

Hyper-eosinophilic syndrome with myocarditis after inactivated SARS-CoV-2 vaccination: A case study

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Case Report

Keywords: Adverse drug reaction, Covaxin, COVID-19 vaccine, Dermatological, Eosinophilia

Posted Date: August 13th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-806335/v1>

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Abstract

A young man without any co-morbidities presented with persistent periorbital baggy swelling along with itchy swelling over fingers, resting tachycardia and exertional breathlessness following first dose of an inactivated SARS-CoV-2 vaccination (COVAXIN). On investigation, patient had elevated blood eosinophils and myocarditis. He was successfully treated with steroid and supportive treatment.

Background

COVID-19 has emerged as a global emergency and has claimed more than 3.9 million lives. The high mortalities caused by SARS-CoV-2 in individuals with co-morbidities and the absence of an effective antiviral stimulated the development of COVID-19 vaccines, few of which were granted emergency use authorization. COVAXIN, manufactured by Bharat Biotech (India) is based on inactivated SARS-CoV-2 virus cultured in Vero cells and was approved on 3rd January 2021. The approval was based on favorable safety and immunogenicity findings in the interim analysis of a Phase 2 trial involving 921 participants.(1) No serious adverse events following immunization (AEFIs) were observed in the trial participants. Similar safety findings have been reported in the phase 3 trial data (preprint only). Since rare but serious adverse events may go undetected in clinical trials, active post-marketing surveillance is of utmost priority.

Here we report the first case of hyper-eosinophilic syndrome and myocarditis developing in a healthy adult male following COVAXIN vaccination.

Case Presentation

A 33-year-old male neurologist noticed swelling under both eyes on day-8 post-vaccination with first dose of COVAXIN (Figs. 1A). Initially, the swelling was more in the morning and tended to decrease with progression of the day but became persistent after a week. The patient had a feeling of uneasiness and regularly monitored his vitals and symptoms. On day-23 of vaccination, he developed severe itching on both heels and on the next day, he developed swelling in the left ring and index fingers, and right ring finger associated with itching (Figs. 1B). Around day-25, he developed shortness of breath on exertion, even occurring while talking. The patient did not have fever, cough or gastrointestinal involvement. There was a background history of post-poliomyelitis residual paralysis in right lower limb since 2-years of age, and occasional allergic rhinitis for the past 10-years which was controlled without any medication for the past one year. On examination, blood pressure in the right and left upper limbs were 126/78 and 124/80 mmHg respectively, without any evidence of orthostatic hypotension. Resting tachycardia was present ranging from 120–130 beats per minute that further increased on exertion. Respiratory and remaining cardiac examinations were non-contributory.

Table 1 (supplementary article) described the laboratory investigations of the patient. The hemogram showed eosinophilia, which increased further with disease progression. ECG on days-24 and 32 showed sinus tachycardia and transthoracic 2D echocardiogram on both occasions were normal. Cardiac magnetic resonance imaging (MRI) on day-38 showed hyperintense areas involving the myocardium on T2 image, suggestive of myocarditis (Fig. 1C-D). A diagnosis of delayed immunological response to inactivated SARS-CoV-2 vaccine with hyper-eosinophilic syndrome was made.

The patient had partial relief in itching with montelukast-levocetirizine combination. On day-25 patient was started on dexamethasone 6mg b.i.d that was administered for five days, and also received ivermectin-albendazole 12mg/400mg single dose as eosinophilia syndromes due to possible worm infestation, endemic in India. As exertional dyspnea became quite distressing and accompanied by palpitations, he began supportive care involving bed rest, small frequent meals, avoiding exertion, laxatives, and proton pump inhibitors. Around day-39 he was also started on extended-release metoprolol (12.5mg) for persistent resting tachycardia and advised salt and water restriction, with fluid intake guided by urine output. He responded to the treatment and was advised cardiac rehabilitation. After three weeks of stopping steroids, swelling under both eyes reappeared and patient complained of increased cardiac symptoms on exertion with resting tachycardia (120 to 130 beats per minute). Patient was restarted on steroids (prednisolone 30mg for 5 days) with plan of slow tapering (followed by 10mg for 20 days followed by 5mg for 2 months then stop after assessing with cardiac MRI imaging and blood eosinophils), fexofenadine, and metoprolol dose was increased to 50mg gradually. Patient has been kept on these medications and cardiac rehabilitation with improvement in symptoms. At present with one month of steroid, patient is improving and undergoing cardiac rehabilitation with gradual escalation of activities as per advice.

Discussion

In the absence of an effective antiviral, vaccination is a crucial step in curtailing the COVID-19 pandemic. The approval of vaccines, however, has been largely based on interim findings of phase 2/3 trials and with a limited follow-up period. Rare but serious adverse events may hence go unnoticed. With their mass roll out, serious AEFIs such as vaccine induced thrombosis and thrombocytopenia (VITT) and myocarditis are being reported with viral vectored vaccines and mRNA vaccines respectively.(2, 3)

The present report highlights the occurrence of a rare but serious form of hypersensitivity reaction and the first such case in a healthy adult male following inactivated SARS-CoV-2 vaccine. It manifested as hyper-eosinophilia with multiorgan involvement of skin, subcutaneous tissue, and myocardium following the first dose. Hyper-eosinophilia can be due to other underlying allergic diseases or parasitic infestations but temporal relationship with COVID-19 vaccine, lack of response to anthelmintic treatment and a good response to steroids points towards the possibility of vaccine induced hyper-eosinophilia in this case. Normal levels of complement proteins and antinuclear antibodies made autoimmune disease less likely. Eosinophilic infiltration of myocardium can lead to eosinophilic myocarditis. Though cardiac markers were normal in the current case, clinical and radiological patterns were suggestive of myocarditis.

Allergic/eosinophilic manifestations of COVID-19 are being reported, but no such cases of hyper-eosinophilic syndrome post-vaccination is described.(4)

Myocarditis cases have been reported predominantly in children, adolescent, and young adult males following the mRNA vaccines of Pfizer and Moderna.(5, 6) Such serious events have not been noticed in the trial data of COVAXIN.(1) It is worth noting that SARS-CoV-2 is also known to cause myocardial injury either directly or following cytokine storm and occurrence of myocarditis in COVID-19 is often associated with poor prognosis. In one case series, possibility of autoimmune myocarditis after COVID vaccination is also considered.(7) With phase 3 trial data showing COVAXIN efficacy close to 80%, decision of mass vaccination should be balanced with a careful assessment of risk of serious adverse events versus benefits of protection against COVID-19. Nevertheless, active post-marketing surveillance of COVID-19 vaccines is required not only to update the safety profile but also to resolve vaccination related hesitation among public.

Various studies have shown that the main stay of treatment for hyper-eosinophilia is treatment of underlying disease followed by steroid. And the alternate therapy may include cytotoxic drugs.(8) In the same way, this patient was treated with steroid and got symptomatically better.

In conclusion, awareness of hyper-eosinophilia presentations as focal subcutaneous edema and myocarditis after inactivated SARS-CoV-2 vaccination (COVAXIN) will clinch the diagnosis at earliest. Prior history of allergic disease like rhinitis may try to avoid in taking this vaccine. Hyper-eosinophilia can present with variable symptoms but the concerned symptom is persistent resting tachycardia and dyspnea. Steroid and antiallergic drugs are successfully used for the treatment of vaccine induced hyper-eosinophilia.

Declarations

Conflicts of interest

We declare that we have no conflicts of interest.

Funding source

None

Acknowledgment

None

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Table 1

Table 1 is included in the Supplementary Files section.

Figures

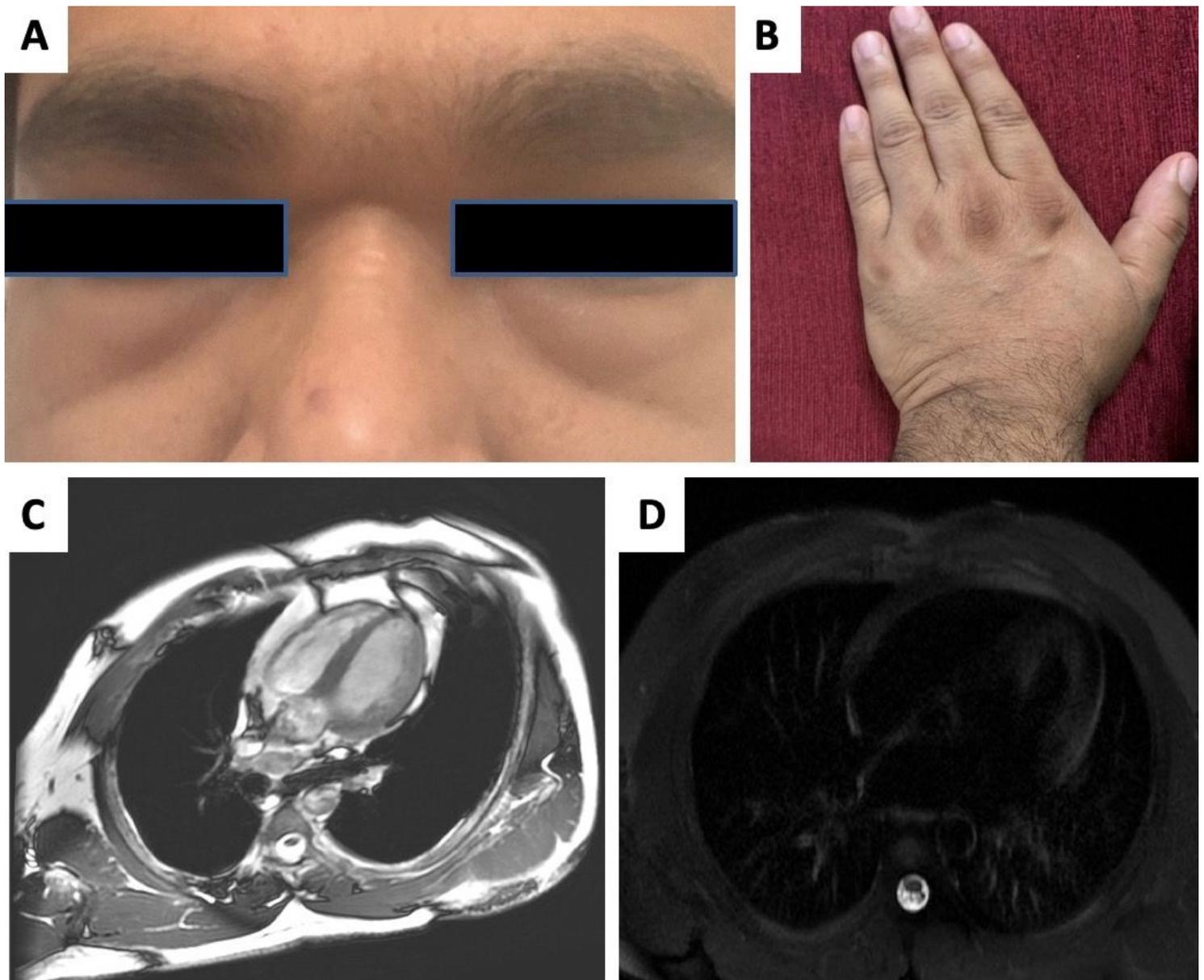


Figure 1

Clinical and imaging findings. (A) shows baggy swelling around eyes; (B) shows itchy swelling in dorsum of right hand (fingers); C & D show four chamber and Axial T2 FS views respectively revealing left ventricular myocardium with T2 hyperintense signal involving its full thickness suggesting myocarditis.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Table1.docx](#)