International Journal of Research in Medical Sciences
Bajpai RG et al. Int J Res Med Sci. 2024 Jul;12(7):2613-2616
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20241609

Case Report

Rare case of immune mediated cutaneous leucoclastic vasculitis with pancytopenia in a rheumatoid arthritis patient with chronic cytomegalovirus infection

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Received: 18 May 2024
Revised: 03 June 2024
Accepted: 04 June 2024

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ABSTRACT

Acute febrile illnesses with systemic involvement can present significant diagnostic and therapeutic challenges, particularly in patients with multiple comorbidities. This case report highlights a complex presentation of acute febrile illness with pancytopenia and immune-mediated cutaneous vasculitis in a patient with type II diabetes mellitus. A 52-year-old male with a known history of type II diabetes mellitus presented with fever, decreased oral intake, loose stools, oral ulcers, dysphagia, and rashes over the trunk and abdomen for four days. Upon admission to the ICU, extensive diagnostic evaluations were performed, revealing significant hematological, biochemical, and serological abnormalities. Imaging studies and histopathological examinations were conducted to further investigate the underlying etiology. Laboratory findings indicated pancytopenia, acute kidney injury, and hyperkalemia. Infectious disease workup was largely negative, except for a positive CMV IgG. Imaging studies revealed medical renal disease, and a skin punch biopsy confirmed cutaneous leukocytoclastic vasculitis. Bone marrow biopsy suggested bone marrow suppression. Multidisciplinary management, including dialysis, IV fluids, antibiotics, blood transfusions, steroids, and Ganciclovir, led to the patient's gradual improvement and stabilization. The comprehensive diagnostic and therapeutic approach in this case underscores the importance of considering immune-mediated etiologies in patients with atypical presentations. Multidisciplinary collaboration was crucial in managing the multifaceted clinical condition of the patient. Early recognition and prompt multidisciplinary management are essential in similar cases. Extensive diagnostic evaluations should be performed to identify the underlying causes, and immune-mediated etiologies should be considered in complex presentations. Further research is recommended to explore optimal management strategies for such multifaceted conditions.

Keywords: Acute febrile illness, Pancytopenia, Cutaneous vasculitis, Type II diabetes mellitus, Multidisciplinary management

INTRODUCTION

Acute febrile illness with pancytopenia and immune-mediated cutaneous vasculitis represents a complex clinical scenario, especially in patients with type II diabetes mellitus (T2DM). The co-occurrence of these conditions underscores the intricate interplay between metabolic disorders and immune system dysregulation. T2DM is a metabolic disorder characterized by insulin resistance and impaired insulin secretion. When compounded by acute febrile illness, pancytopenia, and cutaneous vasculitis, the management and prognosis become considerably more complex. This introduction explores the implications of these comorbid conditions

and their interrelationships. Pancytopenia, a significant reduction in the number of red cells, white cells, and platelets, can complicate the clinical course in diabetic patients, often exacerbated by acute infections or immune dysregulation. Studies report varying incidences and underlying causes of pancytopenia in T2DM, ranging from direct marrow involvement by infectious agents to autoimmune phenomena where the body's immune system mistakenly attacks its own cells.[1] Cutaneous vasculitis in diabetic patients can be a manifestation of underlying autoimmune conditions or a direct immune response to infections. The skin's involvement in T2DM is multifaceted, often reflecting systemic inflammation or direct immune-mediated damage.[2] T2DM itself can alter immune function, leading to an increased susceptibility to infections and an exaggerated inflammatory response, complicating the course of pancytopenia and vasculitis. The dysregulated immune response in diabetes is thought to contribute to the severity and chronicity of these conditions.[3] The concurrence of acute febrile illness, pancytopenia, and immune-mediated cutaneous vasculitis in a patient with type II diabetes mellitus highlights the critical need for an integrated approach to diagnosis and management. Understanding the underlying mechanisms of these interactions is essential for effective treatment and improved outcomes.

CASE REPORT

Chief complaints

A 52-year-old male presented with fever, decreased oral intake, loose stools, oral ulcers, dysphagia, and rashes over the trunk and abdomen for the past four days. He is a known case of type II diabetes mellitus.

Diagnosis

The patient was diagnosed with acute febrile illness with pancytopenia, immune-mediated cutaneous vasculitis, orosystemic involvement, RA factor positive (43.2 IU/ml), cutaneous leukocytoclastic vasculitis confirmed by skin punch biopsy, acute kidney injury (recovering), anemia, acute symptomatic seizure, and type II diabetes mellitus.

Clinical examination and investigations

Upon admission to the ICU, the patient was febrile but hemodynamically stable. Physical examination revealed non-blanchable purpuric rashes over the trunk and abdomen, oral ulcers, and signs of dehydration.

Blood cultures showed no growth. Serological tests for HIV, HCV, and HBsAg were non-reactive. Urine analysis revealed pus cells (2-3/HPF), LE negative, and amorphous urates. Tests for Widal, Typhidot IgM, malaria, scrub typhus, dengue NS1, IgG, and IgM, and PS for MP were all non-reactive.

Imaging and specialist consultations

Echocardiography showed a normal size LA and LV, no regional wall motion abnormality, LVEF of 60%, grade I diastolic relaxation abnormality, normal RV function, trace tricuspid regurgitation, PASP of 26 mmHg, and no intracardiac clot, vegetation, or pericardial effusion. A chest X-ray showed no significant changes.

Table 1: Initial laboratory investigations.

Parameters	Result
Haemoglobin (g/dl)	8.9
Total leukocyte count (x10^9/l)	0.98
Platelet count (x10^9/l)	55
Total bilirubin (mg/dl)	0.75
SGOT (IU/l)	14
SGPT (IU/l)	17
Alkaline phosphatase (IU/l)	95
Albumin (g/dl)	3.86
Blood urea nitrogen (mg/dl)	66.9
Creatinine (mg/dl)	6.78
Sodium (mEq/l)	142
Potassium (mEq/l)	6.42
LDH (IU/l)	144
CPK (IU/l)	112
CKMB (IU/l)	21
HS trop I (ng/ml)	7.1
Calcium (mg/dl)	8.61
Phosphorus (mg/dl)	3.97
Procalcitonin (ng/ml)	4.36
Vitamin D (ng/ml)	33.50
Vitamin B12 (pg/ml)	642
HBA1C (%)	7.5
Folate (ng/ml)	14.13

An ultrasound of the whole abdomen revealed bilateral kidneys with increased cortical echogenicity and multiple cysts, suggestive of medical renal disease, with normal size and maintained CMD. An ultrasound of the neck was normal. A high-resolution CT scan of the chest was also normal. CMV IgG was positive, while rubella IgM, toxoplasma IgM, HSV 1 & 2, CMV IgM DNA, C-ANCA, and P-ANCA were non-reactive. ANA by IFA was negative, anti-CCP was less than 1.50, and the rheumatoid factor was 43.2 IU/ml.

Management and clinical course

A skin punch biopsy confirmed cutaneous leukocyte-clastic vasculitis. Given the acute kidney injury with hyperkalemia and anuria, nephrology consultation led to the initiation of dialysis. A dialysis catheter was inserted under aseptic precautions, and the first session of dialysis was performed. ENT consultation was obtained for managing oral ulcers. Due to pancytopenia, hematology

consultation recommended bone marrow aspiration and biopsy, performed after informed consent. The differential count showed 0% blasts, 8% neutrophils, 86% lymphocytes, 5% eosinophils, and 1% monocytes. Chromosomal analysis revealed normal cytogenetic results. Bone marrow aspiration showed diluted, paucicellular smears with few lymphomononuclear cells. Comprehensive bone marrow biopsy with special stains and reflex IHC showed hypoplastic marrow with a lymphoplasmacytic population. During a dialysis session, the patient developed a seizure, managed with IV anticonvulsants, and dialysis was temporarily halted. It was resumed the following day. Due to low hemoglobin and platelet counts, the patient received one unit of packed red blood cells and two units of single donor platelets. A rheumatology consultation was obtained due to the elevated rheumatoid factor, and the patient was started on steroids. However, there was no significant response, and a dermatology review led to the initiation of Ganciclovir. The patient was managed with IV fluids, IV antibiotics, and other supportive treatments. Gradually, the patient's condition improved, and he was stabilized and discharged in a stable condition.

DISCUSSION

A 52-year-old male with a known history of T2DM presented with fever, decreased oral intake, loose stools, oral ulcers, dysphagia, and rashes over the trunk and abdomen for four days. Upon admission to the ICU, extensive diagnostic evaluations were initiated to identify the underlying cause of his symptoms. Laboratory findings revealed significant abnormalities. The patient exhibited pancytopenia, with a hemoglobin level of 8.9 g/dl, indicating anemia; a total leukocyte counts of 0.98×10^9/l, indicating leukopenia; and a platelet count of 55×10^9/l, indicating thrombocytopenia. Biochemical tests showed elevated BUN at 66.9 mg/dl and creatinine at 6.78 mg/dl, both indicating acute kidney injury. The patient also had hyperkalemia, with a potassium level of 6.42 mEq/l, and an elevated procalcitonin level of 4.36 ng/ml, suggesting a possible infection or sepsis. The infectious disease workup was largely negative, with no growth in blood cultures and non-reactive results for HIV, HCV, and HBsAg. However, the patient was positive for CMV IgG, indicating a past infection. Other serologies, including Rubella IgM, Toxoplasma IgM, HSV, and CMV IgM, were non-reactive, ruling out active infections.

Imaging studies provided additional insights. The echocardiogram showed normal left ventricular size and function, with a LVEF of 60% and trace tricuspid regurgitation. Ultrasound of the whole abdomen revealed increased cortical echogenicity in the kidneys with multiple cysts, suggestive of medical renal disease. HRCT of the chest was normal. Histopathological examination was crucial in confirming the diagnosis. A skin punch biopsy was consistent with cutaneous leukocytoclastic vasculitis, indicating an immune-mediated process. Bone marrow aspiration and biopsy showed hypoplastic marrow with a lymphoplasmacytic population, suggesting bone marrow suppression or failure, possibly related to the underlying vasculitic process or another systemic condition. The patient was managed with a multidisciplinary approach involving dermatology, nephrology, ENT, and hematology consultations. He received dialysis due to renal failure and supportive care, including intravenous fluids, antibiotics, and blood transfusions. Despite initial treatment with steroids, there was no significant improvement in rashes and oral ulcers, leading to the initiation of Ganciclovir based on dermatology recommendations. Over time, the patient showed gradual clinical improvement and was eventually stabilized and discharged in a stable condition. The case underscores the complexity of diagnosing and managing acute febrile illness with systemic involvement in patients with multiple comorbidities. The comprehensive diagnostic and therapeutic approach, along with timely specialist consultations, was pivotal in the successful management of this patient. This case highlights the importance of considering immune-mediated etiologies in atypical presentations and the necessity of comprehensive, collaborative medical care in managing multifaceted clinical conditions.

A study by Reem et al presented cases of two patients with a history of RA treated with methotrexate who developed generalized leukocytoclastic vasculitis (LCV) with pancytopenia following a viral infection.[4] The findings underscore the complexities of managing RA with immunosuppressive therapies, especially during periods of increased vulnerability to infections, such as during the COVID-19 pandemic. The study raises important considerations regarding the monitoring and potential adjustment of immunosuppressive therapy during viral outbreaks to prevent severe complications.[4] A detailed examination of a patient initially presenting with cutaneous vasculitis and psoriasis, who later developed pancytopenia and was diagnosed with polyarteritis nodosa. This case emphasizes the diagnostic challenges posed by the overlapping symptoms of various immune-mediated conditions and the critical need for comprehensive evaluation to accurately diagnose and manage such complex cases.[5] Another study discussed a patient with RA who developed pancytopenia as a complication of methotrexate therapy and subsequently faced serious infections including Pneumocystis jirovecii pneumonia and cytomegalovirus colitis. The complications were linked to immune reconstitution inflammatory syndrome following the recovery from leukopenia. This case highlights the potential risks of immunosuppression in RA, stressing the importance of careful monitoring and possibly preemptive measures during immunosuppressive therapy.[6] A report covered the reactivation of cytomegalovirus in a patient with refractory rheumatoid vasculitis, considered a manifestation of immune reconstitution inflammatory syndrome (IRIS). It discusses the impact of adjusting

immunosuppressive therapy on the course of both vasculitis and viral reactivation. The study suggests that changes in immunosuppressive therapy can prompt significant shifts in patient condition, necessitating vigilant monitoring and flexible treatment strategies to manage both RA and opportunistic infections.[7]

CONCLUSION

The case exemplifies the complexity of diagnosing and managing acute febrile illness with pancytopenia and immune-mediated cutaneous vasculitis in a patient with type II diabetes mellitus. The interdisciplinary approach, involving extensive diagnostic investigations and timely specialist consultations, was crucial for the successful management and stabilization of the patient. The case underscores the importance of considering immune-mediated etiologies in atypical presentations and highlights the necessity of comprehensive, collaborative medical care in managing multifaceted clinical conditions.

ACKNOWLEDGEMENTS

Authors are thankful to the patients; without them the study could not have been done. Authors are thankful to the supporting staff of hospital who were involved in patient care.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Bajpai RG, Garg A. Rare case of immune mediated cutaneous leucoclastic vasculitis with pancytopenia in a rheumatoid arthritis patient with chronic cytomegalovirus infection. Int J Res Med Sci 2024;12:2613-6.