CASE REPORT

Breast malignancy masquerading under the cloak of acute urticaria

Erin O'Donnell, Rachel Havyer

Mayo Clinic, Rochester, Minnesota, USA

Correspondence to
Dr Rachel Havyer,
havyer.rachel@mayo.edu

SUMMARY

Urticaria is a common disorder characterised by well-demarcated and intensely pruritic erythematous skin swellings. Common triggers include infection, allergic reactions or medications. While often idiopathic, the presence of urticaria can be associated with underlying systemic disease. We report a case of a patient who presented with diffuse and refractory urticaria. A thorough workup was conducted to determine the aetiology including routine age-appropriate cancer screening. Mammography revealed four lesions in the patient's left breast with biopsy consistent with invasive ductal carcinoma. Disappearance of the urticarial lesions with mastectomy suggests an association between breast malignancy and urticaria. Thus, refractory urticaria with unknown cause should prompt a thorough history, physical examination and review of age-appropriate cancer screening.

BACKGROUND

Urticaria, 1 of the 10 most common dermatoses, presents in more than 20% of the population in the USA.¹ Urticaria has a diverse presentation ranging from localised wheals to widespread whealing with angio-oedema. The skin lesions appear oedematous, smooth, pink and surrounded by an annular erythematous flare with clearing of the central area.² While often intensely itchy, the wheals are found anywhere on the skin and may vary within the same individual. Physicians classify urticaria into two categories according to the time-course including acute, shorter than 6 weeks, and chronic, longer than 6 weeks with symptoms present daily.

Chronic urticaria is less common with an estimated prevalence of 1–3% and most often is idiopathic. Possible aetiologies of chronic urticaria include allergic reactions, infections, autoimmune, vasculitis, thyroid disease, hormonal problems and rarely cancer. To diagnose urticaria and identify any eliciting factors, a detailed history, physical examination and laboratory tests are performed.

This case represents a rare association between chronic urticaria and invasive breast cancer and demonstrates the usefulness of age-appropriate cancer screening in patients presenting with persistent idiopathic urticaria. When investigating the cause of persistent urticaria, routine cancer screening tests might be worthwhile as the presence of urticaria can be associated with underlying systemic disease.

CASE PRESENTATION

A 58-year-old woman presented to urgent care with a 1-week history of a flat, erythematous, pruritic rash involving her palmar surfaces bilaterally. Treatment with topical steroids and antihistamines gave no resolution of symptoms leading to referral to dermatology. History revealed no antecedent illnesses, new medications, travel or exposure to toxins or allergens. Her medical history included basal cell carcinoma of the left forearm status post-treatment with curettage and cryotherapy, Graves' disease and osteoarthritis.

Over approximately 3 weeks, the rash progressed to generalised oedematous annular plaques located on her forearms, lower extremities, upper abdomen, suprapubic area and buttocks. She then developed deep dermal swelling of her hands, lip and face prompting initiation of systemic steroid treatment, which resolved the eruption. On examination, firm urticated plaques were found on the right pretibial region, left lateral flank, central coccygeal, sacral and intergluteal cleft, and portions of the forearms bilaterally (figure 1). A red-brown discolouration surrounded the urticated plaque and residual inflammatory erythema appeared in resolved areas. Cardiovascular, respiratory and gastrointestinal examinations were unrevealing with no signs of thyroid disease or infectious processes. Owing to unknown aetiology of her presenting symptoms and signs, a thorough workup was pursued.

INVESTIGATIONS

Skin biopsies of the right hand and left thigh were obtained and yielded results consistent with urticaria showing dermal oedema with mixed dermal and pannicular inflammation with abundant eosinophils (figure 2). Owing to unknown aetiopathogenesis, a thorough workup was pursued. Laboratory studies including thyroid function, serum protein electrophoresis, complement, anti-nuclear antibody, autoimmune blistering disease studies, flow cytometry and Lyme disease serology were normal. While the chest X-ray showed negative findings, urinalysis revealed haematuria, which prompted further workup with urine cytology and a CT urogram both showing normal results.

To investigate further possible triggers for this persistent urticaria, the patient followed up with her primary care physician for age-appropriate cancer screening including mammogram and Papanicolaou (PAP) smear. PAP smear was normal but mammography revealed four lesions in her left breast. Ultrasound-guided core needle biopsies

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To cite: O'Donnell E, Havyer R. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-202494

Figure 1 Generalised wheals found on the patient's upper and lower extremities, left lateral flank and central coccygeal regions.

revealed that three of the four lesions demonstrated grade 1 invasive ductal carcinoma. Further testing showed that the cancerous masses were strongly oestrogen receptor positive, progesterone receptor positive and HER2 negative.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for diffuse pruritic plaques includes angio-oedema, urticarial vasculitis, dermatitis herpetiformis, perniosis and granuloma annulare. Once biopsy proved urticaria, search for aetiology ensued due to its severity and persistence. History did not show any new exposures. Other differential includes infection, autoimmune disease or malignancy.

TREATMENT

The first line of treatment for our patient's intensely pruritic urticarial lesions included topical steroids, triamcinolone 0.1% cream and clobetasol 0.05% ointment and antihistamines diphenhydramine and cetirizine. With minimal resolution of the rash, the patient received 40 mg of oral prednisone for treatment, which led to overall improvement of her rash.

Following the diagnosis of invasive ductal carcinoma based on the results from the core needle biopsies, our patient underwent a left breast mastectomy that showed clear margins and a negative left axillary sentinel node biopsy.

OUTCOME AND FOLLOW-UP

After the surgery, our patient was gradually tapered off oral steroids, and at 4 weeks postoperation she showed no evidence of

rash recurrence. A follow-up visit with her dermatologist 4 months later reported that the urticaria and angio-oedema remained clear while receiving no medical therapy.

DISCUSSION

Urticaria is a common dermatosis classified as acute or chronic based on the duration of symptoms. Primary causes of acute urticaria include medications, foods, viral infections, parasitic infections, insect venom and contact allergens.² Although several cases have reported associations between urticaria and underlying internal malignancy, little evidence is present to either confirm or elucidate the causal relationship.

Until today, only one other case report describes the association between urticaria as a preceding marker for breast malignancy.³ A thorough literature search, however, yielded findings of several other cases that suggest a causal relationship between urticaria and other malignancies including lung cancer, papillary thyroid cancers, lymphoma, ovarian cancer, brain tumours and carcinoid syndrome.⁴⁻⁸ Interestingly, these cases have similar outcomes to the breast malignancy presented in this report. In the majority of the cases presented, treatment of the underlying malignancy such as removal of the malignancy or chemotherapy leads to prompt resolution of the urticarial lesions.

While several reports suggest an association between chronic urticaria and malignancy, it remains difficult to prove a relationship that exists beyond simple coincidence. An epidemiological study seeking to evaluate the association between malignant disease and chronic urticaria concludes that urticaria is not statistically associated with malignancy in general. This study evaluated 1155 patients with chronic urticaria and investigated the incidence of cancer in this population, comparing the observed number of cases to the expected number of malignancies. The findings presented suggest that the rate of malignancy within the population with chronic urticaria shows no significant difference compared to the normal healthy population.⁹

So, while on a population level, there may not be increased incidence of malignancy, the refractory and persistent symptoms that resolved with treatment of the breast cancer in our patient's case supports a relationship between breast malignancy and acute urticaria on an individual level. Thus, persistent symptoms and signs of urticaria with unknown cause should increase our index of suspicion for an underlying systemic illness, prompting a thorough history, physical examination and age-appropriate cancer screening.

Figure 2 Right hand skin punch biopsy shows mixed dermal infiltrate composed of neutrophils and eosinophils representing an acute urticarial tissue reaction.

Learning points

- ▶ Urticaria is a common clinical diagnosis that can commonly be idiopathic.
- ▶ When symptoms of urticaria are persistent, thorough history and physical as well as targeted studies to elucidate aetiopathogenesis, including age-appropriate cancer screening are warranted.
- ▶ Although epidemiological studies do not support increased incidence of malignancy with urticaria, resolution of urticaria with appropriate treatment suggests association on an individual level.

Contributors All authors contributed meaningfully to the conception/design, drafting/revising and final approval of the article.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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