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Local myofascitis of the deltoid muscle after administration of the AstraZeneca (AZD1222) COVID-19 vaccine: two cases, infectious and inflammatory

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Case 1

On April 29, 2021, the AstraZeneca vaccine (AZD1222) was administered to a 41-year-old female patient on the direct lateral portion left deltoid muscle (in the center of the deltoid muscle, midway between the acromion and the deltoid tuberosity). About 12 hours after vaccination, a mild fever of 37–38°C with localized heat and tenderness, erythema, and edema developed around the inoculation site. Pain of visual analog scale (VAS) 6 was also accompanied by active movement of the left shoulder. Although she took only 500 mg of acetaminophen three times a day and observed these symptoms without any other special treatments, she showed no improvement even after 3 days.

Hence, she visited our hospital as an outpatient; her body temperature was 36.9°C, and there was erythema of about 7 cm in diameter around the vaccination site, accompanied by swelling and heat. Tenderness was most severe at the injection site. Resting pain was VAS 4–5, and it was most severe with VAS 6 in abduction of the shoulder joint. She did not have any specific underlying medical conditions. Blood analysis indicated an erythrocyte sedimentation rate (ESR) of 28 mm/h and a normal C-reactive protein (CRP) level of 0.3 mg/dL. We recommended magnetic resonance imaging (MRI) in consideration of the possibility of infection because the pain pattern was more severe than that of other patients and the patient had symptoms for a longer period of time. MRI presented edema in the left deltoid muscle and superficial soft tissue and a fluid signal (~120 mm length) on the T2-weighted image (T2WI) (Fig. 1*A*). The radiologist suggested local myofascitis of the deltoid muscle as a preliminary diagnosis. Due to the possibility of infection, a first-generation cephalosporin (2 g/day in 2 divided doses) was administered intravenously for 2 days. She was still taking 500 mg of acetaminophen three times a day. Subsequently, there was VAS 2 pain and mild tenderness, a reduction in the erythema and swelling, and the body temperature was 36.3°C. However, after 5 days, similar symptoms recurred, and the size of the erythema around the vaccination site was reduced to about 5 cm in diameter; the erythema, warmth, and edema decreased; and the tenderness was similar. Resting pain was VAS 4, and pain during active motion was VAS 5. The white blood count, ESR, and CRP level were still within the normal range. In collaboration with an infectious disease physician, we changed the antibiotic to a third-generation cephalosporin (2 g/day in 2 divided doses) to be administered intravenously for 3 days; however, there was no improvement in symptoms. Hence, piperacillin sodium 4 g/ tazobactam 0.5 g was administered 3 times a day every 8 h. Two days later, most symptoms were alleviated, except for mild swelling. On the last follow-up, MRI performed approximately one month after vaccination

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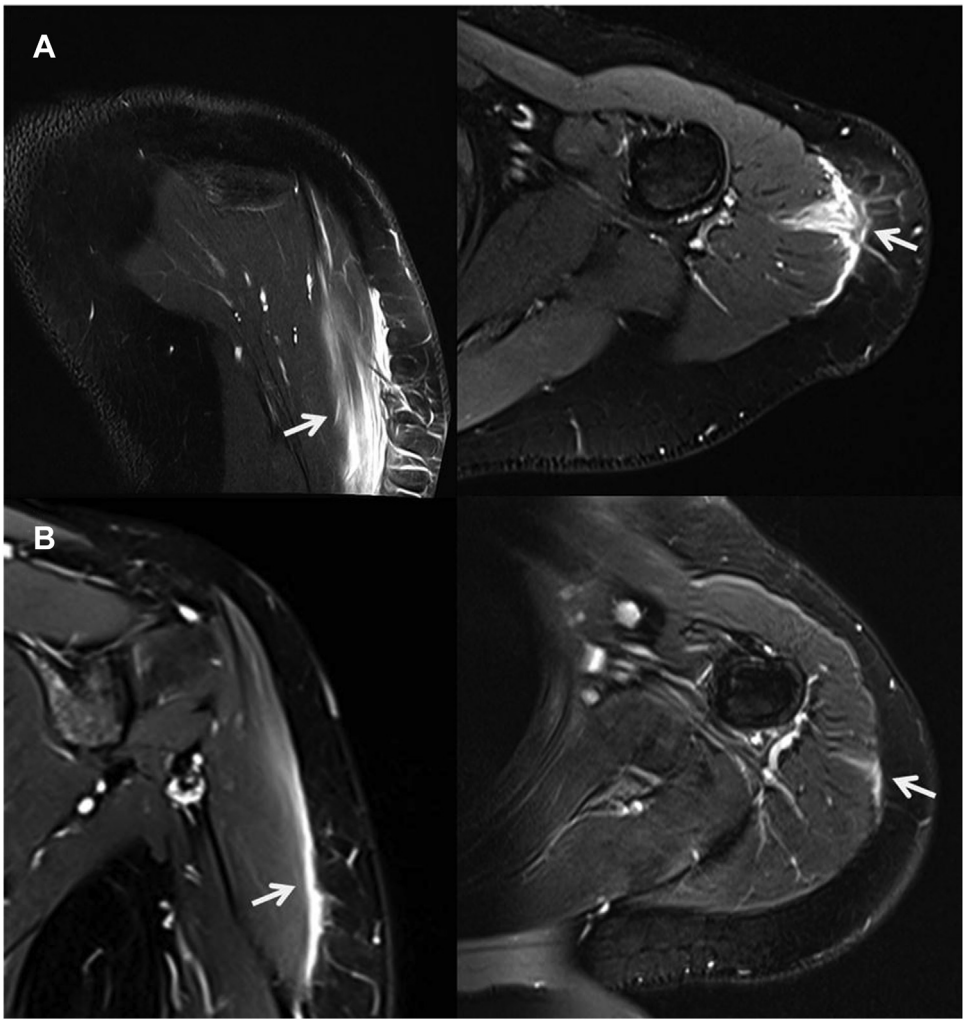

Figure 1 Case 1. (**A**) The MRI presented edema in the left deltoid muscle and superficial soft tissue, and fluid signal (about 120 mm length) on the T2-weighted image. (**B**) After 1 month, the range and intensity of the fluid signal on the T2-weighted image were decreased compared with the previous MRI. *MRI*, magnetic resonance image.

revealed that although edema was present in the deltoid muscle and superficial soft tissue, and the fluid signal (about 74 mm length) had improved compared to the previous MRI (Fig. 1*B*).

Case 2

On April 30, 2021, the AstraZeneca vaccine (AZD1222) was administered to a 41-year-old female patient on the direct lateral portion left deltoid muscle (in the center of the deltoid muscle, midway between the acromion and the deltoid tuberosity). After vaccination, she had no systemic symptoms, only pain and tenderness of VAS 3 around her vaccination site, and a slight warmth. For 24 h after vaccination, although she took 500 mg of acetaminophen three times, her pain worsened to VAS 7. The passive range of motion of the glenohumeral joint was within the normal range, but active abduction was limited to 90–100° due to pain. Also, she had mild tenderness and swelling around the vaccination site, but there was no heat or erythema. She continued to take only acetaminophen for a week without any other treatment. However, after 10 days, her pain did not improve, and she visited our institution's outpatient clinic. She complained of VAS 5 pain and had no systemic symptoms other than local tenderness and mild swelling around her inoculation area. Her body temperature was 36.3 °C. She did not have any specific underlying medical conditions. Blood analysis indicated an ESR of 7 mm/h and a normal CRP level of 0.1 mg/dL. We recommended an MRI for two reasons: persistent pain and exclusion of complications such as infection. On MRI, the T2WI showed a high signal (~65 mm long) and strong enhancement in the lateral portion of the deltoid muscle (Fig. 2*A*). She was not given antibiotics because her blood analysis was within the normal range, and there was no evidence of infection such as localized warmth and erythema. We recommended follow-up while taking analgesics, as symptoms were improving and there were no other obvious signs of infection. She was prescribed 162.5 mg of acetaminophen + 18.75 mg of tramadol hydrochloride three times a day. After 10 days, her pain had improved to VAS 2, and she still had pain during active abduction, but the range of motion was unrestricted. She also showed improvement in tenderness around the vaccination site and no other signs of infection. On the last follow-up, MRI performed approximately 4 weeks after vaccination revealed that the previously seen high signal intensity had decreased on the T2WI (Fig. 2*B*).

Discussion

The replication-defective viral vector (adenovirus) in the AstraZeneca/Oxford vaccine has exhibited an average efficacy of 70.4%.[1,3] AZD1222 can be transported and stored under refrigerated

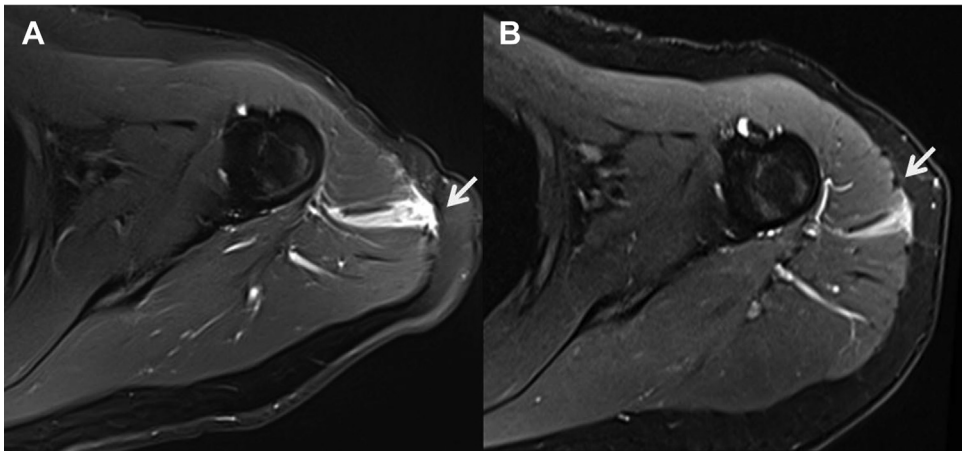

Figure 2 Case 2. (**A**) High signal intensity can be observed along the fascia and muscle of the middle part of the deltoid on the T2-weighted image. (**B**) After one month, the previously seen high signal intensity had decreased on the T2-weighted image.

conditions (2–8°C) for a minimum of six months in the existing healthcare settings.[1] Although the average efficacy of AZD1222 is lower than that of the vaccines produced by Moderna and Pfizer/BioNTech, its recommended storage conditions are noteworthy.[1] Because AstraZeneca/Oxford used a less expensive technology for the production of AZD1222, the total price per dose is lower than that of the other vaccines. Indeed, it is the cheapest, at just 3–4 USD per dose, compared to the other vaccines (Moderna, 32–37 USD and Pfizer/BioNTech, 19.50 USD).[8] For this reason, AZD1222 is an ideal vaccine in low- and middle-income countries with limited resources.[17]

The phase 2–3 trial of the AZD1222 vaccine reported systemic adverse effects such as headache (22.8%), fatigue (21.1%), arthralgia (11.5%), chills, and shivering (14.7%) in 88% of participants aged 18–55 years who received the first injection.[12] Local side effects were commonly reported in the order of tenderness (49.3%), pain (19.1%), warmth (7.9%), and swelling (5.5%). In terms of the safety profile, 13 serious adverse events, such as hemolytic anemia, and transverse myelitis, occurred; however, none was considered related to the study vaccine according to the investigators.[16,21] Various thromboembolic events were reported after vaccination with the AZD1222 vaccine, one of which may be related to post-vaccination immune-mediated thrombocytopenia.[7,14,15]

In general, locally occurring fascitis is mainly caused by the local injection of drugs, and necrotizing fascitis,[11,20] eosinophilic fascitis,[19] and macrophagic myofascitis (MMF) have been reported for various drugs. To date, the most well-known myofascitis occurring after vaccination is MMF. MMF appears as symptoms of myalgia months to years after vaccination and can be diagnosed through muscle biopsy.[6,13] In addition, the cause of MMF is known to be aluminum hydroxide, which is an adjuvant included in some vaccines.[6,9] However, the COVID-19 vaccines developed so far do not contain adjuvants to enhance the effectiveness of the vaccine. Cases of necrotizing fascitis after administration of the measles vaccine have been reported previously,[11] as has local myofascitis after deep subcutaneous injections of somatostatin analogs in patients with acromegaly-gigantism.[10]

With the administration of vaccines for COVID-19 since late 2020, there have been reports of various side effects but none of myofascitis. Here, we report two cases of localized myofascitis after the administration of the AstraZeneca vaccine, which were diagnosed by MRI. In both cases, there was muscle pain and tenderness around the deltoid muscle within 24 hours after administration of the vaccine. Despite taking acetaminophen-based analgesics, the pain improved slowly or was maintained until 10 to 15 days after administration of the vaccine. Tenderness and pain are the most common local side effects that may occur after the administration of the AstraZeneca vaccine, although these symptoms usually resolve within 48 hours. However, in our two cases, the pain became uncontrolled and severe after 48 h, and myofascitis of the deltoid muscle was confirmed on MRI, which also revealed it to be the cause of the atypical severe shoulder pain after the administration of the AstraZeneca vaccine.

In the first case, the patient showed symptoms of pain and heatness, erythema, and tenderness. When an infection is suspected, empirical antibiotics can be used based on symptoms, serological tests, and imaging evidence in situations where it is difficult to identify the causative organism. *Staphylococcus aureus* is known to be the most common causative agent of these diseases.[2,4,5] Gram-negative bacteria may also cause pyogenic myositis or necrotizing fascitis. The best antibiotics recommended for the treatment of cellulitis are first-generation cephalosporins, such as cefazolin, which are effective against *S. aureus* and *streptococci*, and penicillinase-resistant penicillins, such as nafcillin.[18] However, due to recurrence and persistence of symptoms, third-generation cephalosporins and beta-lactam antibiotics that can act against gram-negative bacteria were administered.[5]

Our cases report that myofascitis may occur as one of the complications after receiving the AstraZeneca vaccine. These cases suggest that the possibility of myofascitis should be considered if the pain at the injection site worsens without improvement or maintained after 48 hours post administration of the AstraZeneca vaccine. Patients may not show any abnormalities in the blood test, and they are accompanied by pain to the extent that active shoulder movement is impossible. In addition, tenderness around the injection site is commonly complained of, and some may show signs of infection such as fever, redness, and swelling. It is recommended to consider blood tests to measure the white blood count, ESR, and CRP levels. According to previous reports, rare but serious side effects, such as necrotizing fasciitis, may occur after vaccination. So, if there are signs of local infection and it is difficult to identify the causative agent, empirical antibiotics are recommended. It is suggested to administer broad-spectrum antibiotics including gram-negative bacteria. In addition, if the patient does not respond to these conservative treatments, we suggest considering imaging tests such as MRI in consideration of serious complications such as necrotizing fasciitis.

Conclusion

The possibility of myofascitis should be considered if there is severe pain at the inoculation site that persists even 48 h after the administration of the AstraZeneca vaccine. In addition, the possibility of infection should always be considered, blood tests and imaging tests to rule it out are recommended, and empirical antibiotic administration should be considered.

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