COVID-19 Vaccine-Induced Pneumonitis, Myositis and Myopericarditis

Mariya Farooq 1, Yaser Mohammed 2, Mansoor Zafar 3, Dawpadee Dharmasena 3, Usman Iqbal Rana 2, Osei Kankam 1

1. General Internal Medicine, Conquest Hospital, East Sussex Healthcare NHS Trust, St. Leonards-on-Sea, GBR
2. Internal Medicine, Conquest Hospital, East Sussex Healthcare NHS Trust, St. Leonards-on-Sea, GBR
3. Gastroenterology and Hepatology, Conquest Hospital, East Sussex Healthcare NHS Trust, St. Leonards-on-Sea, GBR
4. Respiratory Medicine, Conquest Hospital, East Sussex Healthcare NHS Trust, St. Leonards-on-Sea, GBR

Corresponding author: Mansoor Zafar, 1mansoorzafar@gmail.com

Abstract

A 63-year-old male, with no significant past history and not on any regular medications previously, had mild respiratory symptoms post the first dose of the AstraZeneca (Cambridge, England) coronavirus disease 2019 (COVID-19) vaccine, which were self-limiting. Following the second dose of the vaccine, he arrived at the emergency department (ED) with worsening shortness of breath.

During this admission, he was assumed to have interstitial lung disease due to a possible past history of occupational exposure. He responded to a short-term course of corticosteroids and antibiotics and was discharged home.

However, he reported again to the emergency department three weeks later, with persistent dyspnoea along with myalgia. His blood tests and imaging from scans suggested myositis, pneumonitis, and myopericarditis. Since he recently had the COVID-19 AstraZeneca vaccine, it was postulated as the most likely cause of the symptoms. He was managed with intravenous (IV) corticosteroids followed by oral corticosteroids with symptom resolution.

Introduction

When dealing with the global pandemic of coronavirus disease 2019 (COVID-19), there was an urgent need for immunity that could boost the natural immune system. The answer was herd immunity from the various vaccines on the market, recommended by the World Health Organization (WHO) [1]. The WHO issued emergency use listings (EULs) for two versions of the AstraZeneca/Oxford (Cambridge, England) COVID-19 vaccine [2]. There was funding, including indemnity given by governments across the globe to accelerate the mass production and availability of COVID-19 vaccines to the masses [3]. Vaccines and, in particular, adjuvant contents of vaccines have been shown to increase the antigen-specific immune response toward immunogenicity. This may also have negative outcomes, inducing autoimmunity [4].

We present a unique case with combined pneumonitis, myositis and myopericarditis post-COVID-19 vaccination, which responded to conservative management, highlighting the need to be aware of the prompt management of such patients with favourable outcomes.

Case Presentation

A 62-year-old male had the first dose of the AstraZeneca/Oxford COVID-19 (ChAdOx1 S [recombinant]) vaccine (AZ) three months after recovery from asymptomatic COVID-19 infection. He developed mild respiratory symptoms and was managed in primary care with oral antibiotics. Respiratory tract symptoms recurred after the second dose of the AZ vaccine two months later; he was again managed in primary care with a course of antibiotics for a lower respiratory tract infection.

After three weeks with persisting symptoms of dyspnoea and chest tightness, he arrived at the emergency department and was referred to the medical team on-call for further assessment. His initial observations showed oxygen saturation of 88% on air and improvement to 94% with 2 litres of oxygen. As a landlord, there was a possible exposure to bird droppings and dust at building sites while visiting various properties he was renovating. Initial blood tests and high-resolution computed tomogram (HRCT) suggested an impression of probable hypersensitivity pneumonitis (Figure 1). He was started on a weaning course of steroids with outpatient follow-up in the respiratory clinic.
There is diffuse and patchy ground-glass attenuation (yellow arrows) with tiny nodules in the upper and mid zones, and there are multifocal areas of peripheral consolidation with tractional bronchiolar dilatation within both lower lobes.

HRCT: high-resolution computed tomogram

Twelve days later, he presented again to the emergency department with a referral to the medical team for review. This time, he was admitted to the respiratory ward in insolation with significant myalgia, weakness and dyspnoea and was detected to have very high creatinine kinase (CK) levels of 4053 u/L (22-198), troponin levels of 472 (0-< 14) ng/ml, aspartate transaminase (AST) of 217 u/L (1-45) and C-reactive protein of 60 (-5) (Table 1).

| Parameter                    | Day 1 | Day 2 | Day 3 |
|------------------------------|-------|-------|-------|
| Troponin                     | 472   | 399   | 204   |
| Creatinine Kinase (CK)       | 4053  | -     | 1526  |
| Aspartate Transaminase (AST) | 217   | -     | 88    |
| C-Reactive Protein (CRP)     | 60    | 27    | 6     |

TABLE 1: Progressive downward trend of biochemical blood markers towards resolution

Although the ECG was non-specific, cardiac magnetic resonance imaging (MRI) did show mild fibrosis of the septum and inferior and lateral walls (Figure 2). MRI of the left quadriceps showed non-specific subcutaneous fat tissue oedema (Figure 3).
FIGURE 2: Cardiac MRI

A. STIR-T2 images: Mild fibrosis of the basal septum and inferior and lateral walls. No myocardial inflammation or infarction. B. Gadolinium study: In the late phase, there is a mild mid-wall enhancement in the basal septum and inferior and lateral walls. There is an area of increased signal in the posterior right lung (white arrow).

STIR: short tau inversion recovery

FIGURE 3: MRI-left quadriceps: axial view

There is diffuse oedema in the subcutaneous fat tissue on the anterolateral sides of both thighs (blue arrows).

A clinical diagnosis of probable AZ COVID-19 vaccine-related inflammatory myositis, myopericarditis and pneumonitis was made. He was managed with IV methylprednisolone for three days followed by oral prednisolone 40 mg daily with weekly tapering, with appropriate proton pump inhibitor (for acid protection) and vitamin D (bone protection) while on steroids. The anti-nuclear antibody (ANA) level was 1:80 while extra-nuclear antibody (ENA) and double-stranded deoxyribonucleic antibody (dsDNA) were negative. There was a gradual improvement of CK, troponin, AST and CRP levels noted. His repeat HRCT also showed significant resolution (Figure 4). Following recovery, the patient was discharged and booked for outpatient
follow-up by the rheumatology and respiratory teams.

**FIGURE 4: HRCT-repeat: axial view**

Almost complete resolution of peripheral areas of radiologically presumed organising pneumonia.

HRCT: high-resolution computed tomogram

**Discussion**

A number of studies have suggested an association of co-morbidities with the COVID-19 infection [5-8]. Similarly, a number of side effects have also been reported with the use of the vaccines. Some were immediate while others present in a sub-acute fashion. These include COVID-19 vaccine-related rashes [9] and dural venous sinus thrombosis [10]. Side effects related to pneumonitis, which has been demonstrated in transgenic mice studies [11]. A number of studies have demonstrated post-COVID-19 vaccine-related myositis [12-14]. There was also cardiovascular involvement including myocarditis and myopericarditis [15-16].

It is questionable whether the introduction of a booster vaccination would have any further impact on side effects [17-18]. Additionally, National Institute for Clinical Excellence (NICE, UK) and Centre for Disease Control (CDC, USA) guidelines would need to be updated. Fortunately, the monoclonal antibody treatment by AstraZeneca has been approved by the Food and Drug Administration (FDA) USA for emergency use on December 8, 2021, for the long-term prevention of COVID-19 among people with weakened immune systems before they have been exposed to coronavirus with six-monthly injections [19]. The UK’s Medicines and Healthcare products Regulatory Agency (MHRA) made the announcement on December 31, 2021, for the pill - Paxlovid, towards reducing the risk of hospitalisation and death [20]. Hopefully, these steps would ensure more safety and more favourable outcomes with a lower incidence of side effects.

We present here a unique case report of a patient who developed an augmented reaction to the second dose of the COVID-19 vaccine with pneumonitis, myopericarditis and myositis that responded well to the tapering doses of steroids. While it would be interesting to see other cases that may be reported and the outcomes of their management, it gives us some hope that there is treatment available to manage such outcomes, albeit short term.

**Conclusions**

Symptomatic management with corticosteroids, either intravenous or oral, depending on the patient’s status is advised and has shown good results. Since, irrespective of vaccination, the incidence of various side effects, including myositis, pneumonitis, myopericarditis and widespread rashes, is more frequent, there is a need to update NICE UK and CDC USA guidelines and for more awareness of management.

In particular, there is an increasing need to update the guidelines related to side effects with plans to roll out booster vaccinations in the upcoming autumn season.
Additional Information

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

Acknowledgements

Dr. Mariya Farooq and Dr. Mohammed Yaser are joint first co-authors involved in the care of the patient; they designed the case report and collected the references. Dr. Mansoor Zafar is the corresponding author and was involved in designing the case report and collecting the references. Dr. Dawpadee Dharmasena was involved in the care of the patient. Dr. Usman Iqbal Rana was involved in the proofreading and editing of the case report. Dr. Osei Kankam was involved in the overall care of the patient and reviewed the manuscript for intellectual input. The authors would like to thank the Respiratory Ward team and Radiology team at Conquest Hospital, East Sussex Healthcare NHS Trust for their help in providing the necessary images highlighting the side-effects post-COVID-19 vaccination. Special thanks to Dr. Rita Joarder, Consultant Radiology, Dr. Bernal, Consultant Radiology, and Dr. Hackikurt, Consultant radiology, for help and support towards identifying and reporting symptom resolution on repeat CT and musculoskeletal MRI images, respectively.

References

1. WHO. Coronavirus disease (COVID-19): vaccines. (2021). https://www.who.int/news-room/q-a-detail/coronavirus-disease-(covid-19)-vaccines?topicurvey=vtk13&gclid=CjwKCAiwyM6dBRBUEiwAAnzIFl5Q067R8Z_1YU0E9e7CEEj6eP44P47ZQWJ2W3l81Qj6BQJdOEw_2g8Q0QAvEALwCw.
2. Oxford/AstraZeneca Covid vaccine research 'was 97% publicly funded'. The Guardian. (2021). https://www.theguardian.com/science/2021/apr/15/oxfordastrazeneca-covid-vaccine-research-was-97-publicly-funded.
3. UK government grants Pfizer civil legal indemnity for COVID-19 vaccine. Jurist. (2020). https://www.jurist.org/news/2020/12/uk-government-grants-pfizer-civil-legal-indemnity-for-covid-19-vaccine/.
4. Cheng MP, Kozoriz MG, Ahmadi AA, Kelsall J, Paquette K, Onrot JM: Post-vaccination myocarditis and myositis in a previously healthy male. Allergy Asthma Clin Immunol. 2016, 12:6. 10.1186/s13223-016-0114-4
5. Zafar M, Karkhanis M, Shahbaz M, et al.: Vitamin D levels and mortality with SARS-COV-2 infection: a retrospective two-centre cohort study. Postgrad Med J. 2021, 10.1136/postgradmed-2021-140564
6. Zafar M, Shahbaz M, Karkhanis M, et al.: A retrospective observational study: is absolute lymphocyte count a prognostic marker in COVID-19?. Cureus. 2021, 13:e16554. 10.7759/cureus.16554
7. Ruan Y, Ryder RE, De P, et al.: A UK nationwide study of people with type 1 diabetes admitted to hospital with COVID-19 infection. Diabetologia. 2021, 64:1717-24. 10.1007/s00125-021-05456-x
8. Zafar M, Randhawa R S, Hegner W, et al.: Can HbA1c levels be used as an independent marker of mortality and morbidity risk in patients with COVID-19 positive swabs? - a retrospective observational study. Univ Tor Med J. 2021, 98: [Epub].
9. Zafar M, Ewenu B, Ahmed S, Iqbal U, Whitehead M: COVID-19 vaccination-induced rash: does the choice of vaccine matter?. Cureus. 2021, 13:e15490. 10.7759/cureus.15490
10. Wolf ME, Luz B, Niehaus L, Bhogal P, Bäzner H, Henkes H: Thrombocytopenia and intracranial venous sinus thrombosis after COVID-19 vaccine AstraZeneca exposure. J Clin Med. 2021, 10:1599. 10.3390/jcm10081599
11. Jiang RD, Liu MQ, Chen Y, et al.: Pathogenesis of SARS-CoV-2 in transgenic mice expressing human angiotensin-converting enzyme 2. Cell. 2020, 182:50-58.e8. 10.1016/j.cell.2020.05.027
12. Theodorou DJ, Theodorou SJ, Axiotis A, Gianniki M, Tsifetaki N: COVID-19 virus-related myositis. QJM. 2021, 114:424-5. 10.1093/qjmed/hca043
13. Mehan WA, Yoon BC, Lang M, Li MD, Rincon S, Buch K: Paraspinal myositis in patients with COVID-19 infection. AJNR Am J Neuroradiol. 2020, 41:1949-52. 10.3174/ajnr.A6711
14. Zhang H, Chermchi Z, Seidman RJ, Anziska Y, Velayudhan V, Perk J: COVID-19-associated myositis with severe proximal and bulbar weakness. Muscle Nerve. 2020, 62:E57-60. 10.1002/mus.27003
15. Nasser M, Nso N, Gonzalez C, et al.: COVID-19 virus-induced myocardiitis: case report with literature review. Diabetes Metab Syndr. 2021, 15:102205. 10.1016/j.dsx.2021.102205
16. Sulemankhil I, Abdelrahman M, Negi SI: Temporal association between the COVID-19 Ad26.COV2.S vaccine and acute myocardiitis: a case report and literature review. Cardiovasc Revasc Med. 2021, [Epub ahead of print]10.1016/j.carrev.2021.08.012
17. COVID-19 vaccination: a guide to booster vaccination - GOV.UK. (2021). https://www.gov.uk/government/publications/covid-19-vaccination-booster-dose-resources/covid-19-vaccination-a-guide-to-
18. Mahase E: Covid-19: booster vaccine to be rolled out in autumn as UK secures 60m more Pfizer doses . BMJ. 2021, 375:n1116. 10.1136/bmj.n1116
19. FDA clears first covid antibody treatment for immunocompromised before exposure. NBC News. (2021). https://www.nbcnews.com/health/health-news/fda-clears-astrazenecas-covid-antibody-treatment-
immunocompromised-rca8150.

20. Pfizer covid pill approved In UK for those most at risk. The Independent . (2021).
https://www.independent.co.uk/news/uk/home-news/paxlovid-covid-pill-pfizer-uk-b1984885.html.