Pleuropericarditis and Exudative Pleural and Pericardial Effusions after Administration of Shingrix Vaccine

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Abstract: The adjuvanted subunit vaccine, Shingrix (GSK, Belgium) is now preferred over the live attenuated virus vaccine Zostavax (MSD, USA) due to its comparatively longer immune response durability. Autoimmune/autoinflammatory Syndrome Induced by Adjuvants (ASIA) refers to immune mediated disease triggered by adjuvants in vaccines intended to enhance antigen-specific immune response. Clinicians should be aware of this syndrome given the replacement of Zostavax by Shingrix. We present the first reported case of pleuropericarditis associated with Shingrix vaccine.

Keywords: Autoinflammatory Syndrome, ASIA Syndrome, Shingrix Vaccine, Pleuropericarditis, Pericardial Effusion, Pleural Effusion.

OBJECTIVE

Symptoms after vaccination can pose a diagnostic challenge. Awareness of ASIA can result in a timely diagnosis and appropriate treatment. Subtle patterns of systemic inflammation can be recognized from the history, EKG, labs, and imaging. ASIA may require a longer treatment course.

Case Report

A 73-year-old man with asymptomatic coronary artery disease after stent placement for a myocardial infarction 10 years prior, and the Shingrix vaccine 2-days prior, developed soreness in his left upper chest, left shoulder, and neck, worsened with activity while working in his yard. He presented to the Emergency Department (ED) after 3-days of symptoms and discharged with a diagnosis of chest pain after review of his EKG and Troponin I. There was mild neutrophilia (6.66 x 10^3/uL). The initial computer interpretation of the ECG stated, “ST elevation suggests acute pericarditis,” which was subsequently amended to “ST (T wave) deviation still present.”

He returned to the ED 3-days later with worsening pleuritic chest pain. Transient QT interval prolongation, and precordial biphasic and inverted T waves were noted on EKG (Figure 1). A CT angiogram demonstrated a moderate sized pericardial effusion, mild bibasilar atelectasis/infiltrates, and small left greater than right pleural effusions (Figure 2). He received Ketorolac 15 mg IV, and was discharged on Amoxicillin/Clavulanate 875-125 mg twice daily for 10 days and Ibuprofen 600 mg every 6 hours prn.

He returned to the ED 3-days later after experiencing episodes of tachycardia for 48-hours lasting up to 2-hours each. His rhythm strip and EKG demonstrated recurrent Supraventricular tachycardia at a rate of 160, requiring Adenosine and Metoprolol to control. An echocardiogram redemonstrated a moderate-sized pericardial effusion which prompted measuring a C-Reactive Protein, elevated at 222 mg/L. A chest x-ray re-demonstrated the left pleural effusion. He underwent thoracentesis of 900 mL of exudative fluid. He was administered prednisone 40mg and colchicine 0.6mg for inflammatory pleuritis and pericarditis with an elevated Rheumatoid Factor and ANA 1:160 with a homogenous pattern. He was discharged on a 5-day course of Prednisone 20mg daily.

He returned to the ED 8-days after discharge, 2-days after finishing his prednisone course, with recurrent pleuritic chest pain. His EKG showed QT prolongation. He was diagnosed with pleurisy and provided Hydrocodone/Acetaminophen.

3-days later, the patient requested another course of prednisone citing that this was an effective treatment for his pain. He was provided a 19-day taper of prednisone with his CRP normalizing on day 7. He experienced a return of chest tightness at a dose of 10mg and therefore his prednisone taper was lengthened to 50 days.

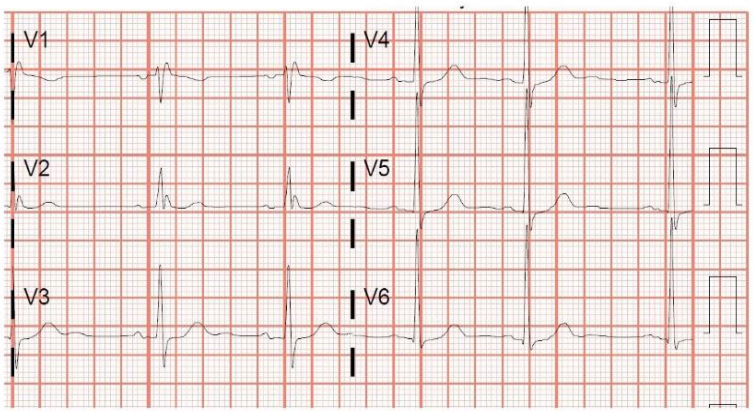
DISCUSSION

Autoimmune syndromes following vaccination are rare and the benefit of vaccines outweigh the risks. Herpes zoster is associated with significant morbidity, with 1:10 developing post-herpetic neuralgia. Zostavax’s declining vaccine efficacy with increasing age motivated the adoption of Shingrix. Shingrix’s adjuvants include: S21, which is a molecule extracted from a South American tree, and MPL which is a lipopolysaccharide derived from the Salmonella minnesota1. These adjuvants stimulate dendritic cells to enhance antigen presentation to T-cells and promote inflammatory reaction. The median onset of symptoms after vaccination has been reported to be one week (2 days – 5 years)2.

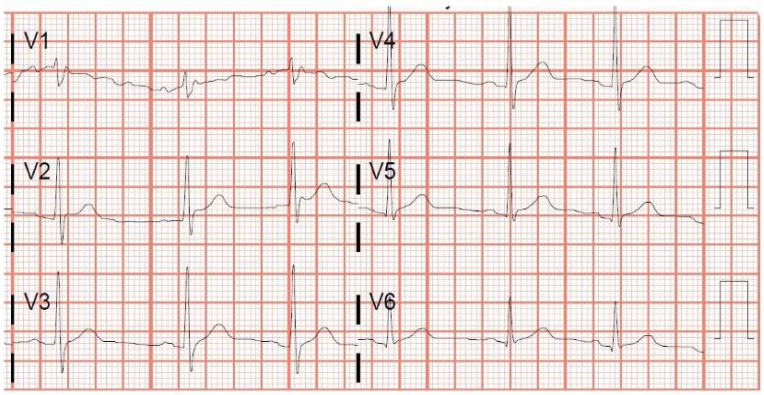
The EKG findings of pericarditis can be subtle and can be seen on the initial EKG with PR-segment depression and ST-segment elevation better appreciated in comparison with his known baseline. On the second EKG, T-wave inversions are seen along with QT-interval prolongation. QT-interval prolongation has been reported in chronic inflammatory arthritis patients with elevated C-reactive protein (CRP) and IL-6 levels3, with dendritic cells being one source of IL-6.

Elevated IL-6 levels cause neutrophilia which can indicate an autoimmune or autoinflammatory state if infection is excluded4. A low-titer homogenous pattern ANA can suggest a drug-induced lupus. As with other autoimmune conditions, a longer steroid course may be appropriate.

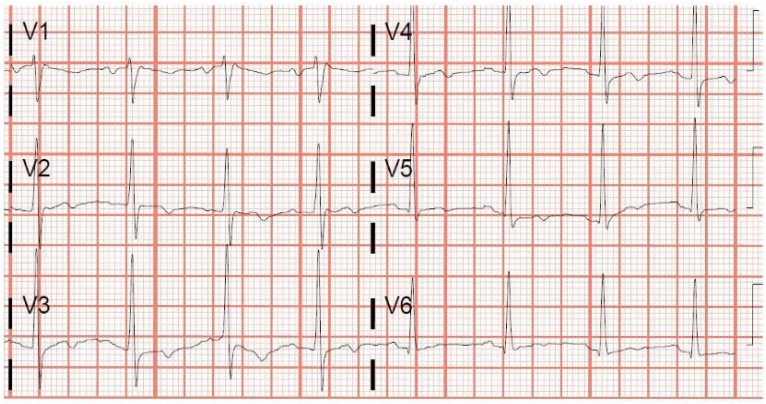
Baseline
QTc 416 ms



Visit 1
Pleuritic chest pain
QTc 429 ms



Visit 2
Pleuritic chest pain
QTc 537 ms



Visit 4.
Pleuritic chest pain
QTc 542 ms

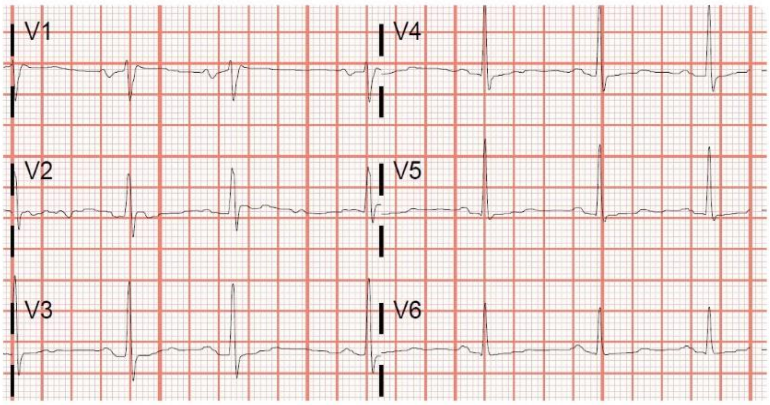


Figure 1: EKG findings in precordial leads comparing baseline to visits for pleuritic chest pain demonstrating subtle ST segment and T wave changes and transient QT interval prolongation.

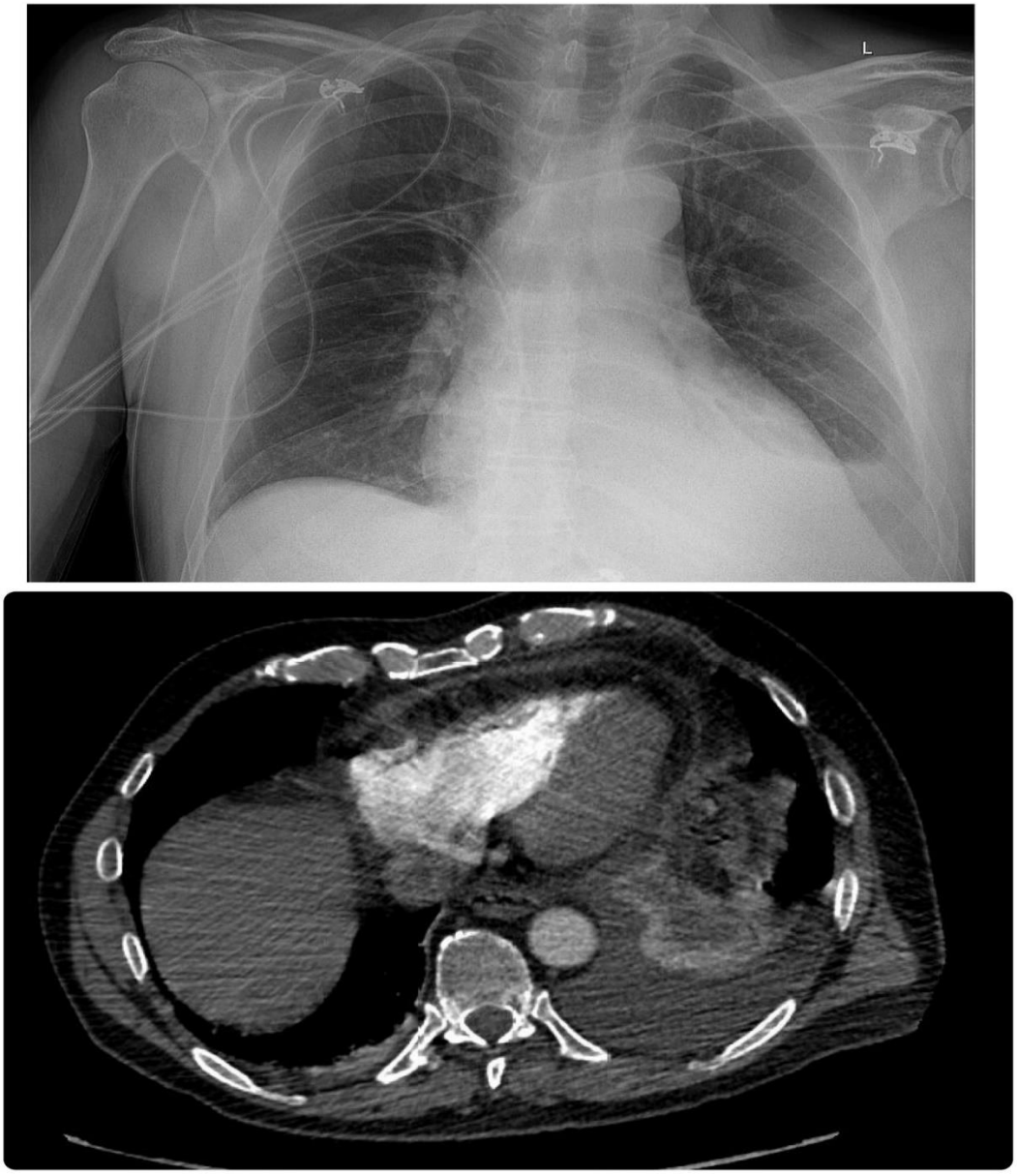


Figure 2: Imaging demonstrating effusions

References

[1] Heydari-Kamjani M, Vante I, Uppal P, *et al.* Uveitis sarcoidosis presumably initiated after administration of Shingrix vaccine. Cureus 2019; [cited 2022 Oct 23]. Available from: https://www.cureus.com/articles/20208-uveitis-sarcoidosis-presumably-initiated-after-administration-of-shingrix-vaccine

[2] Watad A, Bragazzi NL, McGonagle D, *et al.* Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) demonstrates distinct autoimmune and autoinflammatory disease associations according to the adjuvant subtype: Insights from an analysis of 500 cases. Clin Immunol 2019;203:1-8.

[3] Lazzerini PE, Capecchi PL, Bertolozzi I, *et al.* Marked QTc prolongation and Torsades de pointes in patients with chronic inflammatory arthritis. Front Cardiovasc Med 2016; [cited 2022 Oct 23]. Available from: http://journal.frontiersin.org/Article/10.3389/fcvm.2016.00031/abstract

[4] Xu Y, Cheng M, Shang P, Yang Y. Role of IL-6 in dendritic cell functions. J Leukoc Biol 2022;111(3):695-709.