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CASE REPORT

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Myocardial infarction with nonobstructive coronaries (MINOCA) following rabies postexposure prophylaxis: A case report

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Key Clinical Message

This case underscores the importance of considering myocardial infarction with nonobstructive coronary arteries (MINOCA) in patients experiencing acute chest pain following rabies vaccination, emphasizing the need for heightened awareness and further research into the association between MINOCA and Rabies vaccination.

Abstract

Rabies is a vaccine-preventable deadly viral disease prevalent in Asia and Africa that causes thousands of deaths annually. Rabies pre (PrEP) and postexposure prophylaxis (PEP) is highly effective in annulling rabies-associated deaths. The adverse reactions following rabies vaccination are typically mild. Myocardial infarction with non-obstructive coronary arteries (MINOCA) is a rare condition, and its association with rabies vaccination is unprecedented. We present a case of a 43-year-old male with MINOCA following Rabies PEP. A 43-year-old male, nonsmoker and nonalcoholic, presented to the ER with complaints of acute onset left sided chest pain following the completion of the third dose of intradermal rabies vaccine, whose clinical features, ECG changes and lab reports were suggestive of acute presentation of inferior wall MI. Coronary angiography was performed, which however revealed normal coronaries with only slow flow being noted in the left anterior descending (LAD) artery. Echocardiography later showed a normal study with no other relevant diagnosis unveiled on further investigations. Hence a diagnosis of vaccine-induced MINOCA was made. Treatment included antiplatelet therapy, statins, and beta-blockers. MINOCA following rabies vaccination is an unprecedented finding. The clear etiology behind this couldn't be ascertained. The patient's treatment was conventional, emphasizing the need for further research and clinical trials in MINOCA diagnosis and management. This case highlights the need for clinicians to consider MINOCA in patients with acute chest pain post-rabies vaccination. Further research is essential to unravel the

association between MINOCA and rabies vaccination, paving the way for optimal management strategies.

KEYWORDS

case reports, MINOCA, myocardial infarction, postexposure prophylaxis, rabies vaccines

1 | INTRODUCTION

Rabies is a vaccine-preventable deadly viral disease that has a high incidence in Asia and Africa and causes tens and thousands of deaths every year.[1] Despite the high case-fatality rate, the disease is almost completely preventable by pre (PrEP) and postexposure prophylaxis (PEP).[2] The Department of Health Services Nepal has estimated that more than 100 cases of rabies occur in Nepal every year and mostly occur following dog-bites.[3] It is estimated that around 50,000 people seek postexposure prophylaxis in Nepal based on available medical records, vaccine distribution trends, and services provided by private clinics.[3] The most common side effects attributed to rabies vaccination are pain, tingling and itching at the injection site, and headache.[4] Serious systemic anaphylactic and neurological adverse reactions are relatively rare occurrences.[5]

Myocardial infarction with nonobstructive coronary arteries (MINOCA) encompasses a heterogeneous group of conditions that include both atherosclerotic and nonatherosclerotic disease resulting in myocardial damage that is not due to obstructive coronary artery disease.[6] Though rare, there have been reported cases of MINOCA following COVID-19 vaccination in the literature.,[7] MINOCA following rabies vaccination is somehow unheard of. Here, we present a case of a 43-year-old male patient with MINOCA following the rabies vaccine as a part of postexposure prophylaxis.

2 | CASE DESCRIPTION

A 43-year male presented to the ER with the complaints of left sided chest pain for 4 h, acute on onset, with burning sensation around the anterior chest wall, without any radiation and it was associated with sweating. He was referred from another hospital to our tertiary center for ECG changes presenting as ST segment elevation in the leads II, III, and avF. The patient had already received a loading dose of aspirin, clopidogrel and atorvastatin before presenting to our center.

The patient was a nonsmoker and did not consume alcohol. He had no known co-morbidities, however he said that he had just completed his third dose of intradermal rabies vaccine 1 day before. The patient had a history of dog bite 1 week ago for which he was on postexposure prophylaxis. The patient had no history of fever, shortness of breath, limb swelling, dizziness, palpitations, nausea, vomiting, or loss of consciousness. On presentation, his BP was 90/60 mm Hg, pulse rate was 110 bpm, and saturation was 98% in room air. The respiratory, cardiac, neurological, and abdominal examinations were within normal limits. ECG was done in our center immediately which revealed ST elevation in leads II, III, avF, and V2 with reciprocal changes in lead aVR. ECG was suggestive of acute inferior wall MI with probable right coronary artery (RCA) involvement (Figure 1).

Blood investigations were sent which showed elevated WBC count, positive troponin I, and RFT, LFT were within normal limits A screening echocardiography was done in the ER with a portable echo machine which was suggestive of hypokinetic RCA territory. With the evidence of typical chest pain, ECG changes, positive cardiac enzyme and positive echo findings, a primary coronary angiography (CAG) was performed, however, CAG showed normal coronary arteries without any stenosis. (Figure 2A,B) However, slow flow was noted in the left anterior descending (LAD) territory. The procedure was uneventful and the patient was asymptomatic after the procedure. During the hospital stay he was treated with aspirin, clopidogrel, statin, low molecular weight heparin, beta blocker, antibiotics, and other supportive measures. A formal echocardiography was done following the angiography which then showed a normal study with no regional wall motion abnormality and a normal ejection fraction of 60%. Blood samples were repeated the following day, which then showed a normal WBC level and a normal troponin I level. ESR and CRP were also sent which were also within normal limits.

Further investigations were done to evaluate the etiology. NT-Pro BNP were also within normal limits. Moreover, Rh factor, ANA beta 2 glycoprotein IgG and IgM, anticardiolipin Ab IgG and IgM were also found to be negative. Coagulation profile was also sent to rule out any coagulation disorders which were all within normal limits. He had no any constitutional symptoms suggestive of any infections and the increased WBC count

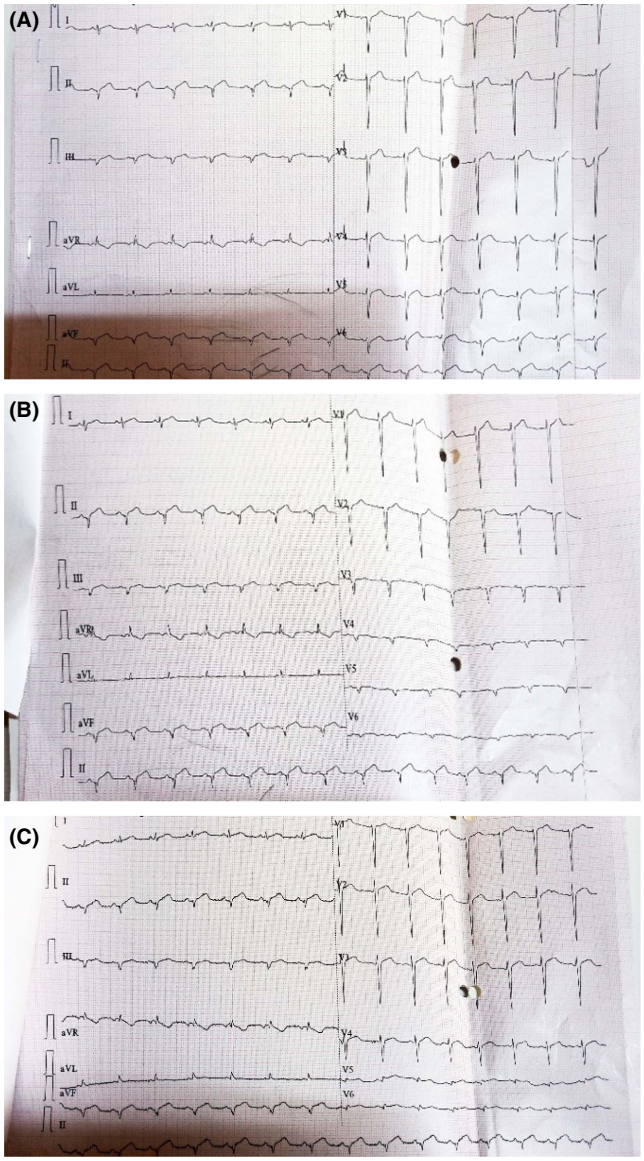

FIGURE 1 (A) ST elevation in leads II, III, and avF with reciprocal change in aVR in left sided ECG suggestive of inferior wall MI. (B) ST elevation in II, III, aVF, V1, and V2 in Right sided ECG suggestive of RCA involvement. (C) ST elevation in limb leads, no posterior wall involvement in posterior ECG.

could be well explained by the fact that he was just recently vaccinated with the rabies vaccine. A diagnosis of MINOCA was made with no relevant possible diagnostic tests explaining his symptoms and clinical diagnosis. His hospital stay was uneventful. His vitals were stable at the time of the discharge and he was discharged with aspirin, clopidogrel, and statin. The patient is under regular follow up and is now discontinued on dual antiplatelet therapy. He is currently under aspirin, statin, ACE inhibitor and beta blocker. The patient is doing all well and aspirin is planned to be discontinued after a year.

3 | DISCUSSION

Without PEP, the average probability of developing rabies following a bite by a rabid animal to the head is 55%, upper extremity 22%, the trunk 9%, and a lower limb 12%.[3] The case-fatality rate of rabies is reported as high as 100%.[8] The anti-rabies vaccines used in Nepal are cell culture vaccines and embryonated egg-based vaccines (CCEEVs) and simultaneous administration of anti-rabies immunoglobulin (RIG) in severe exposures, is close to 100% effective in preventing rabies.[3] Therefore postexposure prophylaxis remains mandatory for suspected exposure to rabid animals.

The common reported side effects after the use of CCEEVs are local reactions like rash, pain, pruritus, and systemic adverse effects like fever, headache, and gastrointestinal symptoms. Immunological and neurological side effects (e.g., Guillain Barre Syndrome) have also been reported, though rare.[9] Severe cardiovascular events following anti-rabies vaccination are relatively unheard of. The diagnosis of MINOCA after rabies vaccination is very uncommon and therefore deems the reporting of this case necessary.

This case report suggests that MINOCA should be considered as a diagnosis in a recently vaccinated patient who presents with signs and symptoms suggestive of acute coronary syndrome. The nonobstructed coronaries in an angiogram shouldn't lead to dismissing of the case. MINOCA remains a puzzling entity for clinicians with the criteria for diagnosis being the same as for acute myocardial infarction with coronary angiography revealing nonobstructed coronaries (stenosis 50%) and no clinical evidence of other diseases that cause acute myocardial infarction (MI) like myocarditis and pulmonary embolism.[10] This patient had signs and symptoms suggestive of acute coronary syndrome with ECG changes suggestive of inferior wall MI and no obstruction in coronary-angiogram, with other viral and autoimmune panels that came negative which led to this case being diagnosed as MINOCA. The elevated WBC count could be attributed to recent vaccination. The echocardiography was relatively normal with hypokinetic apex and slow flow in RCA and LAD. Though cardiac magnetic resonance is an important diagnostic tool in exploring the underlying case that led to MINOCA,[11] this test was not done in our case.

Another entity with similar presentation that still puzzles cardiologists is Takotsubo syndrome and there are controversies surrounding whether it should be classified within MINOCA.[12] The absence of a stressful trigger with lack of apical ballooning and basal hyperkinesia often otherwise seen in Takotsubo syndrome,[13]

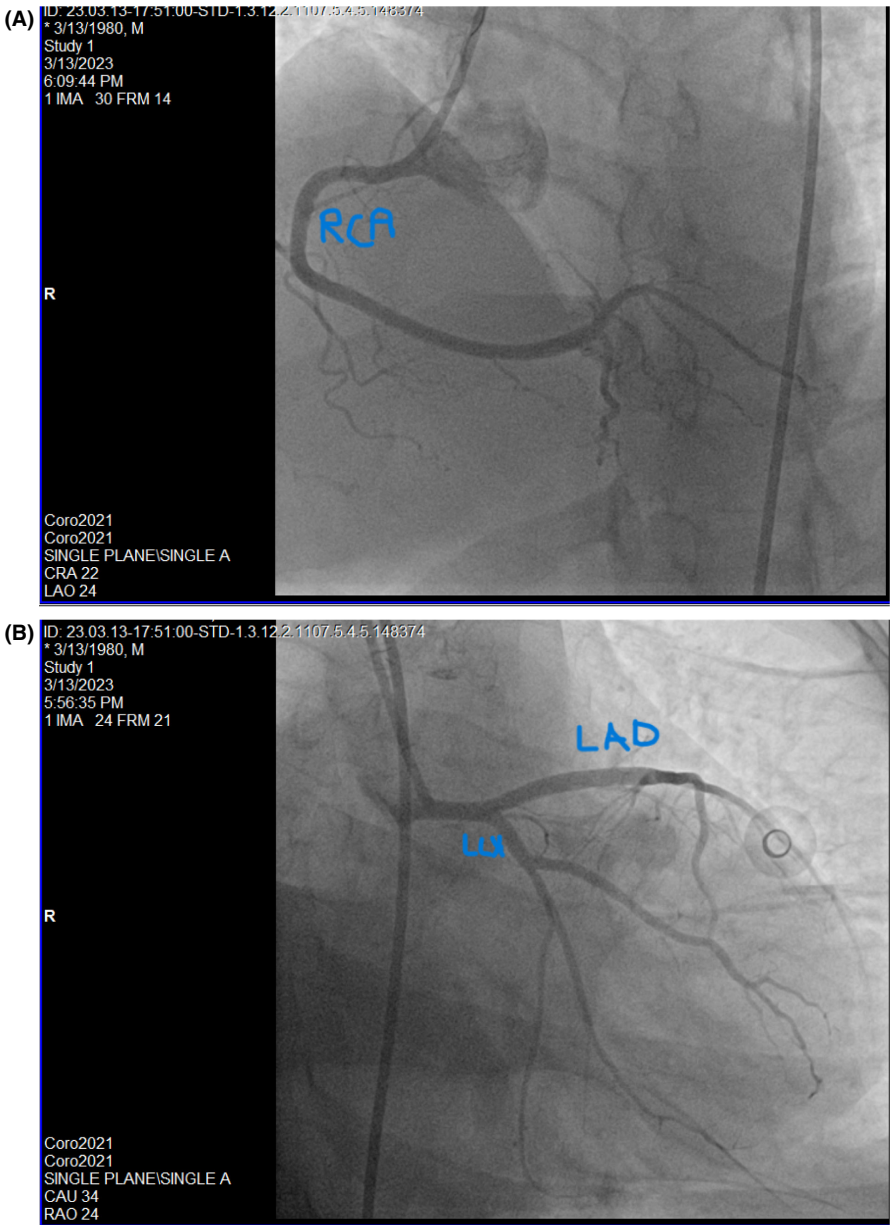

FIGURE 2 (A) Coronary angiography showing nonobstructive RCA (right coronary artery). (B) Coronary angiography showing nonobstructive LAD (left anterior descending) and LCX (left circumflex) arteries.

along with evident hypokinetic RCA territory in echocardiography and ECG showing definitive ST elevation and reciprocal changes in this case led to the cardiology team choose MINOCA as a working diagnosis instead of Takotsubo syndrome.

While a diagnosis of MINOCA is fitting to this patient, it is important to raise the consideration of coronary slow flow phenomenon (CSFP), as the potential contributor to the observed clinical symptoms. CSFP is characterized by delayed contrast opacification in coronary vessels without significant obstructive coronary disease, and can lead to acute chest symptoms and even ECG changes suggestive of acute coronary syndrome (ACS),[14] which adds a layer of complexity to the diagnosis of this case. Further, the mechanism of CSFP involves microvascular dysfunction,[14] and it remains possible that vaccination induced inflammatory changes could lead to such dysfunction. Discerning whether vaccine-induced- MINOCA and CSFP could be distinct or overlapping entities can be very challenging. Further CSFP in MINOCA patients has been recognized in literature as independent predictor of clinical outcomes and is associated with higher risk of adverse events.[15]

Though the long-term prognosis in MINOCA patients is better than that of acute myocardial infarction, MINOCA is not a benign condition and demands prudent treatment.[16] Rather, inhospital mortality within the first 30 days has been shown to be more in MINOCA patients than acute MI patients.[17]

Unlike myocardial infarction, the etiologies of MINOCA are varied and there are no rigid guidelines for the management of MINOCA and the best management

strategy should be to find out the etiology.[18] Large scale randomized control trials on MINOCA patients are the best bet in establishing the efficacy of cardio-protective agents in MINOCA patients. Our patient was however treated in hospital with dual antiplatelet therapy, statins and B-blockers along with other supportive measures and was discharged on dual antiplatelet therapy and statins after the hospital stay was uneventful.

Although it is evident that our patient completed three doses of intradermal postexposure CCEEV prophylaxis, the patient party wasn't able to provide information on the exact type of CCEEV used, which goes down as one of the major limitations of this case report. Nerve tissue vaccines (NTV) were phased out in Nepal in 2006.[3] Since then, CCEEVs have been widely used for pre and postexposure prophylaxis. Different kinds of CCEEVs used in Nepal are human diploid cell vaccine (HDCV); purified vero cell rabies vaccine (PVRV); and purified chick embryo vaccine (PCECV).[19] Studies have shown that the incidence of local side effects is common with intradermal use than intramuscular use however no difference in the incidence of systemic side effects is noted.[20] Among the CCEEVs, PCECVs, and PVRVs are reported to have lesser frequency of local, systemic and neurological side effects than of HDCVs.[21]

MINOCA following rabies vaccination is a relatively rare association and the exact mechanisms linking the two remain unclear. However, vaccine associated inflammatory changes that led to endothelial dysfunction, microvascular inflammation or possible coronary spasm could explain this association.[22] Clinicians should therefore have MINOCA as a working diagnosis in cases of acute chest pain even in the absence of significant coronary artery disease, especially in a post-vaccination setting.

4 | CONCLUSION

In countries where animal bites are common and rabies is endemic, postexposure prophylaxis is considered mandatory keeping in mind the high case-fatality rate for rabies. However, this case report shows that clinicians should keep in mind the working diagnosis of "MINOCA" in cases of acute chest pain following rabies vaccination even in the absence of angiographic evidence of obstructed coronaries. However, owing to the elusive pathophysiology of MINOCA, further research is needed to understand the etiopathogenesis of MINOCA and to develop optimal strategies for its goal-directed management.

AUTHOR CONTRIBUTIONS

Reechashree Dhungana: Conceptualization; formal analysis; methodology; project administration; visualization; writing – original draft; writing – review and editing. **Prajjwal Pokharel:** Conceptualization; data curation; investigation; resources; writing – review and editing. **Chandra Mani Poudel:** Investigation; supervision; validation; writing – review and editing. **Raja Ram Khanal:** Investigation; supervision; validation; writing – review and editing. **Smriti Shakya:** Investigation; supervision; validation; writing – review and editing. **Ratna Mani Gajurel:** Investigation; supervision; validation; writing – review and editing.

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None.

CONFLICT OF INTEREST STATEMENT

None.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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