Vasculitis as a paraneoplastic syndrome has rarely been reported with renal cell carcinoma [1-2]. We report a patient who developed a purpuric eruption on his extremities in conjunction with surgical removal of a renal cell carcinoma. Skin biopsy demonstrated a leukocytoclastic vasculitis. Concurrently, a type-II (polyclonal) cryoglobulinemia was discovered. With deterioration of renal function months later and persistence of the vasculitic skin lesions, a transformation from type-II to type-I (monoclonal) cryoglobulinemia was observed.

A 63-year-old man, previously in good health, presented with a 2-year history of weight loss, paroxysmal episodes of hiccups, shortness of breath, and a decreased appetite with early satiety. Physical examination was unremarkable.

The hematocrit was 27.2% (MCV 74), the erythrocyte sedimentation rate was 113 mm/h, and urinalysis was remarkable for micro-hematuria and 3+ proteinuria. Abdominal ultrasound revealed a soft tissue mass in the lower pole of the right kidney, and a bone scan was not suggestive of metastatic disease. The patient underwent a right nephrectomy. Pathology demonstrated a poorly differentiated clear cell renal carcinoma which extended through the capsule into the perinephric fat.

The postoperative course was complicated by hypertension, seizures, and, on postoperative day 3, the development of non-palpable purpura on both arms and legs and scattered petechiae on the fingertips. The patient’s medications at the time included phenytoin, nifedipine, labetolol and cefazolin. A biopsy of the lesions revealed leukocytoclastic angiitis. The skin lesions resolved completely during the subsequent week.

Serum protein electrophoresis (SPEP) revealed a monoclonal IgM kappa spike and the presence of cryoglobulin. Immunofixation electrophoresis (IFE) of the cryoprecipitate demonstrated the presence of monoclonal IgM kappa and polyclonal IgG kappa. A urine protein electrophoresis (UPEP) revealed kappa Bence-Jones proteinuria. Total hemolytic complement (CH50) was within normal limits. Bone marrow biopsy was refused.

Eight months later, the patient was readmitted for worsening renal function and poorly controlled hypertension. A retrospective review of the earlier surgical specimen revealed glomeruli with...
membranoproliferative changes, intracapillary thrombi, and eosinophilic deposits, suggesting cryoglobulinemic renal disease. One week later, multiple purpuric macules and papules (fig. 1) were again noted on the palms and the lower extremities, but repeat skin biopsy was declined. UPEP revealed a kappa spike similar to the previous study. An SPEP demonstrated a monoclonal IgM kappa spike decreased from the previous study and the persistence of cryoprecipitate in the serum. IFE of the cryoprecipitate demonstrated monoclonal IgM kappa similar to that which was found in the serum, but no polyclonal IgG kappa as before. CH50 was mildly decreased. A skin biopsy was then sent for immunofluorescence studies, which revealed abnormal deposits of fibrin in the vessels of the upper dermis and thin deposits of IgG and fibrin at the dermal-epidermal junction. C3, IgM and IgA studies were negative. These findings are consistent with immune-complex vasculitis.

Three cases of paraneoplastic vasculitis associated with renal cell carcinoma have been reported. Andrasch et al. [1] reported cold-induced ischemia, hypergammaglobulinemia (without cryoglobulinemia), and gangrene of the distal phalanges of the fingers in a 63-year-old woman. A skin biopsy from an erythematous area of the upper extremities disclosed mild angiitis. A sarcomatoid renal adenocarcinoma was discovered and following nephrectomy the digital ischemia and hypergammaglobulinemia improved significantly.

Hoag [2] reported 2 cases of vasculitis which failed to demonstrate a cause-and-effect relationship between neoplasm and vasculitis because the renal cell carcinoma was not recognized until autopsy. In 1 case, a 63-year-old man presented with palpable purpura of his forearms, which was found to be leukocytoclastic vasculitis. Autopsy revealed renal cell carcinoma and vasculitis involving skin, lungs and gastrointestinal tract. The second case was a 77-year-old woman with tender nodules along the temporal arteries. Autopsy revealed both a renal cell carcinoma and giant cell arteritis involving the retinal, cerebral, carotid, coronary and mesenteric beds.

Unlike the previously reported cases of renal cell carcinoma and vasculitis, this case was complicated by the additional association of cryoglobulinemia. The vasculitis in our patient was characterized as small vessel and leukocytoclastic. This form of vasculitis is consistent with a polyclonal cryoglobulinemia (monoclonal cryoglobulinemia is more likely to produce thrombotic vasculitis). Many diverse processes have been associated with leukocytoclastic vasculitis including certain infectious, rheumatic, and allergic diseases [3]. Workup of our patient excluded these possibilities.

Greer et al. [4] proposed multiple mechanisms by which malignancy-associated vasculitis might occur. Tumor antigens might serve as sensitizing agents which may in turn provoke host reactions identical to those of classic hypersensitivity vasculitis. Tumors themselves may produce serum proteins which could precipitate in vessel walls, ultimately predisposing to the development of hypersensitivity vasculitis. Tumor antigens may give rise to antigen-antibody complexes which deposit in vessel walls and produce inflammation. That this may have been the case in our patient is supported by the decreased total hemolytic complement, the presence of cryoglobulins, and the finding of fibrin in the dermal vessels and IgG at the dermal-epidermal junction.

There are several traps in the evaluation of leukocytoclastic vasculitis. Malignancy should be suspected in the patient with chronic unexplained or ‘idiopathic’ vasculitis. Microscopic
hemosccuria should not be presumed to be due to vasculitis, but may be secondary to undiagnosedenal cell carcinoma. When vasculitis develops in a patient with an apparently cured malignancy,
tumor recurrence should be suspected. Workup for recurrent tumor is mandatory before immuno-
osuppressive therapy, which could enhance tumor growth, is instituted.

References
Andrasch RH, Bardana EJ Jr, Porter JM, Pirofs-ky B: Digital ischemia and gangrene preceding
Hoag GN: Renal cell carcinoma and vasculitis: Report of two cases. J Surg Oncol 1987;35: 35-
38.
Fauci AS, Haynes BF, Katz P: The spectrum of vasculitis. Clinical, pathologic, immunologic and
Greer JM, Longley S, Edwards L, Elfenbein GJ, Panush RS: Vasculitis associated with
357