

GIANT URTICARIA AND COLONIC ADENOCARCINOMA

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Background: Paraneoplastic syndromes may represent the only clinical sign of a silent neoplasm and may precede discovery and diagnosis of the tumor itself. Specific skin lesions can be associated with internal malignancy yet these are rare. In many instances their etiology remains a mystery. Early identification of paraneoplastic syndromes is imperative for prompt diagnosis and treatment of the underlying malignancy, resulting in an improved prognosis for the patient.

Objective: The purpose of this case is to evaluate the role of urticaria as an early cutaneous finding of internal malignancy.

Subject: A 60 year-old Caucasian man was referred for evaluation of urticaria of one-year duration. His medical history was significant for an adenocarcinoma of the colon resected three years prior to the onset of his cutaneous lesions. In the interval between his surgery and the referral to our clinic, the patient had no evidence of tumor recurrence. He underwent to a complete workup to rule out both a recurrent colonic adenocarcinoma and a new primary malignancy.

Results: An increase in non-specific tumor antigens was found six months before a recurrent colon adenocarcinoma was identified.

Conclusions: Cutaneous signs may rarely occur as a paraneoplastic phenomenon in patients with a gastrointestinal malignancy. Urticaria has been uncommonly described in association with colon malignancy. We report a case of giant urticaria associated with an internal malignancy recurrence.

Key-words: Colonoscopy - Giant urticaria - Paraneoplastic syndrome - Tumor markers.

TO THE EDITOR

Determining the etiology of chronic urticaria can be a frustrating endeavour for both patients and physicians alike (1). Its pathogenesis often remains an enigma, and the actual frequency is not well known. Since cutaneous paraneoplastic signs may be the only presenting sign of an occult malignancy, one's index suspicion must remain high for the prompt identification of an associated underlying cancer to allow early diagnosis and treatment. The implications of early diagnosis are of considerable importance (2).

A 60-year-old man was diagnosed with adenocarcinoma of the colon in 2001 and was treated with a subtotal colectomy without chemotherapy. Three years later he developed a burning, persistent rash, refractory to topical emollients, corticosteroids and oral antihistamines. After one-year duration he was referred to the dermatology clinic. Examination revealed well-demarcated erythematous plaques and wheals involving the neck, trunk, and legs (Fig. 1). Initially the

lesions lasted less than 24 hours and appeared intermittently. Gradually their frequency increased appearing every other day. No association with medication, topical agents or aeroallergens could be identified. The workup for contact allergies and prick testing was negative. Specific serum IgE for the most common aeroallergens were negative.

Histopathology of a cutaneous lesion revealed a non-specific inflammatory infiltrate and direct immunofluorescence was negative. Laboratory findings, including skin reactivity to autologous plasma, complement fractions, were within normal ranges except for an increa-

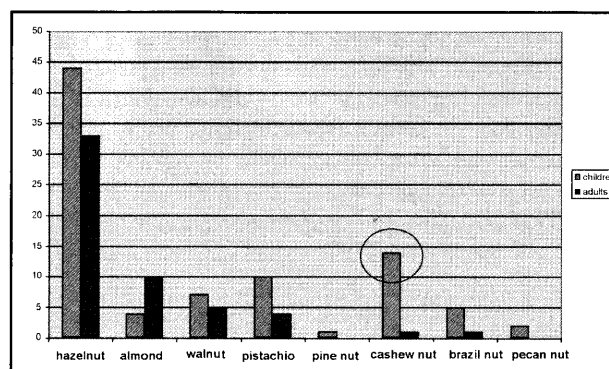


Figure 1: Well-demarcated erythematous plaques and wheals over the trunk. The largest skin lesions measured about 10-cm in diameter.

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se in total bilirubin 4.7 md/dl (n.v. 0.1-1.3) and PCR 22.49 mg/L (n.v.<5) increase. The presence of oncogenesis and other parasitic infections were excluded. As part of his oncologic follow-up the patient was seen every three months after his colon resection. Tumor markers were checked every six months and he underwent annual colonoscopy, which thus far have been negative for recurrent colon adenocarcinoma. Suspecting the presence either a recurrent malignancy or a new primary malignancy, including hematologic malignancies, multiple myeloma, and autoimmune diseases, or mastocytosis, we tested additional tumor markers. CA 72-4: 28 (n.v. <3U/ml) and M2-PK>100 (n.v.<15 U/ml) were found to be increased. Additional workup revealed negative CAT Scans, PET scans, bone marrow biopsy, liver ultrasound and normal lactate dehydrogenase levels but six months later the colonoscopy showed a recurrence. After the colectomy the atypical urticaria disappeared.

Generally urticaria is not associated with an underlying malignancy, but in chronic cases there is an increased risk for an associated internal malignancy (2). Paraneoplastic cutaneous manifestations, consisting of urticaria are exceptionally rare and can be the presenting sign of an asymptomatic cancer.

Paraneoplastic conditions can occur secondary to substances produced by tumor cells, be due to the development of autoantibodies directed against tumor antigens, or develop secondary to the effects of metastasis (3).

In the few cases of urticaria and angioedema reported in the literature the etiologic processes included C1 esterase consumption, alternative complementary way activation, through the C3B-properdin system, cryptoantigen cleavage, antibody production to tumor antigens, and cytokine-like substances produced by neoplastic cells (3).

Paraneoplastic signs may antedate the appearance of the internal malignancy. Some run a course parallel to the tumor and some follow a pattern independent of the neoplasm. A minority of patients have idiopathic chronic giant urticaria. As an indicator for an underlying malignancy, it may not only serve in the early detection of the malignancy, it can also be an indicator of either successful treatment or recurrence of disease. The Swedish epidemiological study strongly suggested that chronic urticaria is not statistically associated with malignancy. When the dermatosis is common, as with urticaria, the possibility increases

that the association has occurred only by chance (4). Our patient remains disease free three years following his colon resection.

An increase in bilirubin, without evidence of liver disease or hemolysis, prompted an investigation of tumoral markers, revealing an increase in CA 72-4 and M2-PK (5). Cells with an increased turnover, like embryonic cells, stem cells, and neoplastic cells, express these antigens. They are not routinely evaluated but when elevated following the EGTM they are associated with a poor prognosis (6). The coincident appearance of chronic urticaria in a patient with colonic adenocarcinoma might be linked to the activation of the coagulation cascade and generation of vasoactive substances (7-8). Our case is of anecdotal value and no other reports of the association of chronic urticaria with malignancy were found on review of the literature.

The association in our patient may be casual but in cases like this the dermatologist plays a critical role in recommending whether or not additional workup for an underlying new or recurrent malignancy is warranted.

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