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CASE STUDY

GLIMEPIRIDE-INDUCED LEUKOCYTOCLASTIC VASCULITIS: A RARE CASE REPORT AND INSIGHT OF THE 1990 ACR CRITERIA FOR THE DIAGNOSIS OF LEUKOCYTOCLASTIC VASCULITIS

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ABSTRACT: Cutaneous drug-induced leukocytoclastic vasculitis accounts for about 10% of all vasculitis cases and usually presents as skin lesions in a palpable purpuric form that likely begins within two weeks after exposure to a particular agent. The use of glimepiride has recently increased with the sharp augmentation of poorly-controlled diabetes mellitus cases, and hence, recognition of this reaction is important as it may lead to fatal consequences, and discontinuation of the offending drug is a cornerstone of the management. To the best of our knowledge, this is the first reported case of Glimepiride-induced leukocytoclastic vasculitis from the Eastern Part of India.

Keywords: Diabetes, Glimepiride, Leukocytoclastic vasculitis

INTRODUCTION:

Diabetes mellitus has been becoming more common as a result of poor eating habits and sedentary lifestyles. In order to treat diabetes mellitus, a large range of oral hypoglycemic agents have lately become accessible. Sulfonylureas are the oldest class of oral antidiabetic medication dating back to the 1950s [1]. Drugs in the sulfonylurea family work by depolarizing the ATP-sensitive potassium channels on the pancreatic beta cells, which stimulates insulin secretion from the pancreatic beta cells [2].

There has been debate on the effectiveness of sulphonylureas in the current long-term management of Type-2 Diabetes Mellitus, who are at high risk of hypoglycaemia, heart failure and/or renal insufficiency. The potential benefits of an oral hypoglycemic agent must be carefully weighed against the risk of developing hazardous adverse effects.

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Leukocytoclastic vasculitis (LCV) is seldom caused by sulfonylureas, but clinical recognition of this reaction is very important because continued use of the culprit drug may lead to fatal consequences. We detail a more peculiar presentation of biopsy-proven LCV in this clinico-pathological case report that was brought on by glimepiride, a second-generation sulfonylurea.

To the best of our knowledge, this is the first reported case of Glimepiride-induced leukocytoclastic vasculitis from the Eastern Part of India.

CASE REPORT:

A 58-year-old female with a decade long history of hypertension treated by Cilnidipine 10 mg daily and a year long history of Type-2 Diabetes Mellitus that was initially treated with diet and metformin by a primary care physician, presented to the out-patient clinic with deranged glycemic profile. She was initiated with glimepiride 1 mg before lunch. Within 43 days after starting glimepiride, the patient presented with non-pruritic eruptions on her legs. The rash first emerged on the neck and abdomen and then appeared on the lower extremities within 3 days. The eruptions also involved the upper extremities with no facial puffiness, tongue swelling, hoarseness of voice, difficulty breathing, or change in her mental status. There was no history of fever or decreased food intake. The patient had been taking a normal diet, appropriate for culture and locality. She denied the use of illicit drugs, sexual risk behavior and the consumption of any other type of medication except her prescribed ones. Physical examination revealed palpable erythematous papules on both lower limbs.

There were no physical signs suggesting clinical evidence of connective tissue or other systemic disease. No mucosal lesions were detected. Otherwise, her systemic examination was unremarkable. There was no reported patient or family history of autoimmune diseases.

Initial laboratory workup revealed leucocytosis (white blood cell count, 22.3×10^9/L). Prothrombin time and partial thromboplastin time were normal. Acute phase reactants and results of kidney and liver function tests were within normal range. Results of additional workup, including tests for antinuclear antibody, antineutrophil cytoplasmic antibodies, rheumatoid factor, herpes simplex virus, hepatitis B and C serology, complement levels and serum protein electrophoresis were within normal limits. Urinalysis was negative for hematuria and proteinuria.

Drug-induced leukocytoclastic vasculitis was suspected and glimepiride was stopped. She underwent a skin biopsy from left leg which revealed superficial perivascular inflammatory infiltrate composed of neutrophils with frequent eosinophils, few fragmented neutrophils, nuclear dust and prominent vascular damage evidenced by the presence of endothelial injury and extravasated red blood cells, suggestive of leukocytoclastic vasculitis. No evidence of fibrosis, giant cell or granuloma formation appreciated.

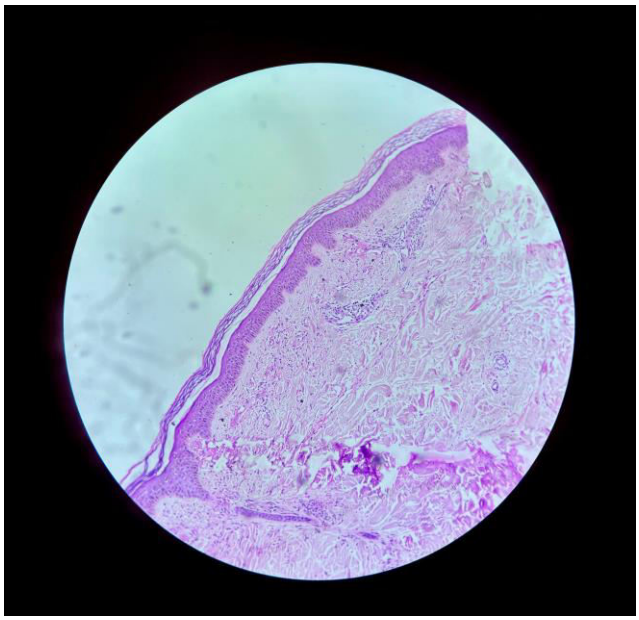

Image 1: Histopathological examination of the skin punch biopsy (Hematoxylin-eosin stain; 10x) showing perivascular inflammation in the papillary dermis.

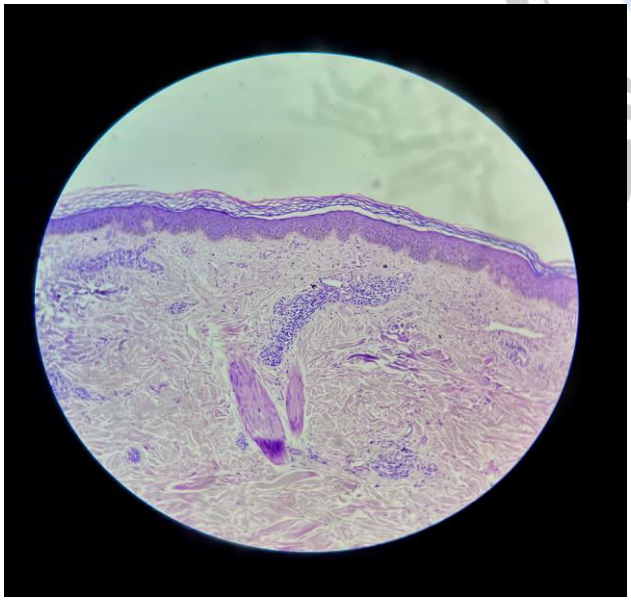

Image 2: Histopathological examination of the skin punch biopsy (Hematoxylin-eosin stain; 10x) showing perivascular inflammation with infiltration of lymphocytes and neutrophils.

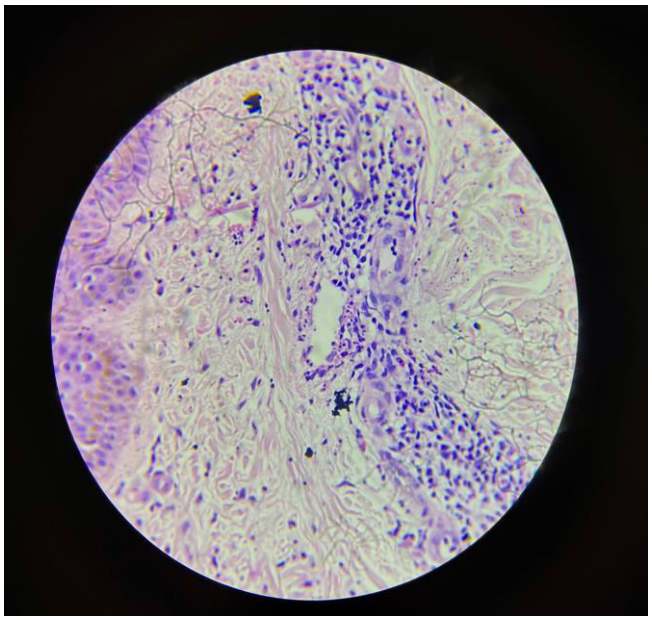

Image 3: Histopathological examination of the skin punch biopsy (Hematoxylin-eosin stain; 40x) showing perivascular inflammation with endothelial swelling and nuclear dust deposition.

The American College of Rheumatology (ACR) proposed criteria [3] to define LCV includes age > 16 at disease onset, history of taking a medication at onset that may have been a precipitating factor, the presence of palpable purpura, the presence of maculopapular rash, and a biopsy demonstrating granulocytes around an arteriole or venule. The presence of 3 or more of these 5 criteria was associated with a sensitivity of 71.0% and a specificity of 83.9% [3]. The patient in our case report scored 5 out of 5, which favours the diagnosis of LCV.

Table 1: ACR proposed criteria (1990) to define leukocytoclastic vasculitis / hypersensitivity vasculitis [3]

Criteria	Definition
Age at disease onset >16 years	Development of symptoms after age 16
Medication at disease onset	Medication was taken at the onset of symptoms that may have been a precipitating factor
Palpable purpura	Slightly elevated purpuric rash over one or more areas of the skin; does not blanch with pressure and is not related to thrombocytopenia
Maculopapular rash	Flat and raised lesions of various sizes over one or more areas of the skin
Biopsy including arteriole and venule	Histologic changes showing granulocytes in a perivascular or extravascular location

According to the Naranjo probability scale [4], ACR proposed criteria [3] & histopathological impression of the skin-punch biopsy, glimepiride-induced leukocytoclastic vasculitis was confirmed.

All lesions resolved spontaneously within 5 days and the patient had no further episodes of skin eruption over a follow-up period of 3 months. She was initiated with Sitagliptin 50 mg and her glycaemic profile was well controlled by sitagliptin and metformin.

DISCUSSION:

In 1995, the FDA approved glimepiride, a second-generation sulfonylurea, for use in improving glycemic control in individuals with type 2 diabetes [5,6]. When used in combination therapy with metformin, it can be used as a second-line medication to treat type 2 diabetes mellitus in individuals who do not have atherosclerotic cardiovascular disease and whose hemoglobin A1c is below their goal level [6]. Notably, the FDA has only authorized glimepiride as a sulfonylurea for use in combination therapy with insulin in patients who do not respond to combination therapy. Glimepiride is thought to preserve myocardial preconditioning by preferentially blocking sarcolemmal ATP-dependent potassium channels in cardiac myocytes as opposed to mitochondrial potassium channels [7].

Leukocytoclastic vasculitis is a small vessel vasculitis that is histologically typified by immune complex-mediated vasculitis of the venules and dermal capillaries [8,9]. Usually limited to the skin, cutaneous LCV seldom manifests as extracutaneous lesions in fewer than one-third of patients [8]. Palpable purpura, lower extremity localization, and tiny vessel involvement are important clinical characteristics of LCV [8].

Up to 50% of LCV patients are idiopathic [10]. Secondary LCV is most frequently caused by infections (such as *Chlamydia*, *Mycobacterium*) and medications (such as vancomycin, thiazides, allopurinol) [10,11]. A number of medications have been linked to leukocytoclastic vasculitis. However, glimepiride induced LCV is an extremely rare clinical entity and a limited number of cases have been

reported worldwide. The onset usually occurs one to three weeks after initiating the medication [10,11]. Once clinical suspicion of leukocytoclastic vasculitis arises, a punch biopsy should be performed and complete blood counts, liver function test and renal function tests along with urinalysis are recommended. If the physician suspects systemic involvement, a more extensive workup needs to be performed. A histopathological analysis is essential to confirm LCV and to rule out medium and large vessel vasculitis and other cutaneous vasculitis.

Most cases of idiopathic cutaneous LCV are mild and resolve with supportive measures such as leg elevation, rest, compression stockings, and antihistamines [10]. In more chronic or resistant cases, a 4-6 week tapering dose of corticosteroids can be used. If an offending drug has been identified, withdrawal of the drug is crucial in the resolution of the vasculitis.

Consent

Patient data were de-identified and verbal informed consent to publish the case was obtained from the patient.

Authors' contributions

SC and PM were responsible for drafting the manuscript and the literature search. SC was responsible for diagnosis of the case. PM and BD both made critical revisions to the manuscript. All authors have read and approved the final manuscript.

REFERENCES:

[1]. Genuth S. Should sulfonylureas remain an acceptable first-line add-on to metformin therapy in patients with type 2 diabetes? No, it's time to move on! Diabetes Care. 2015;38,1:170-5.

[2]. Proks P, Reimann F, Green N, Gribble F, Ashcroft F. Sulfonylurea stimulation of insulin secretion. Diabetes. 2002;51 Suppl 3: S368-76.

[3]. Calabrese, L.H., Michel, B.A., Bloch, D.A., Arend, W.P., Edworthy, S.M., Fauci, A.S., Fries, J.F., Hunder, G.G., Leavitt, R.Y., Lie, J.T., Lightfoot, R.W., Jr, Masi, A.T., McShane, D.J., Mills, J.A., Stevens, M.B., Wallace, S.L. and Zvaifler, N.J. (1990), The American College of Rheumatology 1990 criteria for the classification of hypersensitivity vasculitis. Arthritis & Rheumatism, 33: 1108-1113.

[4]. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, Janecek E, Domecq C, Greenblatt DJ. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther. 1981; 30:239–45.

[5]. Basit A, Riaz M, Fawwad A. Glimepiride: evidence-based facts, trends, and observations (GIFTS). [corrected]. Vasc Health Risk Manag. 2012; 8:463-72. Erratum in: Vasc Health Risk Manag. 2013; 9:1.

[6]. Trerattanavong K, Tadi P. Glimepiride. [Updated 2023 Jul 4]. In: StatPearls [Internet].

[7]. Mocanu MM, Maddock HL, Baxter GF, Lawrence CL, Standen NB, Yellon DM. Glimepiride, a novel sulfonylurea, does not abolish myocardial protection afforded by either ischemic preconditioning or diazoxide. Circulation. 2001 ;103,25:3111-6.

[8]. Baigrie D, Crane JS. Leukocytoclastic Vasculitis. [Updated 2023 Aug 8]. In: StatPearls [Internet].

[9]. Carlson JA (2010) The histological assessment of cutaneous vas- culitis. Histopathology 56.1:3–23

[10]. Fraticelli P, Benfaremo D, Gabrielli A. Diagnosis and management of leukocytoclastic vasculitis. Intern Emerg Med. 2021;16,4:831-841.

[11]. Bouiller K, Audia S, Devilliers H, Collet E, Aubriot MH, Leguy-Seguin V, et al. Etiologies and prognostic factors of leukocytoclastic vasculitis with skin involvement: a retrospective study in 112 patients. Med (United States) 2016;95,28: e4238.

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