中文題目：阿斯特捷利康新冠疫苗可能引起自體免疫壞死性肌肉炎
英文題目：Immune-mediated Necrotizing Myopathy Maybe Triggered by AstraZeneca COVID-19 Vaccine
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Introduction: The AZ vaccine is one of the most effective vaccines against COVID-19 infection. The most frequent adverse effect of the AZ vaccine in patients with autoimmune is similar to that of the general population. However, increased disease activity is observed.[1] Vaccine-induced myopathy, including inflammatory myositis, had been described in past literature. As of July 2021, there are currently 4 cases of myopathy secondary to the AstraZeneca vaccine but non-fatal.[2] Here we described a fetal case of IMNM associated with the AZ vaccine. IMNM is a rare autoimmune disease that causes damage to the muscle. It is characterized by elevated serum creatinine kinase (CK) levels, proximal muscle weakness, and the presence of anti-HMGCR or anti-SRP autoantibodies. It can further classify according to which antibody is present. The disease can be diagnosed with clinical presentation and laboratory data without a muscle biopsy. The treatment of the disease involves IVIG, rituximab, corticosteroids, and immunosuppressants. However, the treatment of the disease is empirical, as there are no RCTs available for optimal regiments.[3]

Case presentation: A middle-aged woman presented to our Emergency Department with a 3-day history of difficulty raising her upper arm. She received her first dose of the AstraZeneca COVID-19 vaccine ten days before the onset of the illness. She denied pain, diplopia, vision loss, paresthesia, dysphasia, or newly developed rash. Her temperature was 37.1^{o}C, blood pressure was 136/7mmHg, heart rate was 80 beats per minute, respiratory rate of 18 per minute, and her oxygen saturation was 100% on room air. Examination showed the weakness of all proximal muscles (4/5), more pronounced in upper limbs than in lower limb muscles. The weakness does not alleviate or exacerbate repetition. All distal limb muscle power was less affected than the proximal muscles. Reflexes were present, and the pinprick sensation was normal. EKG revealed sinus rhythm. There was no muscle atrophy, rash over knuckles, or anterior chest. The rest of her medical record included rheumatoid arthritis diagnosed three years ago. She is currently treated with a combination of methotrexate and etanercept for her RA with DAS 28-ESR of 1.1 points. She had stopped one dose of methotrexate after her COVID-19 vaccination under the recommendation of her rheumatologist.
Laboratory analysis at admission revealed elevated aspartate transaminase (AST) 757U/L and alanine transaminase (ALT) 276U/L. Creatine kinase (CK) was 40368, and C-reactive protein was 5.2mg/dL. The autoimmune panel revealed strong positives for the anti-nuclear antibody (>1280), Anti-RNP antibody (>240 U/mL), and Anti-cyclic citrullinated peptide antibodies (>250.0 U/mL). (Table 1) The elevation of AST is thought to be related to muscle damage. Due to the rapid progression of muscle breakdown

despite treatment with aggressive hydration of 80mg/day of methylprednisolone, the myositis panel (Table 2) revealed a positive for anti-signal recognition particle (anti-SRP).
The patient received IVIG therapy for the treatment of IMNM. However, only moderated decrease in CK level was noted. Methylprednisolone pulse therapy was given as follow-up therapy. Rituximab 1000mg was given as a consolidated therapy at the end of the pulse therapy (Figure 1). Methotrexate and Mycophenolate mofetil was also added according to the recommendation from a review article by Allenbach et al.[3]

The patient's muscle power gradually returned after the combination of IVIG and pulsed therapy. Her swallowing function was first to return, followed by the power of her limbs. However, she developed neutropenia about one week after the addition of MTX. She soon suffered from septic shock and expired despite broad-spectrum antibiotics and vasopressors.

Discussion: Here we report a possible adverse reaction to the AstraZeneca COVID-19 vaccine as ranked by the WHO-UMC category. Although our patient had a history of RA, the disease is well controlled by her medications, as evident by her low DAS 28 ESR score. The onset of myositis developed within one week of vaccination without any other possible explanation. It is thought that her IMNM may be triggered by the vaccine injection. The patient was initially treated as rhabdomyolysis, and inflammatory myositis was not suspected until she deteriorated both clinically and in lab analysis despite standard treatment with hydration. Due to the rarity of IMNM, no guideline was established for treatment recommendations. In this case, we followed the suggestion from a review by Allenbach et al.[3] The patient had good recovery of muscle power and decline of CK level until the addition of MTX, which, she developed neutropenia and deteriorated rapidly, and died from septic shock.

To our knowledge, this is the first case of post-COVID-19 vaccine IMNM. There were cases of inflammatory myositis following other vaccines being reported before, but the instance rate is very low.[4] It is of note that research of the literature showed a case of seronegative IMNM related to COVID-19 infection.[5] This brings the possibility that the spike protein being used as the COVID-19 vaccine is related to the trigger of autoimmune disease instead of the adjuvant.

Conclusion: Despite this complication related to the vaccination, the AZ vaccine is still one of the most effective measures against the COVID-19 pandemic, and the benefit of vaccination still outweigh the possibility of harm.

Reference

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Table 1. Autoimmune profile at admission. Elevated ANA and Anti-CCP are compatible with the patient's history of RA

Lab Finding	**Result**	**Unit**	**Reference Range**
ESR	54	mm/hr	<21
Anti-Nuclear Ab	>1280		
Anti dsDNA	2.7	IU/mL	<10
Anti-La Antibody	0.6	U/mL	<7
La Antibody	0.6	U/mL	<7
Ro Antibody	0.6	U/mL	<7
Anti-RNP Antibody	>240.00	U/mL	<5
Anti-Smith Antibody	19	U/mL	<7
Anti-CCP	>350.0	U/mL	<7

Table 2. Myositis panel. The patient is positive for anti-SRP, which is diagnostic of immune-mediated necrotic myopathy

Lab Finding	**Result**	**Lab Finding**	**Result**
Mi2alpha	negative	Scl 75	negative
Mi-2B	negative	Jo-1	negative
TIF1 r	negative	SRP	+
MDA5	negative	PL-7	negative
NXP2	negative	PL-12	+
SAE1	negative	EJ	negative
KU	Positive	OJ	negative
Scl 100	negative	Anti-ENA-Ro-52	negative