

# Chronic Urticaria Resolving after Resection of Mucinous Breast Cancer

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## Abstract

Chronic urticaria is a common condition characterised by intense pruritus, wheals and erythema. A 56-year-old female presented with chronic urticaria which persisted despite multiple therapies. Laboratory and radiological investigations were performed and a mucinous breast cancer detected. Within days of surgical resection of the breast cancer, the urticaria resolved. This paper outlines the major causes of chronic urticaria and the importance of investigating patients with chronic urticaria.

**Keywords:** Breast cancer; Chronic urticaria; Urticaria; Mucinous; Malignancy

## Introduction

Chronic urticaria can be a distressing condition associated with intense pruritus, wheals and erythema. A causative agent is never found in many cases. Though associations with autoimmune diseases have been commonly reported, an association with malignancies is less common. This case demonstrates a rare association between chronic urticaria and breast cancer and highlights the need to perform investigations in patients with chronic urticaria.

## Case Report

A 56 year old Caucasian female presented to the emergency department in November 2009 with a 7 month history of progressively worsening urticaria. Initially it was intermittent but became constant and severe after taking roxithromycin for a presumed chest infection. There were no obvious triggers or allergens and she had no known allergies. Her past medical history included recurrent basal cell carcinomas on her face and trunk, genital herpes, nephrectomy at age eight for renal agenesis, hypertension and tachycardia. She has a family history of renal agenesis and reflux nephropathy.

In the emergency department she was prescribed oral steroids and antihistamines (fexofenadine and promethazine) and discharged home. She continued to have generalised urticaria requiring oral steroids and was referred to the dermatology outpatient clinic in December.

On examination she had generalised wheals involving her entire body and dermatographism but sparing her face (Figure 1 and Figure 2); there was no purpura and she was reviewed 24 hours later, confirming that the lesions were resolving and moving. Cardiovascular, respiratory and gastrointestinal examinations were unremarkable. There were no signs of thyroid disease or infections (including sinusitis or dental abscess).

Laboratory testing including complete blood count, liver, kidney and thyroid function tests, inflammatory markers, anti-nuclear antibody (ANA), extractable nuclear antigen (ENA) tests, double-stranded DNA and complements were all within normal limits, along with urinalysis and Chest X-ray. For want of other investigations in the setting of a distressed patient with idiopathic symptomatic urticaria, routine age-based health screening was recommended including a mammogram and a PAP smear. Her last mammogram and PAP smear were performed about 12 months before presentation. Mammography and breast ultrasound demonstrated suspicious right breast lesions which were biopsied and diagnosed as a Grade 1 infiltrating mucinous carcinoma and ductal carcinoma in situ (DCIS). Further testing showed the tumour



**Figure 1:** There are generalised wheals and evidence of dermatographism on the patient's back.

was oestrogen receptor positive, progesterone receptor negative and HER-2 negative with no nodal involvement. Within two days of surgical removal of the cancer, the generalised urticarial eruption resolved and she no longer required oral steroids or antihistamines. She has been reviewed at 3 months and 4 months following this for unrelated skin checks and the urticaria has remained clear on no therapy.

## Discussion

Chronic urticaria is an inflammatory response involving the epidermis and dermis characterised by the daily onset of wheals for at least 6 weeks. Wheals represent dermal oedema and can involve any part of the skin. Pathognomonic features of urticaria include pruritus, erythema and wheals which last less than 24 hours [1,2].

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Better understanding about this condition has resulted in various attempts at classification. A consensus meeting in 2008 produced a guideline which defined chronic spontaneous urticaria as “spontaneous wheals and/or angioedema > 6weeks” [2]. This guideline separates chronic urticaria due to external physical factors (eg. temperature, contact, pressure, cholinergic and vibratory) from “spontaneous” chronic urticaria. Kaplan [3], however, states two forms of chronic urticaria exist, namely chronic autoimmune urticaria and chronic idiopathic urticaria. Though physical causes of chronic urticaria, such as symptomatic dermatographism and cold induced urticaria, are often excluded, they are included in other classifications [1].

### Chronic idiopathic urticaria

At least 50% of patients with chronic urticaria have chronic idiopathic urticaria (CIU) where a causative agent is never found. CIU affects 0.1% of the population and has a detrimental effect on quality of life. The urticaria of CIU typically lasts 8-12 hours and is especially pruritic at night [1].

### Autoimmune urticaria

Autoimmune diseases account for 39-50% of cases [4]. Both Hashimoto's and Graves' disease have been associated with chronic urticaria. Other autoimmune associations include bullous pemphigoid (where it is often in fact pre-bullous pemphigoid), systemic lupus erythematosus and juvenile rheumatoid arthritis.

### Other causes of urticaria

There is debate as to whether medications (eg. aspirin, aminoglycosides), infections (eg. H.Pylori) and dietary factors (eg. Salicylates in fruits, tea, coffee) play a role in the aetiology of chronic urticaria.

### Urticaria and malignancy

Malignancies are considered rare causes of chronic urticaria and to date there has been only one reported case of breast cancer [5]. Chronic urticaria has been noted in various case reports as the presenting sign of an underlying malignancy. An association between different types of lung cancer and urticaria is well known [6]. Other cancers reported to be associated with chronic urticaria include leukaemia, lymphoma [7], papillary thyroid cancers [8], ovarian cancer[9], brain tumour [10], colorectal carcinoma and carcinoid syndrome with liver metastases [11].

Some of the published case reports have common features to this case: the urticaria was the initial sign of the occult cancer; patients were asymptomatic from their underlying cancer; haematological tests and thyroid function tests were often normal; antihistamines and steroid therapy was ineffective in managing symptoms of the urticaria; resolution of the urticaria was achieved within 1-4 days of treating or removing the cancer. The age ranges of these patients was 12 years to 73 years. The patient in this case was taking regular oral steroids and antihistamines without effect for more than 4 weeks. The urticaria did not show any signs of abating until complete removal of the cancer. A possible theory is that of a paraneoplastic basis of urticaria. Tumour cells may produce humoral substances (eg. proteins or hormones) that trigger the urticaria [12], as they may produce other hormones that result in other paraneoplastic dermatoses, for example, acanthosis nigricans and necrolytic migratory erythema.



**Figure 2:** Erythematous wheals over the anterior aspect of the chest. There is no breast asymmetry or detectable nipple abnormality.

It is uncertain, however, whether a correlation between tumour aggression and the severity of urticaria exists. Removal of the cancer eliminates the source of these humoral factors and 1-2 days are required for metabolism or excretion of such triggers from the body.

In recent times, reports of an association between solid organ malignancies and chronic urticaria have been dismissed as mere coincidence. A study looking at 1155 cases of chronic urticaria did not find a significant association with internal malignancy [13] and concluded that the rate of malignancy was no different to the normal population. However, this study did not address whether the urticaria resolved following removal of the cancer or not. Despite the conclusions from this large study, which rejected a causal relationship between chronic urticaria and an internal malignancy, this case report along with previously reported cases support a potential causal relationship between chronic urticaria and malignancy. Resolution of the urticaria within days of removing the cancer is unlikely to be incidental, though this definitive relationship cannot be proven as it is impossible to “rechallenge” patients unless simultaneous recurrence of the cancer and urticaria is observed. Symptoms and signs of chronic urticaria must be taken seriously as an underlying malignancy is possible and in patients with a previous malignancy, it may herald its recurrence. Unfortunately, routine haematological tests are often normal and various radiographic investigations are needed to make a diagnosis. But, to what extent does one investigate a patient with chronic urticaria? Knowing that CIU accounts for at least 50% of cases, searching for a diagnosis may be a costly and futile effort. But under-investigation may miss an occult malignancy whose removal could not only rid the urticarial but potentially save or lengthen the life of the patient. To add to this dilemma, extensive testing may reveal false positives resulting in unnecessary invasive tests. Even more, internal disease accounts for only 1.6% of presentations with chronic urticaria [14] and haematological investigations can be normal.



Though it has been suggested that history and examination findings bear more significance than laboratory findings [14], patients with chronic urticaria have no symptoms or signs of an underlying malignancy and hence evaluation on clinical grounds is impossible. Current guidelines do not recommend screening for common malignancies in the workup of patients with chronic urticaria. Standard non-invasive investigations are recommended instead. These include serum testing for full blood count with differential, erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) with thyroid function tests, Helicobacter Pylori testing, autologous serum skin test and lesional skin biopsy reserved for severe or persistent cases [2,4,15]. We suggest performing non-invasive screening tests according to local age-related guidelines for common malignancies such as bowel, prostate, cervical, breast, lung, thyroid cancers and haematological malignancies if the standard investigations return normal.

## Conclusion

Chronic urticaria can severely impact a patient's quality of life, so finding the underlying cause and avoiding precipitants is crucial in managing this condition. Though malignancy is a rare cause of chronic urticaria and often not considered to be associated with urticaria, this case reports a relationship between the urticaria and breast cancer. Further studies will hopefully demonstrate a clear association between malignancies and chronic urticarial, possibly in an older age bracket of patients, and clarify if a correlation with aggressive or indolent cancers exists. Checking the status of age-related cancer screening and referral back to the general practitioner for arranging this would therefore be appropriate. We have advised our patient to return if the urticaria reappears as this may indicate tumour recurrence.

## References

1. Greaves M (2000) Chronic urticaria. J Allergy Clin Immunol 105: 664-672.
2. Zuberbier T, Asero R, Bindslev-Jensen C, Walter Canonica G, Church MK, et al. (2009) EAACI/GA(2)LEN/EDF/WAO guideline: definition, classification and diagnosis of urticaria. Allergy 64 : 1417-1426.
3. Kaplan AP (2004) Chronic urticaria: pathogenesis and treatment. J Allergy Clin Immunol 114: 465-474.
4. Powell RJ, Du Toit GL, Siddique N, Leech SC, Dixon TA, et al. (2007) BSACI guidelines for the management of chronic urticaria and angio-oedema. Clin Exp Allergy 37: 631-650.
5. Wedi B, Wagner S, Werfel T, Manns MP, Kapp A (1998) Prevalence of Helicobacter pylori-associated gastritis in chronic urticaria. Int Arch Allergy Immunol 116: 288-294.
6. Greiner D, Schofer H, Boehncke WH (2002) Urticaria associated with a small cell carcinoma of the lung. Cutis 69: 49-50.
7. Murota H, Shoda Y, Ishibashi T, Sugahara H, Matsumura I, et al. (2009) Improvement of recurrent urticaria in a patient with Schnitzler syndrome associated with B-cell lymphoma with combination rituximab and radiotherapy. J Am Acad Dermatol 61: 1070-1075.
8. Manganoni AM, Tucci G, Venturini M, Farisoglio C, Baronchelli C, et al. (2007) Chronic urticaria associated with thyroid carcinoma: report of 4 cases. J Investig Allergol Clin Immunol 17: 192-195.
9. Reinhold U, Bruske T, Schupp G, (1996) Paraneoplastic urticaria in a patient with ovarian carcinoma. J Am Acad Dermatol 35: 988-989.
10. Shamsadini S, Varesvazirian M, Shamsadini A (2006) Urticaria and lip fasciculation may be prodromal signs of brain malignancy. Dermatol Online J 12: 23.
11. Bofek A, Rachowska R, Krajewska J, Paliczka-Cieslik E, Filipowska B, et al. (2008) Carcinoid syndrome with angioedema and urticaria. Arch Dermatol 144: 691-692.
12. De P, Abbasi R, Senadhira T, Orr P, Ullah A (2005) Urticaria and large cell undifferentiated carcinoma of lung. Dermatol Online J 11: 45.
13. Lindelof B, Sigurgeirsson B, Wahlgren CF, Eklund G, et al. (1990) Chronic urticaria and cancer: an epidemiological study of 1155 patients. Br J Dermatol 123: 453-456.
14. Kozel MM, Bossuyt PM, Mekkes JR, Bos JD (2003) Laboratory tests and identified diagnoses in patients with physical and chronic urticaria and angioedema: A systematic review. J Am Acad Dermatol 48: 409-416.
15. Zuberbier T, Asero R, Bindslev-Jensen C, Walter Canonica G, Church MK, et al. (2009) EAACI/GA(2)LEN/EDF/WAO guideline: management of urticaria. Allergy 64: 1427-1443.

