# CAPECITABINE INDUCED VASCULITIS MIMICKING IGA VASCULITIS IN A PATIENT WITH CHRONIC HEPATITIS B: A CASE REPORT

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**Abstract**

Capecitabine is a cornerstone of adjuvant therapy for colorectal cancer. While dermatologic toxicities such as hand-foot syndrome are well-recognized, cutaneous small-vessel vasculitis remains an exceptionally rare complication. We present the case of a 59-year-old female with stage II mucinous adenocarcinoma of the colon and concurrent chronic Hepatitis B infection. During her eighth cycle of adjuvant capecitabine and oxaliplatin (CapeOx), she presented with extensive palpable purpura on the extremities and evidence of renal involvement. Histopathology of a skin biopsy confirmed leukocytoclastic vasculitis, and direct immunofluorescence demonstrated IgA and IgM deposition. Sustained viral suppression excluded Hepatitis B reactivation, favoring a drug-induced etiology despite positive autoimmune serology. Discontinuation of the chemotherapy resulted in the complete resolution of both cutaneous and renal manifestations. This case illustrates the diagnostic complexity of distinguishing drug-induced vasculitis from viral etiologies in patients with comorbidities and underscores the need for prompt recognition to prevent systemic organ damage.

**Keywords:** capecitabine, leukocytoclastic vasculitis, IgA vasculitis, colon cancer, drug-induced vasculitis, chemotherapy adverse events.

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## Introduction

Adjuvant chemotherapy with the combination of capecitabine and oxaliplatin (CapeOx) is a cornerstone in the management of high-risk stage II and stage III colon cancer, offering a significant survival benefit over surgery alone.[1,2] Capecitabine, an oral fluoropyrimidine, is generally well-tolerated, with a predictable toxicity profile characterized by diarrhea, stomatitis, and palmar-plantar erythrodysesthesia (hand-foot syndrome).[3] However, cutaneous immune-mediated hypersensitivity reactions remain an infrequent complication of fluoropyrimidine therapy. Leukocytoclastic vasculitis (LCV), also known as hypersensitivity vasculitis, is a histopathologic term denoting angiocentric neutrophilic inflammation with fibrinoid necrosis and nuclear dust. [4] While approximately 50% of LCV cases are idiopathic, the remainder are secondary to infections, connective tissue diseases, malignancies, or medications. Drug-induced LCV accounts for roughly 10–15% of all cases, typically manifesting as palpable purpura on the lower extremities within 7 to 21 days of treatment initiation.[5]

The literature on capecitabine-induced vasculitis is sparse, comprising fewer than 20 isolated case reports worldwide.[6,7] Furthermore, the specific subtype of IgA vasculitis (formerly Henoch-Schoenlein purpura) is predominantly a pediatric condition; its occurrence in adults is rare and often carries a poorer prognosis due to increased risk of renal sequelae. Chemotherapy-induced IgA vasculitis is an even more distinct rarity, posing a significant diagnostic challenge when it arises in patients with confounding comorbidities. We present a complex case of LCV with features of IgA vasculitis appearing late during chemotherapy in a patient with controlled chronic Hepatitis B.

## Case report

A 59-year-old female with a history of hypertension and chronic Hepatitis B infection (HBsAg positive, HBeAg negative) presented with high-risk stage II (pT3N0M0) mucinous adenocarcinoma of the colon. Following a right hemicolectomy, adjuvant chemotherapy was initiated with the CapeOx regimen (capecitabine 2,000 mg/m² and oxaliplatin 130 mg/m²) administered on a 21-day cycle. The patient was maintained on daily Lamivudine for viral suppression and tolerated the first seven cycles well, with no significant adverse events. During the eighth cycle, the clinical course was complicated by the sudden eruption of extensive purpuric lesions on the extremities. Notably, the medications administered had the same trade names as in previous cycles, and no additional medicines were introduced during the eighth chemotherapy course. Physical examination revealed reddish-purple palpable purpura predominantly affecting the bilateral thighs and arms. The lesions were non-blanching and asymptomatic, with the patient reporting neither pain nor pruritus **(Figures 1 and 2).**

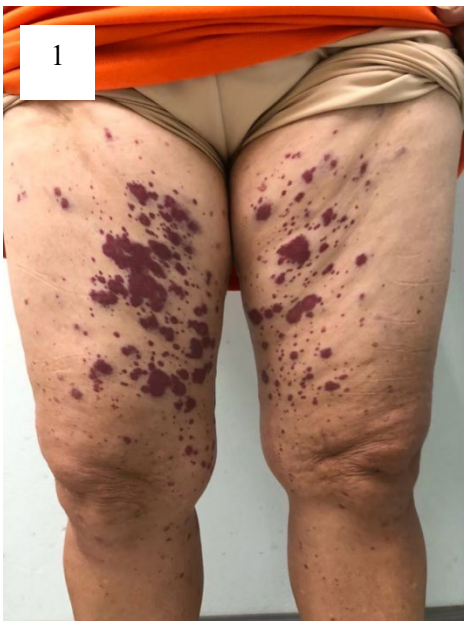
To clarify the etiology, a skin biopsy was performed on the right thigh. Histopathology demonstrated a focal, mild neutrophilic infiltrate within the dermis and subcutaneous fat, accompanied by scattered nuclear dust—classic features of leukocytoclastic vasculitis **(Figure 3).** Direct immunofluorescence revealed mild (1+) vessel wall deposition of IgA and IgM, raising suspicion of IgA vasculitis. A comprehensive serologic workup to exclude systemic mimics revealed a positive ANA (titer 1:80, fine speckled). ANCA, rheumatoid factor, and complement (C3/C4) levels were normal, whereas serum cryoglobulin was positive. Notably, an assessment of her Hepatitis B status confirmed that the viral load remained effectively suppressed (29 IU/mL) on antiviral therapy, ruling out active viral replication or a flare-up as the trigger for the vasculitis **(Table 1).**

Synthesizing the clinical data, the presence of dysmorphic red blood cells in the urinalysis provided critical evidence of renal involvement, consistent with systemic vasculitis. Consequently, the patient was diagnosed with chemotherapy-induced leukocytoclastic vasculitis. Capecitabine was permanently discontinued, resulting in the complete resolution of both the cutaneous lesions and renal abnormalities without the need for systemic corticosteroids or anti-inflammatory agents (e.g., NSAIDs, colchicine). Fortunately, the early cessation of adjuvant therapy did not

**Table 1.** Summary of laboratory investigation results

| Test Name | Initial (Diagnosed Vasculitis) | 3 Months After Holding Capecitabine | Unit |
|---|---|---|---|
| Hemoglobin (Hb) | 11.0 | 11.0 | g/dL |
| Hematocrit (Hct) | 32.9 | 33.0 | % |
| White blood cell Count | 5,200 | 5,800 | cells/μL |
| Neutrophil | 69.0 | 69 | % |
| Lymphocyte | 25.0 | 21 | % |
| Platelet Count | 69,000 | 184,000 | cells/μL |
| ESR | 122 | 68 | mm/hr |
| Antinuclear antibody (ANA) | Positive (Fine speckle 1:80) | - | - |
| Rheumatoid factor (RF) | Negative | - | - |
| c-ANCA (PR3) | Negative (3.1) | - | AU/mL |
| p-ANCA (MPO) | Negative (3.9) | - | AU/mL |
| Creatinine | 0.95 | 1.02 | mg/dL |
| C3 complement | 1.22 | - | g/L |
| C4 complement | 0.24 | - | g/L |
| Cryoglobulin | Positive | - | - |
| BUN | 14 | 20 | mg/dL |
| AST | 44 | 24 | U/L |
| ALT | 19 | 18 | U/L |
| Albumin | 3.8 | 4.3 | g/dL |
| Globulin | 3.5 | 3.8 | g/dL |
| Electrolytes(Na/K/Cl/CO2) | 141 / 4.6 / 104 / 28 | 140 / 4.5 / 102 / 28 | mmol/L |
| Urine analysis | | | |
| Protein/Creatinine Ratio | 1.2 | - | g/dL |
| Appearance | Yellow / Clear | Yellow | - |
| Specific Gravity | 1.015 | 1.006 | - |
| pH | 5.5 | 5.5 | - |
| Albumin | 3+ | Trace | - |
| Blood | 3+ | Negative | - |
| Sugar | Negative | Negative | - |
| Red blood cell | >100 (Dysmorphic) | 2-3 | cell/HPF |
| White blood cell | 10-20 | 0 | cell/HPF |

**ALT (SGPT)**, alanine aminotransferase; **ANCA**, antineutrophil cytoplasmic antibody; **AST**, aspartate aminotransferase; **AU**, arbitrary units; **BUN**, blood urea nitrogen; **Cl**, chloride; CO2, carbon dioxide; **c-ANCA (PR3)**, cytoplasmic antineutrophil cytoplasmic antibody (proteinase 3); **ESR**, erythrocyte sedimentation rate; **HPF**, high power field; **K**, potassium; **Na**, sodium; **p-ANCA (MPO)**, perinuclear antineutrophil cytoplasmic antibody (myeloperoxidase)



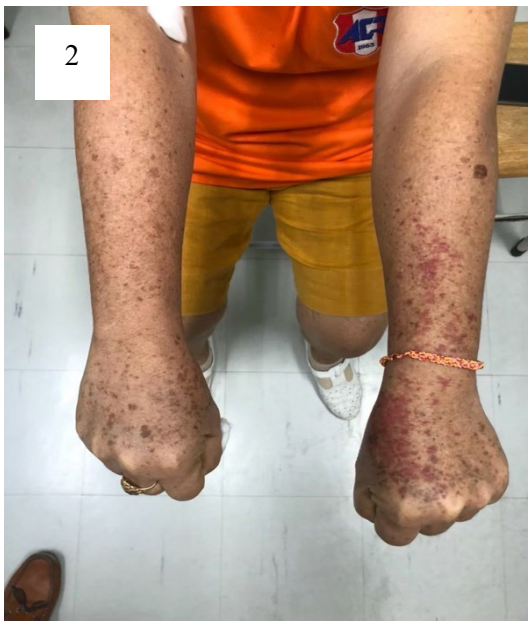




**Figure 1.** Bilateral anterior thighs showing extensive, palpable purpura. Note the coalescing erythematous and violaceous plaques with irregular borders, characteristic of leukocytoclastic vasculitis.
**Figure 2.** Bilateral forearms and dorsal aspect of the hands demonstrating multiple discrete, scattered purpuric macules and papules.

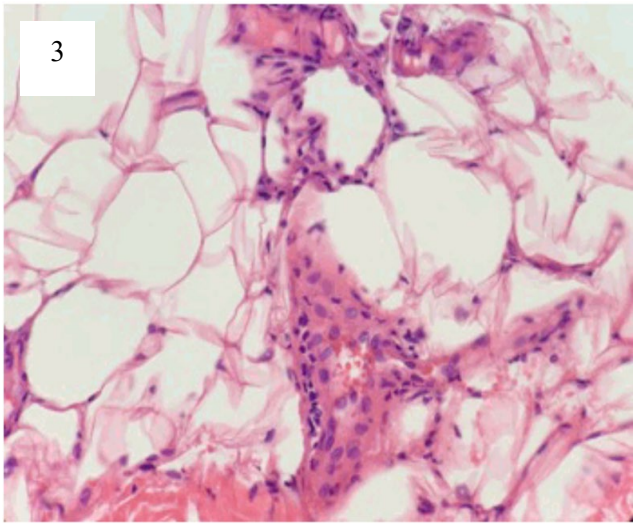



**Figure 3.** Histopathological examination of a skin biopsy (H&E stain, original magnification x400). The section reveals a small vessel in the dermis/subcutis interface surrounded by a dense perivascular inflammatory infiltrate. The infiltrate is predominantly composed of neutrophils with visible nuclear fragmentation (leukocytoclastic) and fibrinoid deposits within the vessel wall, consistent with leukocytoclastic vasculitis.

appear to compromise her oncologic prognosis. Long-term surveillance, including CT and MRI imaging through 2024 and 2025, has consistently demonstrated no evidence of local recurrence or distant metastasis. The patient remains clinically stable with an excellent performance status.

## Discussion

Leukocytoclastic vasculitis (LCV) is a small-vessel cutaneous vasculitis characterized by immune complex deposition, representing a classical type III hypersensitivity reaction.[4] While infections and autoimmune disorders are frequent triggers, pharmaceutical agents are implicated in approximately 10–15% of cases.[8, 9] Capecitabine-induced LCV is exceptionally rare, with fewer than 20 cases reported in the literature.[6] In the presented case, the direct immunofluorescence finding of IgA and IgM deposition strongly points to an immune complex etiology: a drug-induced vasculitis mimicking IgA vasculitis (formerly Henoch-Schoenlein Purpura) with documented renal involvement in

a patient with chronic Hepatitis B.

Mechanistically, it is hypothesized that the chemotherapeutic agents—specifically Capecitabine or Oxaliplatin—function as haptens. These haptens likely bind to serum proteins, forming neoantigens that stimulate antibody production and the formation of immune complexes (containing IgA and IgM).[9] These complexes deposit in the vessel walls, leading to complement activation and subsequent neutrophilic inflammation. The histopathological findings of fibrinoid necrosis and leukocytoclastic (nuclear dust) in our patient are consistent with this mechanism. Notably, the presence of IgA deposition and dysmorphic red blood cells in the urine indicates a systemic presentation resembling IgA vasculitis. This diagnosis is predominantly pediatric and carries a poorer prognosis when arising in adults due to the increased risk of significant renal sequelae.

A major diagnostic challenge in this case was distinguishing drug-induced injury from vasculitis secondary to chronic Hepatitis B infection. Hepatitis B is a well-established cause of secondary vasculitis, including Polyarteritis Nodosa (PAN) and mixed cryoglobulinemia. [10, 11] The patient's initial serology—significant for positive ANA—could have easily led to a misdiagnosis of a viral flare. However, the requisite etiological distinction was made based on the patient's Hepatitis B viral load, which remained effectively suppressed (29 IU/mL) due to concurrent Lamivudine therapy, making a viral-mediated vasculitis flare highly unlikely.

Furthermore, while the presence of IgA on direct immunofluorescence is the diagnostic hallmark of IgA vasculitis,[12] the clinical picture favored a drug-induced etiology. The absence of classic symptoms such as abdominal pain and arthritis, combined with the clear temporal correlation with chemotherapy, distinguished this presentation from idiopathic IgA vasculitis. The Naranjo algorithm supports the causality of capecitabine in this case.[13] First, there was a distinct temporal association; the appearance of lesions during Cycle 8 implies a necessary period of sensitization, a well-recognized phenomenon in drug hypersensitivity. Second, the response to "de-challenge" was positive, as the cutaneous eruption resolved entirely upon discontinuation of the chemotherapy. Finally, alternative etiologies were effectively excluded by the suppressed viral load.

Management of drug-induced vasculitis primarily rests on the withdrawal of the offending agent. The rapid normalization of platelet count, resolution of purpura, and clearance of urinary abnormalities (dysmorphic RBCs and proteinuria) without systemic corticosteroids validated the drug-induced etiology. Finally, this case highlights that the abrupt cessation of adjuvant chemotherapy in the setting of severe immune-mediated toxicity does not necessarily compromise oncologic safety. Despite stopping treatment after the eighth cycle, the patient remains disease-free two years post-diagnosis. Clinicians must remain vigilant for this rare complication, particularly in patients with confounding comorbidities like viral hepatitis, as early recognition and drug withdrawal are critical to preventing irreversible renal damage.

## Conclusion

In conclusion, while capecitabine is a cornerstone of colorectal cancer therapy, clinicians must remain vigilant for rare immune-mediated systemic toxicities. We have presented a unique case of drug-induced IgA vasculitis with renal involvement, clinically complicated by a background of chronic hepatitis B. This case underscores the critical importance of a rigorous differential diagnosis; specifically, the necessity of excluding viral reactivation in patients with comorbid hepatitis before attributing vasculitis to chemotherapy. The prompt recognition of the drug-induced etiology and the subsequent withdrawal of capecitabine prevented permanent renal injury without compromising the patient's oncologic outcome. Ultimately, this case illustrates that in complex clinical scenarios, a multidisciplinary approach integrating oncology, dermatology, and nephrology is essential for safe and effective patient management.

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