Urticarial Vasculitis Occurring in Association with Visceral Malignancy

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This is a report of a solitary patient who had urticarial vasculitis and an adenocarcinoma of the colon. Urticarial vasculitis has not been described in association with malignancy. It is considered that tumor-associated immune complexes might have been involved in the pathogenesis of the vasculitis. ***Key words: Circulating immune complexes; Leukocytoclastic vasculitis; Paraneoplastic.***

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The syndrome of urticarial vasculitis has found its niche in the spectrum of cutaneous vasculitis as attested by reports and reviews which have been numerous in the recent literature (1–5). A case is reported herein of urticarial vasculitis occurring in a patient with a visceral malignancy. The vasculitis was kept well under control with a low-dose regimen of indomethacin. The presence of circulating immune complexes was documented.

CASE REPORT

A 69-year-old white woman presented May 16, 1984 with a

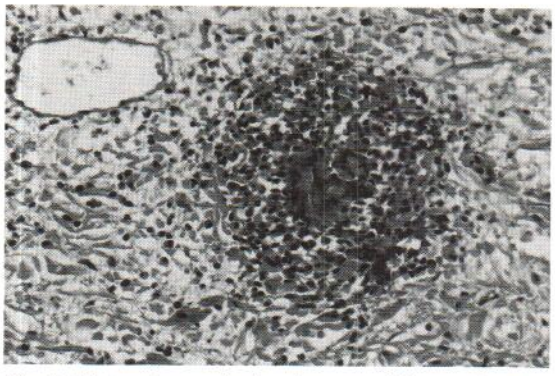

Fig. 1. Photomicrograph showing necrotizing small vessel leukocytoclastic vasculitis in the dermis (H & E stain: ×66). (Photomicrograph courtesy of Robert G. Freeman, M.D.).

history of painful, red, wheal-like lesions since December, 1982. The lesions were migratory, and occurred daily. They occurred on the head, neck, trunk, and extremities. She reported frequent lesions on the 'bra-line', waist-line, and the frontal scalp margin, indicating the possibility of a pathergic mechanism of lesion induction. Healing occurred with post-inflammatory hyper-pigmentation. She reported that the lesions would last 6–7 seven days, "sometimes for weeks." She had no known allergies. During the early development of these lesions, itching was a prominent feature, and then the lesions became painful. The pain was worse than the itching. There was no history of livedo reticularis, Raynaud's phenomenon, purpura, lymphadenopathy, fever, abdominal pain, or arthritis. Review of systems disclosed a history of intermittent slight vaginal bleeding for the preceding 3 years. An abdominal hysterectomy had been performed at the age of 35.

Examination of the skin revealed numerous arciform, annular, and serpiginous urticaria-like lesions on the right medial knee and popliteal flexure, left arm, and right anterior waist. Post-inflammatory hyperpigmentation was a prominent feature, especially along the 'bra-line' and waist-line. Other physical findings included a few hard exudates in the optic fundi, and speculum pelvic examination revealed a friable mass situated in the apex of the posterior fornix which bled very easily on swabbing with a cotton-tipped applicator. The cervix was intact and appeared normal. An excision biopsy of a representative nodule on the medial pole of right popliteal fossa revealed leukocytoclastic vasculitis (Fig. 1). A punch biopsy of the vaginal mass was performed, and this was interpreted as moderately well differentiated adenocarcinoma. Barium enema examination was performed, and revealed an annular carcinoma involving the left transverse colon.

Laboratory studies revealed an erythrocyte sedimentation rate (corrected) of 39 mm/h, negative serum cryoglobulins and cryofibrinogen, non-reactive VDRL, normal CH5O, negative antinuclear antibody test, negative LE prep, normal serum creatinine, and a normal urinalysis and SMA-12. The CBC was normal, with the exception of an anemia with hemoglobin 11.6 Gms/% (normocytic, normochromic). Clq binding assay was 23% (normal less than 13%).

On June 6, 1984 an exploratory laparotomy was performed revealing a Duke-C adenocarcinoma of the transverse colon just proximal to the splenic flexure. Further exploration revealed bilateral ovarian tumors which on histologic examination proved to be Krukenberg tumors (metastases to both ovaries). The left ovary was adherent to and eroded into the posterior vaginal fornix. The primary colon tumor was resected and the colon was repaired with an end-to-end anastomosis. A bilateral salpingo-ophorectomy was performed, with resection of the cervix, upper vagina, and rectosigmoid enbloc. A primary anastomosis was made between the colon and upper anorectum, using a stapling device.

On July 11, 1984 she estimated a 75% decrease in the intensity of the vasculitis compared with the pre-operative situation. On July 31 she reported increased eruption, especially around the abdominal surgical scar and axillae. On August 8 she was given a prescription for fourteen dapsone tablets (100 mg) with instructions to take one daily. This was not helpful. She was next placed on indomethacin using a 75 mg sustained release capsule each morning. She reported complete clearing the day after starting this, but complained that it produced "fatigue." Because of this she stopped the indomethacin. A 2-week trial of colchicine 0.6 mg twice daily was not helpful. Following this a 2-week trial of hydroxychloroquine 200 mg daily failed to help. At this time indomethacin 25 mg twice daily was prescribed, and she reported complete clearing within 3 days of starting treatment. This regimen was free of side effects. On March 26, 1985 she reported increased intensity of the vasculitis. The indomethacin was increased to 25 mg three times daily, which produced drowsiness. She decreased it to b.i.d., and this controlled the problem well.

On September 11, 1985 a recurrence of adenocarcinoma involving the upper vagina was confirmed by repeat biopsy. Exploratory laparotomy was performed revealing recurrent tumor on the area of the vaginal cuff and base of the bladder, a metastatic nodule in the omentum, and a nodule in the abdominal wall in the surgical scar. A permanent colostomy was performed, and she underwent palliative radiation treatment. Indomethacin 25 mg b.i.d. continued to control her vasculitis until she expired as a result of her metastatic disease on January 7, 1988.

A review of the English literature failed to reveal any reports of urticarial vasculitis occurring with visceral malignancy.

DISCUSSION

Although a direct immunofluorescence investigation was not performed on the skin biopsy of this patient, this does not detract from the reportability of this case. Since immunoreactants are present transiently at the onset of a lesion, the frequency of negative direct immunofluorescence of the lesional skin in vasculitis is understandable. Cutaneous leukocytoclastic vasculitis can be a manifestation of a wide variety of diseases, drugs, chemicals, or foreign pro-

teins. Only rarely has leukocytoclastic vasculitis been associated with neoplasia.

In this patient, the discovery of a malignancy occurred concurrently with the urticarial vasculitis, hence, a 'paraneoplastic' association. When the tumor was removed, the vasculitis improved for a time. Callen described a patient with cutaneous leukocytoclastic vasculitis in which the presence of skin disease occurred before the discovery of a colonic adenocarcinoma (6). After the removal of the tumor, his leukocytoclastic vasculitis promptly resolved. However, he was unable to demonstrate circulating immune complexes in this patient. He speculated that tumor-derived antigens may have led to the formation of circulating immune complexes which resulted in the vasculitis.

The case reported here is noteworthy in that findings of circulating immune complex disease were present. It is reasonable to consider tumor antigen – antibody complexes as a possible mechanism of a vasculitic syndrome. Greer's recent report of 13 cases strengthens the paraneoplastic association (7). This suggests that malignancy should be suspected in patients with chronic unexplained cutaneous vasculitis, even in the absence of systemic vasculitis.

The message from this case is clear; the presence of leukocytoclastic vasculitis should prompt a search for an antigen source, including a malignant neoplasm. Although circulating immune complexes were documented in this patient with urticarial vasculitis, we can only speculate that tumor antigens were the progenitor of the circulating immune complexes.

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