

# World Journal of *Clinical Cases*

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### REVIEW

- 3369** Superior mesenteric artery syndrome: Diagnosis and management  
*Oka A, Awoniyi M, Hasegawa N, Yoshida Y, Tobita H, Ishimura N, Ishihara S*

### MINIREVIEWS

- 3385** Astrocytes in the central nervous system and their functions in health and disease: A review  
*Gradisnik L, Velnar T*
- 3395** Progress in diagnosis and treatment of acute injury to the anterior talofibular ligament  
*Chen RP, Wang QH, Li MY, Su XF, Wang DY, Liu XH, Li ZL*
- 3408** Synchronous manifestation of colorectal cancer and intraductal papillary mucinous neoplasms  
*Mirchev MB, Boeva I, Peshevska-Sekulovska M, Stoitsov V, Peruhova M*
- 3418** Clinical infections in neurosurgical oncology: An overview  
*Velnar T, Kocivnik N, Bosnjak R*
- 3434** Effectiveness and safety of subthreshold vibration over suprathreshold vibration in treatment of muscle fatigue in elderly people  
*Mohamed AA, Khaled E, Hesham A, Khalf A*

### ORIGINAL ARTICLE

#### Clinical and Translational Research

- 3444** Establishment of a prognostic model related to tregs and natural killer cells infiltration in bladder cancer  
*Yang YJ, Xu XQ, Zhang YC, Hu PC, Yang WX*

#### Retrospective Study

- 3457** New native tissue repair for pelvic organ prolapse: Medium-term outcomes of laparoscopic vaginal stump-round ligament fixation  
*Kakinuma T, Kaneko A, Kakinuma K, Imai K, Takeshima N, Ohwada M*
- 3464** Demographic characteristics of patients who underwent anterior cruciate ligament reconstruction at a tertiary care hospital in India  
*Malv SK, Mahmood A, Vatsya P, Garika SS, Mittal R, Nagar M*
- 3471** Usefulness of transcatheter arterial embolization for eighty-three patients with secondary postpartum hemorrhage: Focusing on difference in angiographic findings  
*Kim BM, Jeon GS, Choi MJ, Hong NS*
- 3481** Chronic otitis media and middle ear variants: Is there relation?  
*Gökharman FD, Şenbil DC, Aydın S, Karavaş E, Özdemir Ö, Yalçın AG, Koşar PN*

**Observational Study**

- 3491** Observation of the effect of angiojet to treat acute lower extremity arterial embolization  
*Meng XH, Xie XP, Liu YC, Huang CP, Wang LJ, Liu HY, Fang X, Zhang GH*
- 3502** Outbreak of methanol-induced optic neuropathy in early COVID-19 era; effectiveness of erythropoietin and methylprednisolone therapy  
*Tabatabaei SA, Amini M, Haydar AA, Soleimani M, Cheraqpour K, Shahriari M, Hassanian-Moghaddam H, Zamani N, Akbari MR*

**META-ANALYSIS**

- 3511** Impact of heart failure on outcomes in patients with sepsis: A systematic review and meta-analysis  
*Zhu MY, Tang XK, Gao Y, Xu JJ, Gong YQ*

**CASE REPORT**

- 3522** New clinical application of digital intraoral scanning technology in occlusal reconstruction: A case report  
*Hou C, Zhu HZ, Xue B, Song HJ, Yang YB, Wang XX, Sun HQ*
- 3533** Rare adult neuronal ceroid lipofuscinosis associated with *CLN6* gene mutations: A case report  
*Wang XQ, Chen CB, Zhao WJ, Fu GB, Zhai Y*
- 3542** Enzyme replacement therapy in two patients with classic Fabry disease from the same family tree: Two case reports  
*Harigane Y, Morimoto I, Suzuki O, Temmoku J, Sakamoto T, Nakamura K, Machii K, Miyata M*
- 3552** Immune-mediated necrotizing myopathy: Report of two cases  
*Chen BH, Zhu XM, Xie L, Hu HQ*
- 3560** Retroperitoneal cavernous hemangioma misdiagnosed as lymphatic cyst: A case report and review of the literature  
*Hou XF, Zhao ZX, Liu LX, Zhang H*
- 3571** Malignant melanoma resection and reconstruction with the first manifestation of lumbar metastasis: A case report  
*Guo ZX, Zhao XL, Zhao ZY, Zhu QY, Wang ZY, Xu M*
- 3578** Promising way to address massive intragastric clotting in patients with acute upper gastrointestinal bleeding: A case report  
*Liu SX, Shi B, Liu YF, Shan JY, Sun B*
- 3583** Pyogenic spondylitis caused by *Escherichia coli*: A case report and literature review  
*Zou LC, Qian J, Bian ZY, Wang XP, Xie T*
- 3592** Primary ovarian choriocarcinoma occurring in a postmenopausal woman: A case report  
*Dai GL, Tang FR, Wang DQ*

- 3599** Treatment of severe open bite and mandibular condyle anterior displacement by mini-screws and four second molars extraction: A case report  
*Huang ZW, Yang R, Gong C, Zhang CX, Wen J, Li H*
- 3612** Application of apical negative pressure irrigation in the nonsurgical treatment of radicular cysts: A case report  
*Chen GP, Zhang YZ, Ling DH*
- 3619** Treatment of postherpetic neuralgia by bone marrow aspirate injection: A case report  
*Honda Pazili T*
- 3625** Non-target lung embolization during portal vein embolization due to an unrecognized portosystemic venous fistula: A case report  
*Alharbi SR, Bin Nasif M, Alwaily HB*
- 3631** Acute abdomen caused by spontaneous rupture of degenerative hysteromyoma during pregnancy: A case report  
*Xu Y, Shen X, Pan XY, Gao S*
- 3637** Atypical progress of frozen shoulder after COVID-19 vaccination: A case report  
*Jo HS, Kim HM, Han JY, Park HK*
- 3643** Co-existing squamous cell carcinoma and chronic myelomonocytic leukemia with *ASXL1* and *EZH2* gene mutations: A case report  
*Deng LJ, Dong Y, Li MM, Sun CG*
- 3651** Diagnosis based on electromagnetic navigational bronchoscopy-guided biopsied peripheral lung lesions in a 10-year-old girl: A case report  
*Meng FZ, Chen QH, Gao M, Zeng L, Lin JR, Zheng JY*
- 3658** Relationship between intralobar pulmonary sequestration and type A aortic dissection: A case report  
*Wang YJ, Chen YY, Lin GH*

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## Atypical progress of frozen shoulder after COVID-19 vaccination: A case report

Hyun-Seok Jo, Hyeong-Min Kim, Jae-Young Han, Hyeng-Kyu Park

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### Abstract

#### BACKGROUND

After vaccination was mandated worldwide, various adverse effects associated with the coronavirus disease 2019 (COVID-19) vaccination, including shoulder pain, have been reported. Here, we report a case of new-onset shoulder pain after BNT162b2 (Comirnaty, Pfizer-BioNTech) mRNA vaccination.

#### CASE SUMMARY

A 50-year-old man visited our rehabilitation center with left shoulder range of motion (ROM) limitation that had persisted for more than 5 mo. The history included no specific noteworthy events, except vaccination. The pain in the patient's left deltoid muscle appeared 1 day after the second BNT162b2 vaccination and intensified to severe pain. The patient self-administered aspirin, with which the pain subsided immediately, whereas ROM limitation persisted. At the first visit, the patient complained of dull pain and ROM restriction of the left shoulder (flexion 130°, abduction 110°, and external rotation 40°). Among the diagnostic studies conducted for the evaluation of the shoulder, magnetic resonance imaging showed a thickened coracohumeral ligament. Nerve conduction studies and needle electromyography showed no electrodiagnostic abnormalities. The patient received comprehensive rehabilitation for 7 mo and had an overall improvement in pain and ROM of the left shoulder.

#### CONCLUSION

In this case of severe shoulder pain after COVID-19 vaccination that subsided

immediately with aspirin treatment, the exact cause and mechanism of pain are unclear. However, the clinical symptoms and diagnostic workups in our report suggest the possibility that the COVID-19 vaccination triggered an immunochemical response that resulted in shoulder pathology.

**Key Words:** COVID-19; Vaccination; Adhesive capsulitis; Frozen shoulder; Mechanism; Case report

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**Core Tip:** In this case, the patient experienced severe pain immediately after coronavirus disease 2019 (COVID-19) vaccination and was diagnosed with a frozen shoulder. Pain resolved immediately after taking aspirin. The pain of frozen shoulder is associated with inflammatory mediators, such as cytokines. Although the pathogenetic mechanisms of frozen shoulder after COVID-19 vaccination are unknown, an association between some cytokines and frozen shoulder after COVID-19 vaccination likely exists.

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## INTRODUCTION

Vaccination to prevent the coronavirus disease (COVID-19) has been administered worldwide, and various adverse effects have been reported for the different types of COVID-19 vaccines, for which the most common injection site is the deltoid muscle. Post-vaccination side effects include pain, redness, itching, edema, allergic reactions, fever, local soreness, rash, and others[1] and most of these symptoms are usually mild and transitory, and disappear within 2 to 3 d after vaccination[2]. However, shoulder pathology, including frozen shoulder that is associated with chronic persistent symptoms, can occur after vaccination, including the COVID-19 vaccination[3]. The exact pathogenesis of frozen shoulder remains unclear. Frozen shoulder is a severe dysfunction that takes more than a year to resolve with treatment. In 30%-40% of patients, mild to moderate symptoms can persist at 2 to 3 years of follow-up, and many patients can experience symptoms for even longer than 6 years[4].

The treatment includes surgery or nonoperative treatments, such as physiotherapy and intraarticular or subacromial corticosteroid injections. However, the data on management strategies and outcomes vary[5]. Here, we report an atypical case of frozen shoulder that occurred after BNT162b2 (Comirnaty, Pfizer-BioNTech) mRNA vaccination that differed in terms of the clinical course.

## CASE PRESENTATION

### Chief complaints

A 51-year-old Korean man presented with stiffness and limitation of active and passive range of motion (ROM) in the non-dominant left shoulder for more than five months.

### History of present illness

Approximately 5 mo earlier, the patient received the second BNT162b2 vaccination dose into the left deltoid muscle. The next day onward, the patient experienced left shoulder pain (VAS; Visual Analogue Scale, 7-8) and decreased range of motion. There were no adverse effects reported about people who vaccinated on the same day with the same lot number. Owing to persistent pain and impaired overhead activities, the patient visited another local hospital and received conservative treatment, including transcutaneous electrical nerve stimulation, superficial heat therapy, ultrasound as pain modalities and oral NSAIDs (Ibuprofen, three capsules per day, each containing 400 mg ibuprofen) for 1 mo. However, the left shoulder pain persisted and the ROM decreased further. Therefore, the patient self-administered aspirin 500 mg per day for 2 d without a doctor's prescription following which the pain resolved immediately although the shoulder ROM limitation persisted. After 3 mo, the patient visited our department with stiffness and limitation of active and passive ROM in left shoulder.

**History of past illness**

The patient engaged in office work and had not experienced any significant shoulder pain, stiffness, and trauma prior to the administration of the COVID-19 vaccine.

**Personal and family history**

The patient had no specific family history and no allergic reactions prior to the vaccination.

**Physical examination**

At the first visit, the ROM of shoulder was ascertained as shoulder flex 130, abduction 110, internal rotation 30, and external rotation 40. The strength at the shoulder was normal. The patient had a negative O'Brien test and a positive Hawkins test, without any local tenderness, swelling, sensory disturbance, and apparent trauma or shoulder pathology. There was neither atrophy around the deltoid or shoulder girdle nor any scapular winging.

**Laboratory examinations**

All laboratory test results were within the reference values.

**Imaging examinations**

Standard anteroposterior and lateral radiographs of the affected shoulder were checked and found to be within normal limits. Magnetic resonance imaging (MRI) was conducted and showed no rotator cuff tear; however, coracoacromial ligament thickening (6.2 mm, whereas normal value < 4 mm; [Figure 1](#)) was noted.

**Other examinations**

For facilitating the differential diagnosis, an electrodiagnostic study was conducted and revealed results that were within normal limits.

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**FINAL DIAGNOSIS**

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The patient was accordingly diagnosed with frozen shoulder.

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**TREATMENT**

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An intra-articular shoulder joint injection of saline and lidocaine (0.5% lidocaine) was administered once, but did not improve the ROM immediately nor after the 1-week follow-up. Moreover, the patient underwent a rehabilitation program that included ROM exercises and pain modalities such as transcutaneous electrical nerve stimulation, superficial heat therapy, ultrasound for improving shoulder ROM at least 2 times per week. The exercise types included finger to wall climbing exercise, both forward and sideways to improve forward flexion and abduction, respectively, until the symptoms had subsided. Pendulum exercises and anterior posterior capsular stretching were also undertaken.

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**OUTCOME AND FOLLOW-UP**

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After 5-mo rehabilitation, the shoulder ROM improved as follows: Shoulder flex 150, abduction 140, external rotation 65, and internal rotation 15, with no complaints of pain ([Table 1](#)). And there was no adverse event.

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**DISCUSSION**

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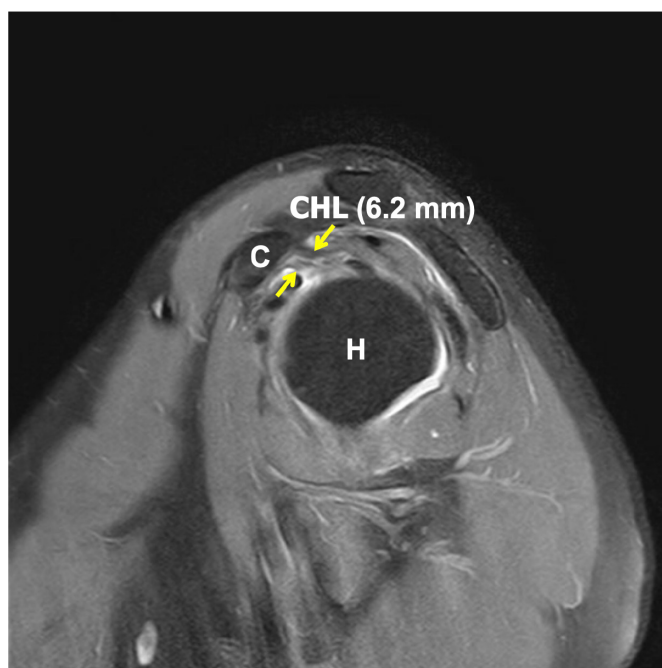
In general, vaccines are frequently injected intramuscularly into the deltoid muscle, and the guidelines for vaccination, including the needle length and depth of injection, have been specified[6,7]. However, injection too high in the deltoid muscle can result in shoulder stiffness[1]. Another mechanism of injury that can occur after vaccination includes an antigen-antibody reaction that can occur in the muscle. Nonetheless, in general, the injury is transitory and progresses moderately. However, in some cases, antibodies from previous infections or vaccinations can lead to considerably longer-lasting inflammatory reactions[8,9] and can cause adhesive capsulitis of the shoulder[10]. Furthermore, vaccination in the shoulder can induce localized autoimmune reactions in the shoulder that can lead to a frozen shoulder[3].



**Table 1 Physical examination of the patient**

	Before rehabilitation	After rehabilitation
Numerical rating scale	7	3
Range of motion		
Flexion	130°	150°
Abduction	110°	110°
External rotation	40°	65°
MMT (Rt. U/E/Lt. U/E)	(5/5/5)/(4/5/5)	(5/5/5)/(4/5/5)

NRS: Numerical rating scale, MMT: Manual muscle test, U/E: Upper extremity.



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**Figure 1 Magnetic resonance imaging of left shoulder.** On magnetic resonance imaging study of left shoulder, the thickness of coracohumeral ligament was increased to 6.2 mm; arrows, thickness of coracohumeral ligament. C: Coracoid process, CHL: Coracohumeral ligament, H: Humerus.

Historically, vaccination is generally administered as an intramuscular injection into the deltoid muscle. However, the patient did not complain of severe pain at the injection site after the vaccination and, after vaccination, there was no erythema, swelling, burning sensation, and other complications.

Any painful condition of the shoulder joint after a vaccination was termed shoulder injury related to vaccine administration, by Atanasoff in 2010[8]. Shoulder injury after or related to vaccine administration have been defined as any pain and dysfunction of the shoulder that occur within 48 h of vaccination and lasts for more than 7 d. However, the presentation and prognosis of the COVID-19 vaccination-related shoulder dysfunction, including frozen shoulder, is unclear[3]. Age-related degenerative change can be considered in this case. However, the symptoms, including pain and ROM limitation, occurred immediately post-vaccination in this case, as reported in prior research.

A frozen shoulder is diagnosed based on the clinical presentation of shoulder stiffness and pain as well as the absence of radiological, laboratory, or other pathologies, as in the present case[1].

Some patients typically present with severe pain immediately after vaccination, especially when the needle enters the subacromial bursa or injures the peripheral nerves[11]. Furthermore, there may be an increase in fluid within the subacromial or subdeltoid bursae that is evident on imaging[12]. However, in the present case, the MRI and electrodiagnostic studies showed no bursitis and nerve injury.

In most cases of vaccination-related injury, patients suffer persistent symptoms, including pain and chronic ROM limitation[8]. Furthermore, the pain of the frozen shoulder may be nociceptive, as a result of peripheral abnormalities associated with capsular structures. In addition, inflammatory mediators can mediate the process of peripheral sensitization[13]. Several studies of frozen shoulder have revealed

immune cells and inflammatory mediators, including cytokines such as interleukins, tumor necrosis factor, and immune mediators[14]. Moreover, cytokines such as the Alarmins high mobility group box 1 (HMGB1) are associated with pain in the frozen shoulder and peripheral nerve ingrowth[15]. In addition, cytokines such as HMGB1 are associated with the severe acute respiratory syndrome coronavirus 2 infections[16]. In the present case, the pain resolved with aspirin intake, which can suppress endogenous prostaglandin synthesis *via* inhibition of cyclooxygenase activity and its effects on the concentration of interleukins[17]. In addition, aspirin decreases the levels of cytokines such as HMGB1[18]. Accordingly, the pain in the present case may have improved immediately. Frozen shoulder after vaccination has been previously reported. But in this case, the progress was somewhat different from the general course including progress of pain.

## CONCLUSION

We report the case of a patient who experienced severe shoulder pain after BNT162b2 vaccination and whose pain resolved immediately after taking aspirin. Physicians usually recommend injections, pain modalities, or physiotherapy for frozen shoulders. There are reports that the HMGB1 signaling pathway is associated with acute lung injury and acute respiratory distress syndrome in COVID-19 patients. However, studies of the association of cytokines, such as HMGB1, and frozen shoulder after COVID-19 vaccination have not been reported. Nonetheless, the exact cause of pain is unclear although the clinical symptoms and diagnostic workup in our case suggest the possibility of an association between cytokines, such as HMGB1, and shoulder pathology. Further studies are needed to understand the pathophysiology of shoulder pain after COVID-19 vaccination and to ascertain the relationship between cytokines, pain, frozen shoulder, and aspirin.

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