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REVERSIBLE RENAL FAILURE IN 88 YEAR OLD FEMALE -PPI THE CULPRIT

Medicine

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ABSTRACT

Granulomatous interstitial nephritis (GIN) is rare entity detected in 0.5-0.9 % of renal biopsies and a proton-pump inhibitor-induced GIN is infrequent. Our patient, a 80-year-old female (2019), on antihypertensive with normal renal function, after 30 days of rabeprazole presented with raised serum creatinine (6.5mg/dl), biopsy revealed GIN, workup for secondary causes were negative, on detailed inquiry, the patient was receiving rabeprazole for the last 1 month on the prescription of her primary physician for dyspeptic symptoms. On stopping rabeprazole, serum creatinine reduced to baseline (1 mg/dl) at 15 days, confirming the diagnosis of rabeprazole-induced GIN.

KEYWORDS

Transitional Cell Carcinoma, Urinary Bladder, Cd 34, Microvessel Density

BACKGROUND

Granulomatous interstitial nephritis (GIN) is a form of chronic inflammation, characterized by the formation of granuloma within the affected tissue with giant cells,macrophages, and monocytes. Less than 1% of the kidney biopsies reveal GIN.[1] Causes are predominantly drugs followed by infections, autoimmune diseases, foreign body reaction, and rarely idiopathic.[2] GIN can occur even in an immune deficiency state. However, it is seldom reported in patients on proton pump inhibitors. As a class of drugs , proton pump inhibitors (PPI) have reported side effects, however they have been implicated in several case reports in the etiology of GIN and mechanism is predominantly immune mediated. Here, we present a case of proton-pump inhibitor (PPI)-induced GIN in a patient, which successfully resolved to stopping the offending drug.

Granulomatous interstitial nephritis (GIN) is rare entity detected in 0.5-0.9 % of renal biopsies and a proton-pump inhibitor-induced GIN is infrequent. Our patient, a 80-year-old female (2019), on antihyp ertensive with normal renal function, after 30 days of rabeprazole presented with raised serum creatinine (6.5mg/dl), biopsy revealed GIN, workup for secondary causes were negative, on detailed inquiry, the patient was receiving rabeprazole for the last 1 month on the prescription of her primary physician for dyspeptic symptoms. On stopping rabeprazole, serum creatinine reduced to baseline (1 mg/dl) at 15 days, confirming the diagnosis of rabeprazole-induced GIN.

CASE PRESENTATION

A 80-year-old with hypertension and mature cyst in ovary . Baseline creatinine was 1.2 mg/dl, on amlodipine and telmisartan .She was doing fine till february 2019, when she presented to her primary physician with complaints of epigastric burning sensation and belching, on the clinical diagnosis of gastritis, rabeprazole 20 mg once daily was commenced. One month of therapy, she presented to us with a rising serum creatinine from 1.2 mg/dl to 6mg/dl , urine routine revealed no albuminuria , erythrocyturia, or leukocyturia. The patient underwent a renal biopsy which showed four glomeruli, all being normal.Interstitium revealed multiple nonnecrotizing granulomas with surrounding inflammation and giant cell reaction [Figure 1], and the Ziehl–Neelson stain for acid-fast bacilli (AFB) was negative. No evidence of viral inclusions including cytomegalovirus (CMV), polyomavirus, and adenovirus.The biopsy was suggestive of GIN. Urine for AFB and the polymerase chain reaction for *Mycobacterium tuberculosis*, polyomavirus, CMV, and Epstein–Barr virus were negative. Serum calcium (9.2 mg/dl) and angiotensin-converting enzyme levels (36 mcl) were normal, computed tomography of the chest and abdomen was not contributory. After ruling out other causes, we kept the possibility of rabeprazole-induced GIN, and the PPI was changed to the H2 blocker (Ranitidine) over a period of 15 days, her creatinine returned to the baseline of 1 mg/dl without steroid therapy.

DISCUSSION

In the current manuscript, we report the successful management of rabeprazole -induced GIN in a old female .The incidence of PPI induced GIN is around 0.3%. [3] There may be an underestimate of GIN because of difference in frequency of kidney involvement in systemic granulomatous disease, indications of biopsy and sampling error. In native kidney biopsies, the major causes for GIN in the developing countries are predominantly of infectious origin; tuberculosis is the leading cause among infections followed by fungal infection, other reasons are drug-induced; systemic diseases such as sarcoidosis, antineutrophil cytoplasmic antibodies-associated vasculitis, and tubulointerstitial nephritis with uveitis. Similar to the native kidney, infection remains the leading cause of GIN [4]. However, the presence of granuloma with giant cell reaction in interstitium suggests GIN. Fungal, mycobacterial infection,[3] and systemic disease like sarcoidosis[3] are the usual suspects. Farris *et al*.[4] reported drug-induced GIN in five patients, of the five cases,two were due to co-trimoxazole and one each because of dapsone, foscarnet, and omeprazole/acyclovir. In the index case, all the infec tious workup were negative, and there was no evidence to support systemic disease, and regarding the drugs, she was on antihypertensive drugs amlodipine and telmisartan and additional PPI (rabeprazole) for dyspeptic symptoms for the last 1 month. PPIs are well-known cause of acute interstitial nephritis in native kidneys,[4] and are not class specific. Nadri and Althaf[4] also reported a case omeprazole-induced GIN in native kidneys. Even though drug-induced GIN is rare, the possibility of PPI-induced GIN was considered and rabeprazole was stopped. The casual relationship was established as the serum creatinine returned to baseline, 2 weeks after discontinuing the drug without the use of any steroids.To conclude, our report highlights PPI as a potential cause of GIN , and cautious approach needs to be inculcated for routine use of PPIs in the older patients .

CONCLUSION
LEARNING POINTS

1. Detailed history and inquiry regarding drug intake, provide an important clue to diagnosis of unusual cause of allograft dysfunction
2. One should be very cautious while using PPI even in renal transplant patients.

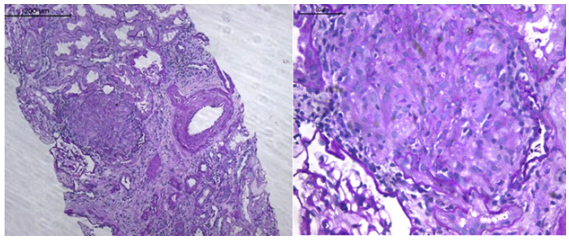

Figure 1: (Right) A nonnecrotizing epithelioid cell granuloma with surrounding mononuclear inflammation along with normal glomeruli and tubules (×20, Periodic acid–Schiff stain). (Left) Granuloma showing epithelioid cells, no central caseation is seen and is surrounded by dense lymphocytic infiltrate (×40, Periodic acid–Schiff stain)

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