Journal of Advanced Research in Medicine
Volume 6, Issue 4 - 2019, Pg. No. 10-12
Peer Reviewed & Open Access Journal

Case Report

Terlipressin Induced Skin Ischemia: A Case Report

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DOI: https://doi.org/10.24321/2349.7181.201918

I N F O

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How to cite this article:
Kumar N, Bohania N, Kumar S. Terlipressin Induced Skin Ischemia: A Case Report. *J Adv Res Med* 2019; 6(4): 10-12.

Date of Submission: 2020-03-24
Date of Acceptance: 2020-04-02

A B S T R A C T

Terlipressin is a synthetic vasopressin analogue used in the treatment of cirrhotic patients with variceal bleeding and hepatorenal syndrome. Side effects associated with terlipressin are usually mild but some rare serious complications can also be seen. Terlipressin induced skin ischemia is one such serious complication. We report a case of 57-year-old lady, a case of chronic alcoholic liver disease presented with variceal bleeding. Patient was given bolus injection terlipressin every 4 hour and patient developed skin ischemia within 48 hours of terlipressin administration. Skin ischemic changes showed marked improvement after stoppage of terlipressin. Treating clinicians should be more vigilant about this rare adverse effect of terlipressin. Early recognition and treatment of the ischemic skin complication gives a better outcome.

Keywords: Terlipressin, Vasopressin Analogue, Hepatorenal Syndrome, Skin Ischemia

Introduction

Terlipressin is a synthetic vasopressin analogue used for the treatment of acute variceal bleeding. It is a nonselective V1 vasopressin agonist. Terlipressin induced skin ischemia is one of the rare side effects of terlipressin. Here, we report a case of 57-year-old lady, case of chronic alcoholic liver disease presented with variceal bleeding. She was treated with terlipressin and developed skin necrosis.

Case Report

A 57-year-old lady presented to medical emergency with history of two episodes of hematemesis in last five hours. Patient was apparently well 8 months back, when she developed mild fatigue for last eight months. She didn't seek any medical attention for her fatigue. Now, she presented with two episodes of passage of frank blood in vomitus (around 200 ml blood in each episode). Patient had a history of alcohol consumption, 30 gm of alcohol per day for last 15 years. There was no past history of jaundice or bleeding manifestations. There was no history of fever. On examination, patient's blood pressure was 110/72 mmHg. Pulse rate was 110/min, regular and low volume. On general physical examination, there was no pallor, icterus, pedal edema or any other significant finding apart from mild bilateral parotid enlargement. She was afebrile. All peripheral pulses were palpable. Per abdomen examination revealed normal shape, central and inverted umbilicus and no visible veins over abdomen. Liver span was 11 cm and spleen was enlarged on percussion but spleen was not palpable beyond the costal margin. Shifting dullness was present. Blood investigations (Table 1) showed normocytic normochromic anaemia with mild transaminitis. On further investigations, patient was found to have features of

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chronic liver disease with portal hypertension with grade 2 oesophageal varices. Her HIV, HBsAg, Anti HCV was nonreactive. 2D echo done was normal in this patient. Patient was started on pantoprazole infusion along with injection terlipressin 1 mg iv every 4 hours. Patient didn't have any further episode of hematemesis, although she had melena which persisted for next two days. On day 2, she developed ischemic changes in bilateral lower limbs as shown in Figure 1. Analysing the temporal relationship with administration of terlipressin and development of ischemic necrosis it was suspected that terlipressin is the culprit agent and it was stopped. On day 3, patient underwent upper GI endoscopy and band ligation of varices was done. After stopping terlipressin there was marked improvement in ischemic lesions over 2-3 days. Skin lesions gradually improved and the patient was discharged on day 8 with full functional recovery of bilateral lower limbs. Patient was then told to follow up in Gastroenterology department for management of chronic liver disease and also to follow up in deaddiction clinic for alcohol deaddiction.

Table 1.Laboratory Investigations of the Patient

Parameters	Results	Normal range
Haemoglobin (gm/dl)	10.4	12-15
Total leukocyte count (cells/µL)	6180	4000-11000
Platelet count (cells/mm^3)	159,000	150,000-400,000
Blood Urea (mg/dl)	43	15-40
Serum Creatinine (mg/dl)	1.0	0.6-1.1
Total bilirubin (mg/dl)	0.6	0.2-1.1
AST /ALT (U/L)	116 /122	<50
Alkaline Phosphatase (U/L)	140	45-130
Total protein (gm/dl)	6.2	5.7-8.2
Serum albumin (gm/dl)	3.4	3.5-5.5
Serum Ca^{2+} (mg/dl)	10.1	8.8-10.6
Serum phosphorus (mg/dl)	3.9	2.3-4.0
ANA by IF, SLA, anti-LKM-1	Negative	
HIV, HBsAg, Anti HCV	Negative	
Chest X-ray	Normal study	
INR	1.1	<1.3
USG Abdomen	Liver 10 cm in size with coarsened echotexture; spleen 12.5 cm in size; portal vein-13 mm; multiple collaterals seen; moderate free fluid present	
UGI endoscopy	Grade II varices seen	
Urine routine	Normal	
Peripheral smear	Normocytic normochromic anaemia	
Ascitic fluid analysis	SAAG: 1.3; Cells: 90 (80% lymphocytes)	
Urinary copper levels (ug/24 hr)	43	20-50
Doppler Upper limbs	Normal study	

ISSN: 2349-7181
DOI: https://doi.org/10.24321/2349.7181.201918

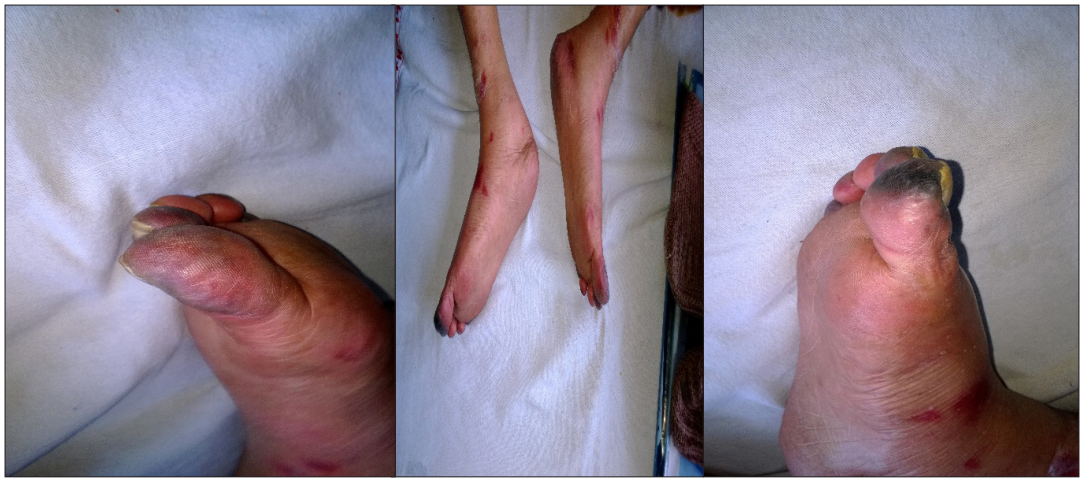

Figure 1.Bilateral lower limbs showing terlipressin induced ischemic skin changes

Discussion

Terlipressin is a synthetic long-acting vasopressin analogue (vasopressin-1 receptors) used in the treatment of cirrhotic patients with variceal bleeding and hepatorenal syndrome. Vasopressin is a potent splanchnic vasoconstrictor. Side effects associated with terlipressin are usually mild and include headache, abdominal pain, pallor, bradycardia and hypertension. Serious complications like ischemic colitis, myocardial infarction and skin necrosis are rare with terlipressin.[1,2,3]

Majority of cases of skin necrosis with terlipressin affected the extremities but there are also cases of involvement of trunk, foreskin and scrotal necrosis in male. Skin necrosis and ischemia may also be caused by other factors like primary skin disorders, atypical infections and coagulation abnormalities. However, in the present case blood culture and other haematological tests did not reveal any other abnormality. Conditions like severe atherosclerosis, vasculitis, infective endocarditis, septic emboli can also cause this kind of peripheral ischemic skin changes but our patient didn't have any of these conditions. It has also been observed that local necrotic complications are more commonly observed if it has been given as continuous infusion rather than bolus administration. Other predisposing factors for terlipressin induced skin ischemia are hypovolemia, concomitant use of other vasopressors, ischemic heart disease and spontaneous bacterial peritonitis.[3,4,5,6]

Apart from terlipressin, other drugs (noradrenaline, midodrine, excessive diuretic use causing hypotension) used in treatment of chronic liver disease related complications like Hepatorenal Syndrome (HRS), can cause peripheral skin ischemia. But in our patient, except terlipressin, none of the above mentioned drugs were used and blood pressure of the patient always remained within normal range. Incidence of terlipressin induced skin necrosis is very rare, although exact incidence is not known. In all the above mentioned reports of terlipressin induced skin ischemia, most of the cases developed ischemic skin changes over 2-3 days, similar was the scenario in our case. In a review article published in 2018, authors could find only 33 cases of terlipressin induced ischemia after extensive literature search.[7]

Conclusion

Early recognition and treatment of the ischemic skin complication caused by terlipressin might give a better outcome. For administering terlipressin bolus IV mode should be preferred over continuous infusion.

Conflicts of Interest: None

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ISSN: 2349-7181
DOI: https://doi.org/10.24321/2349.7181.201918