COVID-19 vaccine-associated myositis – a case report.

Ponnu Bose[1], Usha Goenka[1], Saibal Moitra[1], Sanjib Majumdar[1], Mahesh Goenka[1], and Srijita Sen[1]

[1]Apollo Multispeciality Hospitals Ltd, Kolkata

March 31, 2022

Abstract

Myositis is one of the uncommon adverse events following COVID–19 vaccination, and its mechanism is still unclear. In the hope of aiding in its better understanding, we present a case of myositis following the first dose of the ChAdOx1 nCoV-19 Corona Virus Vaccine, evidenced by serology and MRI.

TITLE PAGE

Title : COVID-19 vaccine-associated myositis – a case report.

Authors : 1. Ponnu Bose, Department of Clinical Imaging and Interventional Radiology, Apollo Multispeciality Hospitals Ltd, Kolkata, Email- ponnubose1947@gmail.com.

2. Usha Goenka, Department of Clinical Imaging and Interventional Radiology, Apollo Multispeciality Hospitals Ltd, Kolkata, Email- dr.ushagoenka@gmail.com.

3. Saibal Moitra, Department of Allergy and Immunology, Apollo Multispeciality Hospitals Ltd, Kolkata, Email- saibal.moitra@gmail.com.

4. Sanjib Majumdar, Department of Clinical Imaging and Interventional Radiology, Apollo Multispeciality Hospitals Ltd, Kolkata, Email- sanjib_dr@yahoo.co.in.

5. Mahesh Kumar Goenka, Institute of Gastrosciences and Liver, Apollo Multispeciality Hospitals Ltd, Kolkata, Email- mkgkolkata@gmail.com.

Corresponding author : Srijita Ghosh Sen, Department of Clinical imaging and Interventional radiology, Apollo Multispeciality Hospitals Ltd, 58, Canal Circular Road, Kolkata, West Bengal, India – 700054, Mobile no: +91 9831323402, Email- srijita20@yahoo.com

Data availability statement: Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflicts of Interest : The authors have no conflicts of interest to declare.

Ethical approval: Our institution does not require ethical approval for reporting individual cases or case series.

Patient consent statement: Written informed consent was obtained from the patient for his anonymized information to be published in this article.

Key words : adverse effect, case report, vaccine-associated myositis, COVID-19 vaccine.

ABSTRACT

Myositis is one of the uncommon adverse events following COVID–19 vaccination, and its mechanism is still unclear. In the hope of aiding in its better understanding, we present a case of myositis following the first dose of the ChAdOx1 nCoV-19 Corona Virus Vaccine, evidenced by serology and MRI.

MAIN DOCUMENT

COVID-19 VACCINE-ASSOCIATED MYOSITIS – A CASE REPORT

INTRODUCTION:

Vaccine-related adverse events are fairly common and generally mild, including transient pain, redness, and edema at the injection site[1], fever, fatigue, and myalgia[2]. Apart from these, the COVID-19 vaccine has also been reported to cause a few rare and life-threatening adverse reactions like thrombosis with thrombocytopenia syndrome[3], Guillain-Barré syndrome[4], vasculitis[1], autoimmune hepatitis[5], inflammatory myopathies[1] and myocarditis[6], which are now thought to be caused by immune-mediated mechanisms. With 28 million doses of COVID-19 vaccine being administered daily, the reporting of such rare adverse events is essential not only for a better understanding of its pathogenesis but also to aid clinicians in promptly recognizing the symptoms and effective management.

CASE REPORT:

A 53-year-old man presented with severe pain and soreness in his left upper arm. The pain started 2 days after the first dose of the ChAdOx1 nCoV-19 Corona Virus vaccine into his left deltoid muscle. The pain initially developed in the left upper arm, followed by the right upper arm and bilateral calf muscles (left more than right). The pain gradually increased, and he had difficulty walking and moving his left arm at the time of presentation. He also reported generalised muscle weakness, more pronounced in the proximal upper and lower limbs than the distal ones. There was no history of heavy manual labour or vigorous exercise before the onset of symptoms. There was no malaise or fever. There was no history of any skin rash, breathlessness, dry cough or joint pain. He was non-diabetic and non-hypertensive, with no history of any connective tissue disorders or allergic reactions to drugs or vaccines. There has been no evidence of COVID-19 infection in the past.

On local examination, there was no swelling or erythema. There was tenderness over the left deltoid muscle and bilateral calf muscles, more so on the left side. The MMT score for the left deltoid muscle and left calf muscles was 3/5, and for the same muscles on the right side it was 5/5.

Serologic testing yielded mildly increased serum creatine kinase (187 U/L, reference range 40 – 171 U/L) and alanine transaminase (50 U/L, reference range 10 – 40 U/L) concentrations. Urine analysis excluded myoglobinuria. Initial laboratory findings are summarised in Table 1.

Suspecting skeletal muscle damage, MRI of all the limbs was suggested. At MRI, there was edema in the left deltoid muscle with a thin layer of subfascial fluid adjacent to the muscle belly (Insert Figure 1). Deltoid muscle architecture was preserved. Subtle edema was also noted in the medial head of the left gastrocnemius muscle, with the edema fluid tracking along the intermuscular plane between the gastrocnemius and soleus (Insert Figure 2). No collection or abscess was seen. MRI of the right arm and leg was normal. Based on these findings, a diagnosis of COVID-19 vaccine-associated myositis was made. EMG, muscle biopsy, and immunological workup could not be done as the patient did not give consent.

The patient was advised to rest and take nonsteroidal anti-inflammatory drugs (NSAIDs) for 1 week. Steroids or IVIg were not given, as the symptoms were relatively mild and the liver enzymes were not elevated. On follow-up after 1 week, the pain and tenderness had reduced considerably. The MMT score for the left deltoid muscle and left calf muscle was 5/5. However, the difficulty in walking persisted. Repeat serum creatine kinase after 5 weeks was normal (121 U/L, reference range 40 – 171 U/L). A repeat MRI was not done, as the patient significantly improved after initial management. A timeline of the events following vaccination is given in Table 2.

DISCUSSION:

ChAdOx1 nCoV-19 is a recombinant, replication-deficient chimpanzee adenovirus vector which encodes the SARS-CoV-2 Spike (S) glycoprotein. When administered, it causes the genetic material of part of the coronavirus to be expressed, thereby stimulating an immune response. Direct inoculation of vaccine via an intramuscular route exposes the muscle to these modified contaminant agents and elicits an immune response to the antigen injected [7].

Autoimmunity associated with vaccines can be attributed to the cross-reactivity between antigens or to the effect of adjuvants [8]. ASIA (Autoimmune/inflammatory Syndrome Induced by Adjuvants) is a complex entity referring to the autoimmune manifestations that appear to be caused by adjuvants and may be related to specific HLA phenotypes, the development of autoantibodies, or even evolve into a rheumatological disorder [9]. ASIA is characterised by inflammatory musculoskeletal, neurocognitive, and/or constitutional symptoms on exposure to an external stimulus and improves when the stimulus is withdrawn[9]. Recently, Das et al.[10] have reported a case of ASIA syndrome following the first dose of the ChAdOx1 nCoV-19 vaccine in a 47-year-old patient, manifesting as subacute thyroiditis.

It is known that COVID-19 can lead to myositis and rhabdomyolysis due to immune hyperactivation and excessive cytokine release[11]. The antibodies against SARS-CoV-2 spike glycoproteins cross-reacting with structurally similar host proteins (molecular mimicry) have been suggested as a possible cause for this acute autoimmune response. Other proposed mechanisms include cytokine-mediated autoinflammation, CD8 T-cell overactivation, formation of antigen-antibody complexes, and structural deformity of myocytes caused by intake of viral antigen[11]. It has been suggested that the COVID-19 vaccination could also trigger such a response[12]. However, the exact mechanism remains unclear. The clinical features suggestive of COVID-19-induced myositis include proximal muscle weakness, myalgia, features of muscle inflammation in MRI, dermatomyositis, and rhabdomyolysis evidenced by elevated CK and myoglobinuria[11].

Theodorou et al.[7] have reported a case similar to ours, with a 56-year-old woman presenting with myalgia and progressive muscle weakness that started 8 days after the second dose of COVID-19 vaccination. As opposed to our case, the symptoms were limited to the left upper arm, where the vaccination was given. Myositis was diagnosed based on elevated CK and typical MRI findings. Maramattom et al.[1] have recently reported three similar cases, all of which showed features of inflammatory myositis on MRI, while one patient showed features of vasculitis in addition to myositis on biopsy.

CK levels in myositis are variable. Though CK levels are raised in most cases of inflammatory myopathy, they may be minimally elevated or even normal in some cases like inclusion myositis. Although injection site myositis has been reported following various vaccinations, it is usually associated with elevated CK. Our case showed myositis in the injection site and in other muscles following the COVID-19 vaccine, though CK was only mildly raised, with radiologic evidence of myositis and considerable patient symptoms and activity limitation. This merited medical attention since ChAdOx 1 nCoV 19 is a newly developed vaccine that is under Emergency Use Authorization.

Although muscle biopsy was not performed in our patient, the temporal link between the vaccination procedure and the patient's symptoms, imaging features, the reversible nature of symptoms, and lack of alternative cause suggests a diagnosis of COVID-19 vaccine-associated myositis as the cause. In addition, the other possible causes of muscle edema, like trauma, infection, neoplastic infiltration, and infarction (as in microvascular disease like diabetes mellitus), were not present in this case. Though the symptoms were mild, they incapacitated the patient for some time, resulting in a loss of work days, which was relieved with rest and NSAIDs, not requiring treatment with steroids. Hence, we are reporting this case, which might lead to the formulation of newer studies to look into the mechanistic pathways of COVID-19 vaccine associated myositis.

CONCLUSION:

ChAdOx1 nCoV-19 vaccine-associated myositis is reported, was mild, and the patient is on treatment. This type of adverse effect can be seen in the vaccine, but it is not a deterrent factor for the ongoing vaccination

programme.

Aknowledgements: None.

Conflicts of Interest : None.

Author contributions: Ponnu Bose: aquisition of data, interpreting and evaluating the MRI images, and drafting the original manuscript. Saibal Moitra: patient management, review and editing of the original draft. Usha Goenka, Sanjib Majumdar and Srijita Ghosh Sen: interpretation and evaluation of the MRI images, editing and supervision of the original draft. Mahesh Kumar Goenka: patient management, review and editing of the original draft.

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Ethical approval: Our institution does not require ethical approval for reporting individual cases or case series.

Ethical statement: Written informed consent was obtained from the patient for his anonymized information to be published in this article.

REFERENCES

1. I.R.B. Godoy, T.C. Rodrigues and A. Skaf. Myositis ossificans following COVID-19 vaccination. QJM: An International Journal of Medicine, 2021, 1–2. doi: 10.1093/qjmed/hcab161.
2. Clodoveo Ferri, Michele Colaci, Carlo Umberto Manzini, Marco Sebastiani, Dilia Giuggioli, and Lucio Brugioni. Polymyositis following Pandemic Influenza A (H1N1) and 2009-10 Seasonal Trivalent Vaccines. Case Reports in Rheumatology Volume 2012, Article ID 836930, 3 pages. doi:10.1155/2012/836930.
3. Greinacher A, Thiele T, Warkentin TE, Weisser K, Kyrle PA, Eichinger S. Thrombotic thrombocytopenia after ChAdOx1 nCov-19 vaccination. N Engl J Med 2021; 384: 2092–101.
4. Maramattom BV, Krishnan P, Paul R, et al. Guillain-Barré syndrome following ChAdOx1-S/nCoV-19 vaccine. Ann Neurol 2021; 90: 312–14.
5. Mohamed Rela, Dinesh Jothimani, Mukul Vij, Akila Rajakumar, Ashwin Rammohan. Autoimmune hepatitis following COVID vaccination. Journal of Autoimmunity 123 (2021) 102688. https://doi.org/10.1016/j.jaut.2021.102688.
6. Guy Witberg, Noam Barda, Sara Hoss, lan Richter, Maya Wiessman, Yaron Aviv et al. Myocarditis after Covid-19 Vaccination in a Large Health Care Organization - nejm.org October 30, 2021 - DOI: 10.1056/NEJMoa2110737.
7. Theodorou DJ, Theodorou SJ, Axiotis A, Gianniki M, Tsifetaki N. COVID-19 vaccine-related myositis. *QJM: An International Journal of Medicine* , 2021, 1–2. doi: 10.1093/qjmed/hcab043.
8. S. Goriely, M. Goldman. From tolerance to autoimmunity: is there a risk in early life vaccination? J. Comp. Pathol. 137 (2007) S57–S61, https://doi.org/10.1016/j. jcpa.2007.04.013.
9. Matthew P. Cheng, Michael G. Kozoriz, Amir A. Ahmadi, John Kelsall, Katryn Paquette and Jake M. Onrot. Post-vaccination myositis and myocarditis in a previously healthy male. Allergy Asthma Clin Immunol (2016) 12:6. DOI 10.1186/s13223-016-0114-4.
10. L. Das, S. K. Bhadada, A. Sood. Post-COVID-vaccine autoimmune/infammatory syndrome in response to adjuvants (ASIA syndrome) manifesting as subacute thyroiditis. Journal of Endocrinological Investigation. https://doi.org/10.1007/s40618-021-01681-7
11. Ahmad Saud, R Naveen, Rohit Aggarwal, Latika Gupta. COVID-19 and Myositis: What We Know So Far. Current Rheumatology Reports (2021) 23: 63 https://doi.org/10.1007/s11926-021-01023-9.
12. Karolina Akinosogloua, Ilektra Tzivakia, Markos Marangosa. Covid-19 vaccine and autoimmunity: Awakening the sleeping dragon. Clinical Immunology 226 (2021) 108721. https://doi.org/10.1016/j.clim.2021.108721.

TABLE 1: Laboratory findings at admission.

	Admission	Reference range
Haemoglobin	14.8	13.0 – 17.0 g/dl
Packed cell volume	43.7	40 – 50 %
WBC count	7400	4000 – 10000 /cu mm
Platelet count	1.59	1.5 – 4.0 lacs/cu mm
Creatine kinase	187	40 – 171 U/L
Bilirubin total	0.7	Upto 1 mg/dl
AST	34	10 – 42 U/L
ALT	50	10 – 40 U/L
GGT	19	7 – 64 U/L
ALP	88	53 – 128 U/L
CRP	< 0.33	< 0.5 mg/dl

AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; ALP: Alkaline phosphatase; GGT: Gamma glutamyl transpeptidase; ALP: Alkaline phosphatase; CRP: C-reactive protein.

TABLE 2: Timeline of events following vaccination.

18 JUNE 2021 (DAY 0)	First dose of ChAdOx1 nCoV – 19 Corona Virus vaccine in left deltoid muscle
21 JUNE 2021 (DAY 3)	Development of myalgia, initially in the left arm followed by right arm and bilateral calf muscles.
29 JUNE 2021 (DAY 11)	Hospital visit following worsening of symptoms. Edema and perifascial fluid in left deltoid and left gastrocnemius muscles in MRI, mildly elevated serum creatine kinase - diagnosis of ChAdOx1 nCoV-19 Coronavirus vaccine-associated myositis made.
6 JULY 2021 (DAY 18)	First follow up, symptoms reduced
2 AUGUST 2021 (DAY 45)	Second follow up, serum creatine kinase returned to normal

FIGURE LEGENDS

Figure 1: Coronal Short tau inversion recovery magnetic resonance (STIR MR) images of left arm (A and B) showing edema in deltoid muscle with adjacent perifascial fluid.

Figure 2: Coronal (A) and axial (B,C) STIR MR images of left leg showing subtle edema in medial head of left gastrocnemius muscle and fluid in the sub fascial and intermuscular plane.