there are different approaches for its management. Many still use unlicensed medications to control the condition. We are putting forward a practical approach in the management of this challenging medical problem.

Keywords: Urticaria Angioedema Immunosuppressant Antihistamine.

Introduction

Urticaria is a skin condition that typically involves extremely itchy wheals, which may be associated with surrounding erythema or redness [1]. Urticarial lesions usually last less than 24 hours before resolving but rarer diseases such as urticarial vasculitis may cause more severe and long lasting urticaria — like lesion symptoms [2]. The condition may also occur in conjunction with angioedema and less commonly angioedema may present on its own. This disease can be categorized broadly into acute or chronic with the latter lasting more than six weeks by definition [3]. Urticaria can also be grouped into a spontaneous or triggered category. The inducible category of urticaria may be triggered by stress, cold, heat or some medications and the management of this subgroup is mainly through reassurance and avoidance of the relevant trigger [4].

Causes when identified include; drugs, infections including COVID-19, and type 1 hypersensitivity reactions, however, no cause is identified in more than 50% of people with acute urticaria and in many of those with CSU, thus it is termed chronic spontaneous Urticaria (CSU) [5]. Only the idiopathic variant of angio-oedema without weal's is now classified as part of chronic spontaneous urticaria, while all forms of C1 esterase inhibitor deficiency should be referred to immunology departments for further investigation and management, as per the with National and International Consensus Guidelines [5]. CSU is estimated to affect 1% of the population of the United Kingdom with a female to male preponderance of 2 to 1[6]. The majority of chronic urticaria patients fall into this idiopathic category, although 50% of patients can go into remission after 6 months, however, symptoms may last 20% and 10% for 10 to 20 years respectively [5,7]. causing a conundrum for both clinicians and patients alike [4]. Due to this fact we have decided to provide an up-to-date management protocol directed towards primary care physicians and community dermatologists to provide the best and most efficient treatment to improve patients' quality of life with CSU. We hope that such a protocol will both help the patient and reduce the burden on the National Health Service.

Assessment

Detailed history and physical examination can guide the evaluation of CU. Polypharmacotherapy, is common in older subjects, thus it is worth reviewing patient`s medication. Aspirin and other NSAIDs can aggravate chronic urticaria in about 30% of patients, moreover, the Committee on Safety of Medicines in UK, over a 40-year period of spontaneous reports has also pinpointed antibiotics, bupropion, selective serotonin re-uptake inhibitor antidepressants, angiotensin-converting enzyme inhibitors (ACEI), H2 and H1 antihistamines, and systemic antifungals [8, 9].

Dietary exclusion is not advised routinely, unless indicated to play a role by history [5]. It is difficult to judge as the time interval may vary from minutes and up to 24 hours after eating this diet, although CSU is not a manifestation of IgE-mediated food allergy, food can cause fluctuations in the symptoms of CSU. This is believed to be due to pseudoallergens, which include naturally occurring aromatic compounds in certain foods (many fruits and vegetables, seafood, others), as well as artificial preservatives and dyes in processed food [10].

As per guidance, investigations are not needed for making the diagnosis of urticaria. However, the following can be considered if indicated during assessment, to identify curable associated illnesses and trigger factors, or to rule out other possible diagnoses; the initial laboratory investigations can be limited to CBC and ESR and/or CRP, eosinophil count may be elevated in parasitic infections and in some drug-induced reactions. An elevated neutrophil count may be associated with urticarial vasculitis [5]. Moreover, an elevation with Erythrocyte Sedimentation Rate (ESR) or C-reactive protein (CRP) can be seen in infections and autoimmunity. Thyroid function tests (TFTs) and thyroid autoantibodies — the presence of thyroid autoantibodies is associated with chronic urticaria in both children and adults and suggests a diagnosis of autoimmune urticaria. There is evidence that people with urticaria are more likely to have thyroid autoimmunity than people without urticaria [11]. Several studies have shown that thyroid autoimmunity in euthyroid patients with chronic angioedema and/or urticaria is more prevalent than in the general population [12]. The presence of thyroid autoantibodies may also indicate a poorer prognosis with longer symptomatic periods and requirement for oral corticosteroids and higher doses of antihistamines. Skin biopsies are not routinely recommended except to rule out vasculitis.

Helicobacter pylori testing is guided by the presence of gastrointestinal symptoms, there is some evidence that H. pylori infection is associated with an increased risk of chronic urticaria [13]. However, it is controversial as to whether eradiation of H. pylori alleviates CSU [14]. Allergy testing: this may include patch testing or skin prick testing for suspected contact urticarias, or IgE test for specific allergens. In treatment-resistant patients, it is worth considering testing for total IgE levels and IgG histamine-releasing autoantibodies to assess the choice between the second-line treatment agents omalizumab or cyclosporin [15]. While Skin prick tests and/or blood tests for allergen specific IgE usually not helpful in chronic urticaria but can confirm the cause of type 1 hypersensitivity, if suspected [16].

Management

It is important to educate the patient about their condition and to provide an information educational leaflet from the British Association of Dermatologists or another well referenced organization. It is pivotal to explain to patients with CSU that the treatments you are providing are directed at relieving symptoms and do not necessary cure the condition. Thus, it is important to consider a validated scoring system to assess severity, score can be relied on as it is both; clear, practical and convenient for the patient and objective tool for the physician [17, 18]. The psychological impact should also be addressed by providing access to support and treatment for anxiety and depression [5]. Treatment outcome measures use 9 points scales, involving the following criteria: Disease control, decrease in urticarial activity, adverse effects, quality of life, time to clinical effect, relapse and when to stop treatment. this helps how improvement is defined [5]. Once a diagnosis has been made and no triggers have been identified and the patients' symptoms have lasted for more than 6 weeks on most days you will be able to categorize the patient into the CSU group. The management of this condition revolves around antihistamines and the following algorithm is widely accepted in the United Kingdom. First line management consist of stepped wise approach, starting with the licensed dose of second generation H1 antihistamine, with up dosing to four-fold the licensed dose if no adequate response obtained and if tolerated with the absence of contraindications. Then, we consider switching to another type of the second generation H1 antihistamine, for patients whose symptoms do not respond considerably, or if they cannot tolerate, the first drug at the starting or after increasing the doses. Within the first line of management steps, montelukast can be added to the antihistamine tried. However, no sufficient data to recommend two different second-generation H1-antihistamines at the same time. It is advised to follow 2-4 weeks of management with of each option.

There is insufficient evidence to recommend routine addition of H2-antihistamines to second-generation H1-antihistamines in case of no response, however, famotidine is the preferred agent if dyspepsia is present [19]. On the other hand, montelukast in combination with a second-generation H1- antihistamine can be effective in certain subtypes of CSU, and can be added if increasing the dose of antihistamine was not adequate [5, 20, 21]. Regarding first-generation H1-antihistamines, these are not recommended unless there is no alternative, due to concerns about their short- and long-term effects on the central nervous system, moreover, up dosing is not advised [5]. If the response to the first line medication was inadequate, and the weekly urticaria area severity score (Figure 1) is more than or equal to 28 then Omalizumab can be used if the patient meets the eligibility criteria (age >/= 12 years) [22]. It may be also relevant to consider measuring total IgE levels and tests for IgG releasing Autoantibodies (BHRA) when available. This can help to inform the choice between the second-line treatment agents omalizumab or ciclosporin [23]. Although indicative and not yet subject to a national quality assurance scheme, it was found that positive BHRA may signal a higher probability of the urticaria response to ciclosporin [5]. Omalizumab or ciclosporin are indicated in its lower effective dose with periodic interruption in addition to second generation H1 antihistamine. Omalizumab is a humanised monoclonal antibody that attaches to circulating immunoglobulin E (IgE) and negatively affects basophils and mast cell production of inflammatory mediators. The recommended dose for the treatment of chronic spontaneous urticaria is 300 mg by subcutaneous injection every 4 weeks. Some patients may show good symptom control with a dose of 150 mg every 4 weeks [24].

Systemic steroid is considered as rescue treatment within the second line management step in the lower effective dose of 0.5 mg/kg for few days [5]. Oral steroid is not expected to heal the patient but at least to bring urticaria flare under control bringing urticarial to its previous basic level of severity and should be clearly explained to the patient. Third-line treatment options are not licensed in UK for treatment of urticaria, these are azathioprine, dapsone, doxepin which is a first-generation antihistamines with concerns regarding central nervous system side effects, hydroxychloroquine (especially for urticaria occurring in association with systemic lupus erythematosus), methotrexate, IVIg, mycophenolate mofetil, narrowband ultraviolet (UV)B (usually in a 30 sessions course, repeated after 12 months if needed, and not as a continual treatment [25].

Score	Wheals or hives	Itch
0	None	None
1	Mild (<20 wheals/24 h)	Mild
2	Moderate (21-50 wheals/24 h)	Moderate
3	Intense or severe (>50 wheals/24 h or large confluent areas of wheals)	Intense or severe

Scoring 0-6

Figure 1: Urticaria area severity score

Conclusion

The management of chronic urticaria can be challenging. Many approaches, advice and guidelines have been proposed. We are putting a simplified approach in the management of chronic urticaria. However, more comprehensive guidelines have recently been published [26, 27].

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