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Original research article

Coronary vasospasm: A rare side effect of tacrolimus in post kidney transplant recipient

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Abstract

Tacrolimus, cornerstone of immunosuppression in post kidney transplant can rarely cause coronary vasospasm.

Vasospastic angina might be induced by medications, most commonly with cocaine and other examples which include catecholamines such as epinephrine, norepinephrine, isoproterenol, dopamine, and dobutamine. Parasympathomimetic agents include acetylcholine, methacholine, and pilocarpine. It is rarely caused by tacrolimus. The clinical evaluation includes an electrocardiogram and echocardiogram. The confirmed di- agnosis is done by coronary angiography. Cardiac catheterization is indicated in such cases to rule out coronary artery disease.

24 year old male patient with typical ECG changes and raised cardiac marker on Tacrolimus underwent thalium scan which shows non transmural infarct. Patient was treated with by calcium channel blockers and reduced dose of Tacrolimus. Later patient underwent coronary angiography which showed normal coronary angiography after treatment. This supports coronary vasospasm due to tacrolimus.

Keywords: Tacrolimus, vasospasm, immunosuppression, kidney transplant.

Introduction

Tacrolimus, the corner stone of triple immunosuppression in renal transplant can rarely cause coronary vasospasm. It functions through calcineurin inhibition that subsequently reduces T-lymphocyte proliferation. Vasoconstrictive properties of tacrolimus contribute to its commonly encountered nephrotoxicity. Cardiovascular toxicity manifests in the form of hypertension, but focal or diffuse coronary spasms are rarely encountered. We report the first such case from India to the best of our knowledge.

Case Report: 27 yr old male, who underwent living related renal transplant 6 weeks back was admitted with chest tightness and giddiness since 3 days, his past history included hypertension, Biopsy proven FSGS and ESRD on MHD, echocardiography done prior to transplant was normal on presentation in casualty his ECG showed ST depression in inferior leads and in v3 to v5 chest leads, troponin I and CPK mb were significantly raised.

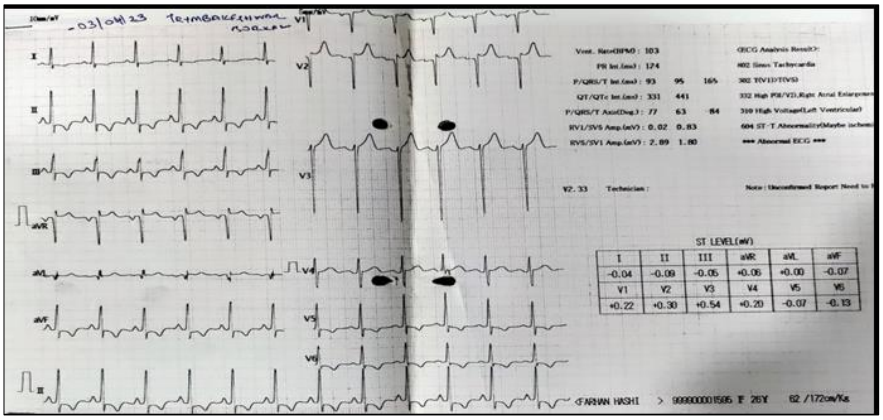

Fig 1: At admission, ECG changes s/o inferior wall ischemia.

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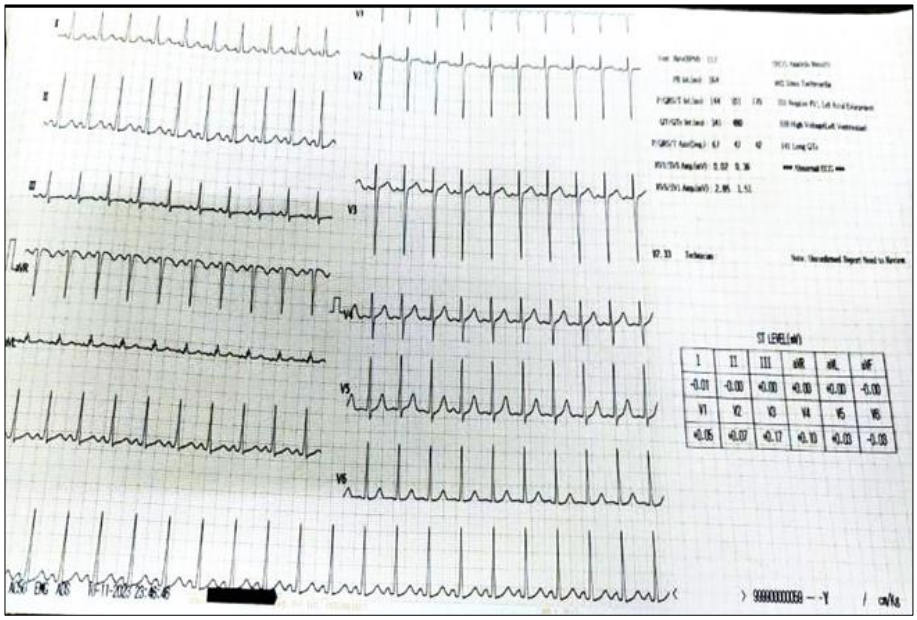

Fig 2: Resolution of ECG changes post reduction in TAC level and CCB.

Physical examination was remarkable for tremor and uncontrolled hypertension. Tacrolimus level at presentation was 9.52. The normal tacrolimus serum range is (3-7 ng/mL). He subsequently underwent adenosine stress test which showed reduced resting EF 39 with post stress non transmural infarct in RCA territory.

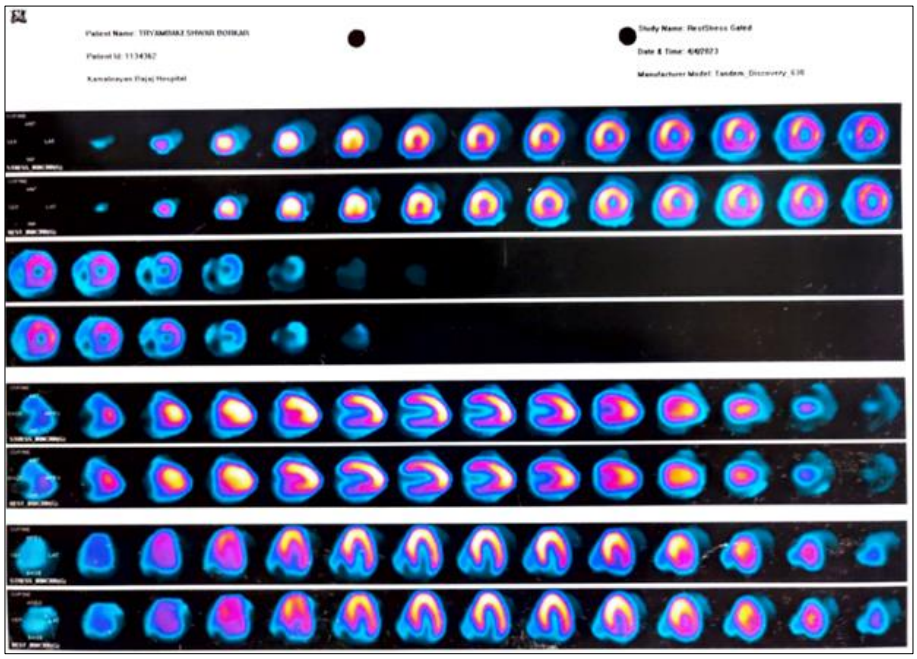

Fig 2: Post stress non transmural infarct in RCA territory.

He was managed initially with enoxaparin and antiplatelets later tacrolimus dose was reduced and calcium channel blockers were added, with significantly reduced symptoms followed by decreased enzymes level and ECG changes reverted to normal. Coronary angiography done on day 3 was normal.

Discussion

In teenagers and young adults, the use of illicit substances, primarily cocaine, is an important cause of drug-induced myocardial infarction secondary to coronary spasm. Recreational drugs marijuana and amphetamine, alcohol, weight losing ephedrine containing drugs are known to cause coronary vasospasm [1].

Tacrolimus adds to this list of drugs, recent case reports both from around the world and Asia point to this adverse drug reaction [3, 4]. The mechanism underlying vasoconstriction induced by tacrolimus have different theories. First, tacrolimus binds FK-binding protein (FKBP) and forms a complex which then

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inhibits calcineurin, a Ca^{2+}-dependent phosphatase. Thus, it increases intracellular calcium concentration, a known spam trigger. Increased tone of vascular smooth muscle, reduced nitric oxide production, and activation of endothelin-1 receptor are other possible explainations [2, 5].

Calcium-channel blockers is the established therapy for coronary artery spasms, and the decrease in frequency of variant angina is explained by their rampant use. Long-acting nitrates were also found to be efficient, and their vasodilatory effect may be additive to calcium antagonists [1].

In our case, this 24 year old male with typical ECG changes and raised troponin indicate ACS typically NSTEMI, his adenosine stress test point too showed RCA territory ischemic, but coronary angiography done on day 3 was normal, the resolution of symptoms, decreasing troponin level after reduction in Tacrolimus dose and calcium channel blockers support the hypothesis.

Conclusion

Coronary vasospasm due to Tacrolimus can mimic acute coronary syndrome, early recognition leads to effective management and avoids false alarm in physicians.

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