

ANCA Negative Vasculitis in Early Gastric Cancer: A Case Report

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Abstract: Crescentic glomerulonephritis associated with malignancy is extremely rare. It can be diagnosed prior to or on follow up of diagnosis of malignancy. Most of these are reported in association with C or P-ANCA. ANCA negative vasculitis in association with malignancy is extremely rare. We report a case of ANCA negative pauci immune crescentic glomerulonephritis associated with early gastric cancer, which showed dramatic response to surgical curative treatment and short duration of immunosuppressant.

Keywords: Crescentic, Glomerulonephritis, Malignancy, Vasculitis

1. INTRODUCTION

Malignant neoplasms are rarely associated with glomerular pathologies. Most commonly reported is membranous glomerulonephritis and other glomerular pathologies such as minimal change disease, Mesangiocapillary glomerulonephritis, IgA Nephropathy, Chronic glomerulonephritis and Amyloidosis are also reported. Paraneoplastic vasculitis as crescentic GN is very rare. ANCA negative vasculitis is extremely rare in that situation.

2. CASE REPORT

69 year old lady, who is hypertensive and diabetic presented with history of polyarthralgia and right ankle arthritis for 1 year. She also had history of reduced appetite, loss of weight and generalized weakness for same duration. No history of abdominal pain, altered bowel habit, GI bleed or jaundice. She underwent endoscopic evaluation 6 months ago, which was normal. Since she was continued to be symptomatic with progressive weight loss and loss of appetite, she was further evaluated with CT imaging of abdomen which showed increased thickening of gastric mucosa. Her urine analysis showed microhematuria and mild proteinuria, but urine culture was sterile repeatedly and urine TB PCR was also negative. USG KUB was normal. Repeat upper GI endoscopy at this time showed 2cm ulcerated area on the antral wall with thickened mucosa (gastric ulcer) and biopsy was reported as poorly differentiated adenocarcinoma with signet ring cells. Her renal

functions were normal at this time with persistent microhematuria and mild proteinuria.

After relevant pre-operative evaluations, she underwent radical D2 subtotal gastrectomy. Operative details showed hard growth in mid body of stomach with no serosa involvement. No evidence of peritoneal tumour deposits/ascites/liver metastasis. Microscopy of surgical specimen also confirmed adenocarcinoma without muscle invasion (stage pT1b N0). She was not offered any chemo considering her tumour staging/age/performance status.

Post-operative period showed deranged renal parameter and persistent fever spikes. No documented intraoperative events like hypotension or nephrotoxic medications. Eventhough she had leucocytosis, and other sepsis markers were normal. Urine routine showed pus cells/RBC, however urine culture was sterile. Urine PC ratio at this time was 1.5. USG KUB repeated didn't reveal any new findings. All cultures were negative. Fluoroscopy did not show any active extravasation or leak. CT abdomen was taken to rule out intra-abdominal collection and it showed normal study except for mild ascites and bilateral mild pleural effusion with basal lung atelectasis. She was treated with broad spectrum antibiotics. Despite all her renal function showed rapidly worsening trend. Serum creatinine became 4 mg/dl from pre-operative value of 0.9mg/dl by one week time.

In view of unexplained renal dysfunction, microscopic haematuria and proteinuria, renal

biopsy was done, which showed 32 glomeruli, 4 obsolescent which are small and sclerotic. Viable glomeruli showed segmental fibrinoid necrosis, breaks in capillary loops with crescents in 27 of them (84.4%, 8 cellular, 17 fibrocellular, 2 fibrous). Tuft appears non proliferative. Tubules showed epithelial vacuolation, simplification and RBC cast in tubules. Tubular atrophy and loss noted in 10% of cortex with surrounding mild interstitial fibrosis. Interstitium reveals diffuse edema and marked inflammatory infiltrate composed of lymphocytes, plasma cells, neutrophils, histiocytes. Interlobular arteries showed fibrinoid necrosis and granulomatous reaction. IF was negative for C3, C4, IgA, IgG and IgM. Biopsy was reported as Pauci Immune Crescentic Glomerulonephritis with acute tubulointerstitial nephritis and vasculitis

involving interlobular arteries and arterioles. Her serological evaluation was negative for C&P ANCA, ANA, Anti GBM antibodies and C3/C4 levels were normal.

She was started on steroid pulsing for 3 days. There were no further episodes of fever spikes. Her general condition improved slowly. IV Steroid was changed to oral steroids. She also received intravenous cyclophosphamide 2 doses 3 weeks apart. Her RFT showed a steadily improving trend. Her steroid was tapered and stopped over a period of 2 to 3 months and no further immunosuppressant was given in the form of CYA or Azathioprine. Her RFT settled with ads. creatinine of 1.6 mg/dl by 2 months time and last follow up after 1 year of surgery revealed as. creatinine of 1.5 mg/dl with no active sediments in urine. Presently she is on regular follow up and RFT is stable.

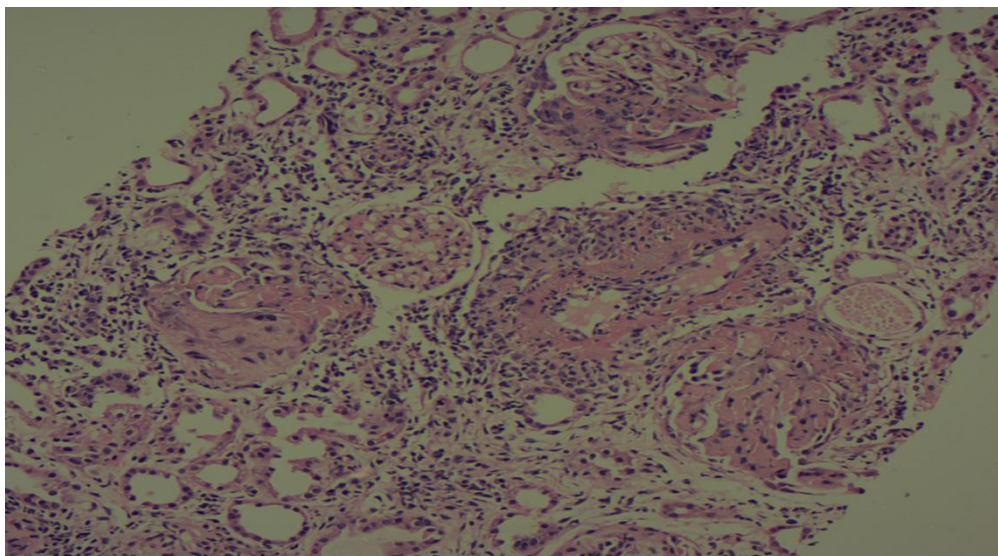


Figure1: H&E stain of renal biopsy specimen showing glomerular crescents with vasculitic changes

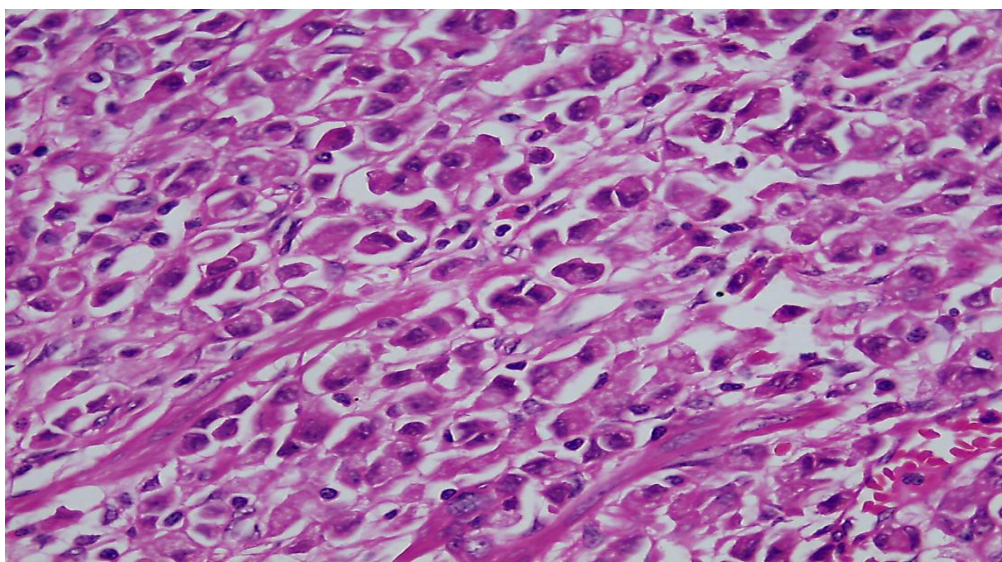


Figure2: Gastrectomy specimen showing adenocarcinoma diffuse type, grade 3 invading submucosa and lymph vascular invasion

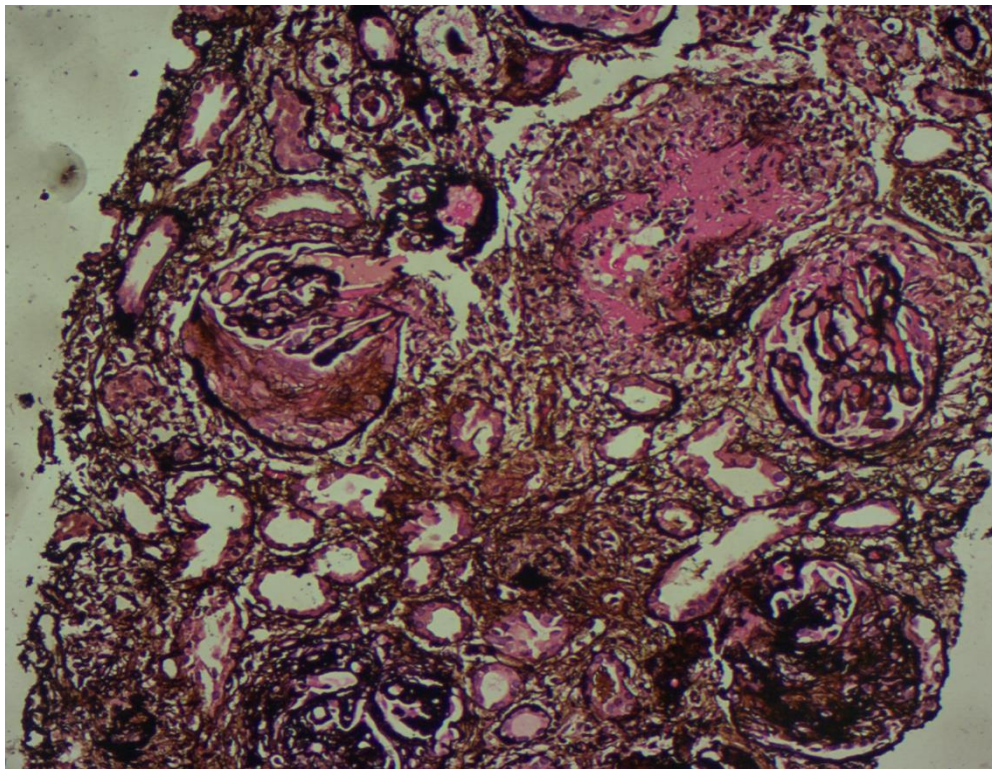


Figure3: Silver staining of renal biopsy specimen showing crescents with fibrinoid necrosis

3. DISCUSSION

Vasculitis can be secondary to infections, drugs, autoimmune diseases and neoplastic conditions. When associated with malignancy, it has been reported to occur before and after diagnosis of malignancy or it can give a clue to recurrence. [1, 2, 3] Overall vasculitis associated malignancy is very rare and malignancies are rare causes of RPGN. The most common clinical vasculitis manifestation associated with malignancy is cutaneous vasculitis, although vasculitis may also affect internal organs. [1, 2] Malignancy may present initially as vasculitis. Five percentages of patients with vasculitis have an occult malignancy, which may not be clinically obvious at the time of presentation. Underlying malignancies found in patients with pauci-immune crescentic glomerulonephritis includes carcinoma prostate, TCC bladder, adenocarcinoma of lungs, occult gastric carcinoma, Myelodysplastic Syndrome, Myeloproliferative disorder and leukemia. Of all solid neoplasm's, bronchogenic carcinoma is the most frequently associated with vasculitis. [2, 3] The path physiology of the two disease processes, malignancy and vasculitis, may be interrelated. Several mechanisms by which tumour-associated vasculitis might occur can be postulated [2, 3] (a) The formation of immune complexes of tumour-associated antigens/antibodies which deposit in vessel walls and produce inflammation; (b) the deposition of

tumour antigens in the vessel wall which allows in situ immune complex formation; (c) direct effects of tumour cells on the endothelium. Also by deregulated T-cell response, elaboration of various cytokines and lack of secreted proteins like uteroglobins from epithelial tumor cells. [4]

Our case is an interesting case with vague symptoms going on for long time with microscopic haematuria, mild proteinuria, normal renal function and rapidly progressive renal failure at the time of diagnosis of adenocarcinoma stomach and in the postoperative period. Whether immunosuppressive regimens should be employed in the treatment of the vasculitis is a matter for discussion, since these drugs have the theoretical risk of provoking malignancy or its dissemination. In our patient, treatment with steroids and 2 doses of cyclophosphamide resulted in rapid renal response within few weeks and then maintained stable renal function despite stopping all immunosuppressive medications. However, the short duration of immunosuppressant didn't cause any harm in malignancy management also. Following removal of the tumour, persistent remission of glomerular pathology favours the possibility of paraneoplastic nephritis. Thus elderly patient with RPGN without evident aetiology; malignant tumour could be kept in mind as underlying possibility. Paraneoplastic vasculitis does not necessarily have bad prognosis. Sanchez Guerrero et al

reported nine out of 11 cases in which vasculitis resolved spontaneously and in the remaining two cases treatment with steroids was successful. [3]

This case has two interesting aspects, one its nature of progression as vague symptoms for long duration with initial negative gastric evaluation and normal renal functions. Second, being ANCA negative. Till now no case reports available with ANCA negative vasculitis in carcinoma stomach. Even though she is started on immunosuppressant, she showed dramatic improvement in renal function within one or two weeks of curative surgical treatment and could be able to taper and stop all immunosuppressants in a short period.

4. CONCLUSION

Vasculitis associated with malignancy is extremely rare. We report the first case of ANCA negative vasculitis in early gastric cancer which is successfully managed with short duration of immunosuppression and surgery and the patient doing well on follow up.

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