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Guillain-Barré syndrome after vaccination against COVID-19

Guillain-Barré syndrome after vaccination against COVID-19 has been reported worldwide.[1,2] Albeit rare, Guillain-Barré syndrome after vaccination is of great public concern given that it could potentially result in life-threatening paralysis. We report the findings of two patients with Guillain-Barré syndrome after receiving the BNT162b2 vaccine (tozinameran, Pfizer–BioNTech) who were in complete remission from diffuse large B-cell lymphoma.

An 80-year-old woman (patient 1) visited the Research Institute and Hospital of National Cancer Center (Goyang, South Korea) on June 30, 2021, and reported a 5-day history of gradual weakness in her right hand and both legs, preceded by a tingling sensation. She was in complete remission from diffuse large B-cell lymphoma; the last round of chemotherapy had been administered in March, 2015. Patient 1 received the second dose of the BNT162b2 vaccine on June 19, 2021.

On neurological examination of patient 1, distal dominant weakness was noted with absent deep tendon reflexes. A nerve conduction study showed axonal type sensorimotor peripheral polyneuropathy. Detailed evaluation is shown in the appendix (pp 1–2). To rule out lymphoma relapse, ^{18}F-fluorodeoxyglucose (^{18}F-FDG) PET and CT was performed. Mild-to-moderate irregular increased ^{18}F-FDG uptake along a neurovascular bundle was observed (figure, video).

Since the initial clinical manifestation in patient 1 was not typical of Guillain-Barré syndrome, high-dose methylprednisolone therapy was initiated under the suspicion of inflammatory peripheral polyneuropathy or a lymphoma relapse. However, the symptoms of patient 1 progressed to quadriparesis. A follow-up nerve conduction study and an electromyographic study revealed subacute polyradiculoneuropathy. The acute motor and sensory axonal neuropathy form of Guillain-Barré syndrome was suspected, and intravenous immunoglobulin (IVIG; 2 g/kg) was administered. After IVIG infusion, the patient's pain and weakness improved slightly. She was referred to a rehabilitation facility after 22 days of hospital treatment.

A 76-year-old woman (patient 2) presented with a tingling sensation in her upper and lower limbs, which had started from late June, 2021. She visited the emergency room of the Research Institute and Hospital of National Cancer Center on Aug 9, 2021, for repeated falls caused by bilateral lower limb weakness. The patient was in complete remission from diffuse large B-cell lymphoma; the last chemotherapy treatment was in February, 2021. Patient 2 received the second dose of the BNT162b2 vaccine on June 8, 2021.

On neurological examination of patient 2, quadriparesis was observed, with the absence of deep tendon reflexes. Findings of a nerve conduction study indicated sensorimotor peripheral

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See Online for appendix

See Online for video

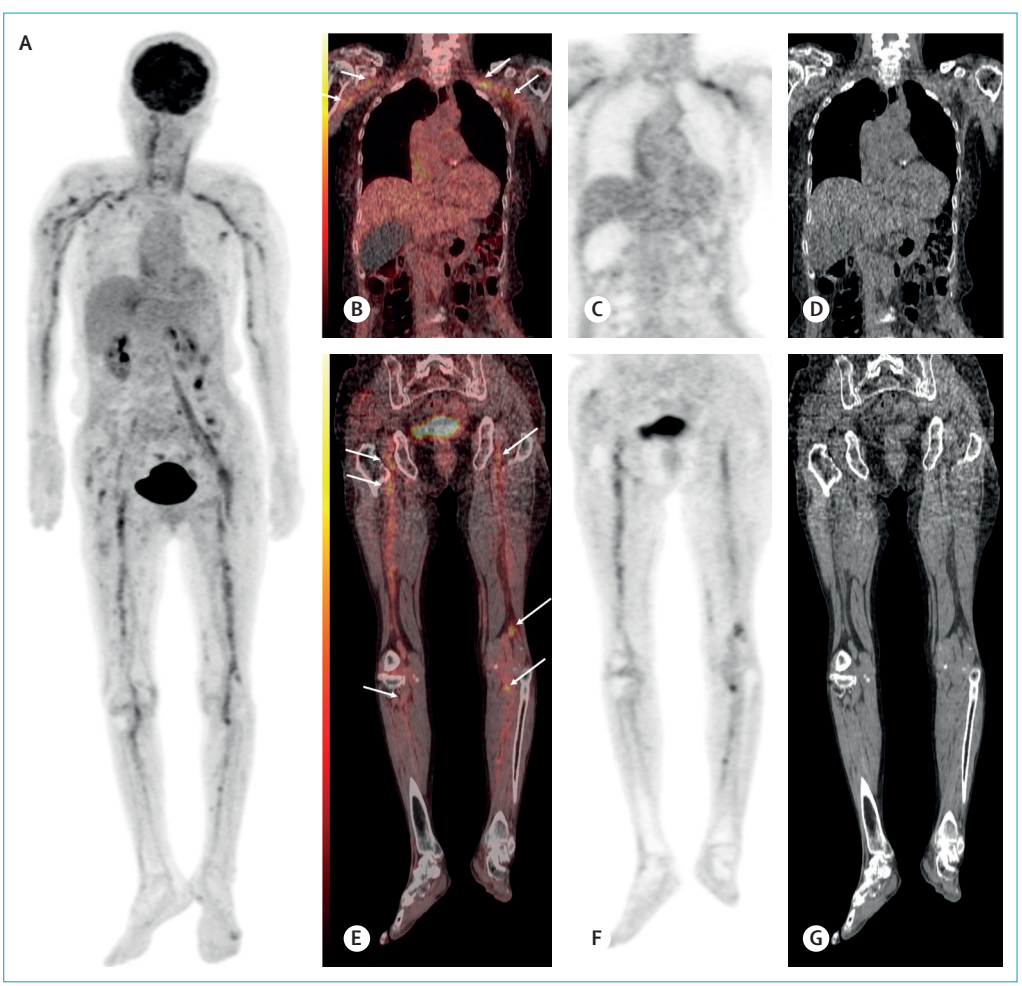

Figure: **^{18}F-FDG PET and CT findings of patient 1**
(A) Maximal intensity projection image of patient 1. ^{18}F-FDG PET/CT exhibited diffuse irregular ^{18}F-FDG uptake along the peripheral nerves, involving bilateral brachial plexus, ulnar, sciatic, and tibial nerves. Fusion coronal ^{18}F-FDG PET and CT (B), PET (C), and CT (D) images of the thorax. Increased ^{18}F-FDG uptake along bilateral brachial plexus is seen (SUV_{max} on right side, 3·73; SUV_{max} on left side, 3·81). Fusion coronal ^{18}F-FDG PET and CT (E), PET (F), and CT (G) images of lower limbs (SUV_{max} on right sciatic nerve, 4·23; SUV_{max} on left sciatic nerve, 3·45). White arrows indicate involved nerves. Colour bar (in B and E) indicates SUV_{max} range from 0 (white) to 5 (black).
^{18}F-FDG=^{18}F-fluorodeoxyglucose. SUV_{max}=maximum standardised uptake value.

polyneuropathy compatible with Guillain-Barré syndrome. CSF analysis showed cytoalbuminologic dissociation. The patient was diagnosed with the acute inflammatory demyelinating polyneuropathy subtype of Guillain-Barré syndrome, and IVIG (2 g/kg) was administered. Proximal weakness of the upper limbs, and the tingling sensation, were relieved. Patient 2 was referred to a rehabilitation facility after 4 days of treatment in hospital.

In South Korea, ChAdOx1 nCoV-19 (AZD1222, Oxford–AstraZeneca) and BNT162b2 vaccines had been predominantly used until August 2021, and thereafter a mixed combination of these vaccines was used (ChAdOx1 nCoV-19 for first dose and BNT162b2 for second dose). In November 2021, use of the ChAdOx1 nCoV-19 vaccine was ceased in South Korea.

In July 2021, the European Medicines Agency and US Food and Drug Administration recommended increased awareness of Guillain-Barré syndrome after ChAdOx1 nCoV-19 and Ad26.COV2.S (Janssen) adenoviral vector vaccines.[3,4] As of Aug 15, 2021, according to the adverse event reports after COVID-19 immunisation in South Korea, acute paralysis events (including Guillain-Barré syndrome) occurred in 620 (0·0059%) of 10409265 recipients after at least one dose of the ChAdOx1 nCoV-19 vaccine and in 382 (0·0055%) of 6908787 recipients after at least one dose of the BNT162b2 vaccine; no significant difference was noted (p=0·25).[5] A caveat is that cases were not always refined by experienced neurologists.

In this case series, two older women in remission from diffuse large B-cell lymphoma developed Guillain-Barré syndrome (acute motor and sensory axonal neuropathy and acute inflammatory demyelinating polyneuropathy subtypes) after receiving the BNT162b2 vaccine. Patient 1 fulfilled level 2 of the Brighton criteria for diagnostic certainty and patient 2 fulfilled level 1 of these criteria.[6] The calculated Naranjo adverse reaction scale score was 7, suggesting a probable association between the vaccination and Guillain-Barré syndrome.[7] However, we cannot confirm the causal relation between Guillain-Barré syndrome and the BNT162b2 COVID-19 vaccine, since the two cases of Guillain-Barré syndrome reported could be coincidental, and our report presents the temporal relation (within 4 weeks) only. Notably, both patients had underlying B-cell lymphoma. Aberrant B-cell function, even in remission status, could trigger the development of Guillain-Barré syndrome after vaccination and would be a potential predisposing factor. Such an extensive vaccination drive that is underway, including all age groups (from young people to older adults), is an unprecedented event in the COVID-19 era. Therefore, we might now observe the development of Guillain-Barré syndrome among patients with diffuse large B-cell lymphoma. Collectively, we suggest that clinicians should be vigilant in suspecting a diagnosis of Guillain-Barré syndrome, particularly among patients with B-cell lymphoma.

Additionally, to our knowledge, this is the first report of Guillain-Barré syndrome variants using ^{18}F-FDG PET and CT. Patient 1 had visited hospital immediately after symptom onset, and ^{18}F-FDG PET and CT showed mild-to-moderate irregular uptake of ^{18}F-FDG along the peripheral nerves, possibly related to active inflammatory processes. Considering the previous history of these two patients, neurolymphomatosis could be a differential diagnosis, which we could not completely exclude.[8] Nonetheless, neurolymphomatosis usually exhibits intense ^{18}F-FDG uptake, up to the maximum standardised uptake values (5·0), with thickening of the involved nerve, and we did not see these findings in patient 1.[9] Large vessel vasculitis would be another differential diagnosis. However, a large vessel, such as the aorta or femoral artery, was not involved, which led us to suspect polyneuropathy rather than vasculitis in patient 1.[10]

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