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BRIEF REPORT

Title

Multisystem inflammatory syndrome in a male adolescent after his second Pfizer-BioNTech COVID-19 vaccine

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Multisystem inflammatory syndrome (MIS) in children (MIS-C) is a complication of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, while myocarditis is a rare adverse effect to messenger ribonucleic acid (mRNA) SARS-CoV-2 vaccines, especially in males aged 12-17 years.[1,2] As far as we are aware, no cases of MIS-C after mRNA SARS-CoV-2 vaccinations have been reported in children or adolescents. However, one case of MIS after the Pfizer-BioNTech mRNA vaccine has been described in a 44-year-old woman without a previous SARS-CoV-2 infection.[3]

We present details on a 17-year-old previous healthy male adolescent who fulfilled the diagnostic criteria for MIS-C after the Pfizer-BioNTech vaccine.[4] He developed fever, vomiting, myalgia and chest pain five days after his second dose of the Pfizer-BioNTech vaccination. After two days, he was admitted to hospital with high levels of inflammatory parameters and multisystem involvement of the gastrointestinal tract, skin, central nervous system, kidneys, liver, coagulation, lungs and heart (Table 1). The patient developed myocarditis, with a severely reduced ejection fraction of 20%. He received therapy in the intensive care unit for six days with norepinephrine infusion, high-flow oxygen therapy, steroids, intravenous immunoglobulin and antibiotics. The patient was discharged after 10 days of hospitalisation. Cardiac magnetic resonance imaging the day after discharge revealed normal left ventricular ejection fraction of 62% and was consistence with myocarditis with subepicardial late gadolinium enhancement. During a follow-up visit eight days after discharge, the patient was asymptomatic, except fatigue, with no obvious clinical sequelae (Table 1). He returned to school the week after discharge from the hospital.

In-depth investigations excluded a wide range of differential diagnoses, including septic shock and toxic shock syndrome, meningitis, Kawasaki syndrome, macrophage activation syndrome, SARS-CoV-2 vaccine-induced immune thrombotic thrombocytopenia, *Legionella pneumophila* and cat-scratch disease. The following viral infections were also excluded: enterovirus, parechovirus, adenovirus, cytomegalovirus, Epstein-Barr-virus, herpes simplex virus, norovirus, rotavirus, influenza virus and human parvovirus B19. The patient's polymerase chain reaction SARS-CoV-2 test was negative on admission and he had negative nucleocapsid SARS-CoV-2 immunoglobulin G, but a

high level of SARS-CoV-2 spike glycoprotein immunoglobulin G (> 5.680 IU/ml). The case was reported to the European Medical Agency. The patient and his parents agreed that his details could be published.

To our knowledge, this is the first reported case of an adolescent who developed fever and multisystem inflammation following an mRNA SARS-CoV-2 vaccination. He fulfilled the diagnostic definition for a level one definitive case of MIS-C after COVID-19 vaccination, as defined by Vogel *et al*.[4] Differential diagnoses were thoroughly investigated and excluded, including a previous SARS-CoV-2 infection.

Although the mRNA vaccine cannot be established as the cause of this case of MIS-C, it was compatible with the known spectrum of vaccine reactogenicity. The side effects of mRNA vaccines, which have been reported to occur in up to one-third of adolescents, are fever, headache and myalgia. In addition, myocarditis, often accompanied by fever and myalgia, is a rare adverse effect of mRNA vaccines.[1,2] Furthermore, myocarditis occurs more frequently in male adolescents after the second vaccine.[1,2] This was in accordance with our male adolescent developing MIS-C with myocarditis a few days after the second vaccination.

If the inflammation in our patient was caused by the Pfizer-BioNTech vaccine, it still remains an extremely rare condition as no other cases fulfilling the criteria for MIS-C after COVID vaccination have been reported in adolescents, despite nine million vaccinated children in the USA.[1] This contrasts with MIS-C after SARS-CoV-2 infection, which has been reported to occur in one in approximately 4,000 children and adolescents.[5]

In conclusion, this case raises suspicion of a rare association between the Pfizer-BioNTech mRNA SARS-CoV-2 vaccine and MIS-C in a male adolescent.

ABBREVIATIONS

SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; MIS, multisystem inflammatory syndrome; MIS-C, MIS in children; mRNA, messenger ribonucleic acid;

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

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Table 1. Details of clinical findings, investigations and treatment

Hospitalisation status	**Day 1[§] Ward**	**Day 2 Ward**	**Day 3 ICU**	**Day 4 ICU**	**Day 5 ICU**	**Day 6 ICU**	**Days 7-10 ICU/ward**	**Day 18 Follow-up**
Clinical findings	Fever, headache vomiting, lethargy, myalgias	+Diarrhoea +Diffuse rash +Dehydration	+Hypotension (80/40 mmHg) +Dyspnoea	+Chest pain	Ending of fever, headache, vomiting, rash		Clinical stable	Fatigue. No obvious clinical sequelae
Investigations	Blood cultures: Negative	Chest X-ray: Normal Urine culture: negative	Chest CT: Bilateral infiltrations, pulmonary oedema, pleural effusions Abdominal CT: Mesenteric adenitis, periportal oedema Lumbar puncture: Normal CSF Blood culture: Negative TTE: LV ejection fraction 40%		TTE: LV ejection fraction 20% Chest X-ray: Bilateral infiltrations, pleural effusions	TTE: LV ejection fraction 45%		TTE: Normal
Treatment	Fluid therapy Antipyretics Antiemetics	Fluid therapy Antipyretics Antiemetics	Norepinephrine infusion Hydrocortisone (IV) Antibiotics High-flow oxygen	Norepinephrine infusion IVIG (100 grams) Hydrocortisone (IV) High-flow oxygen Antibiotics	High-flow oxygen Methylprednisolone (IV) Antibiotics	Methylprednisolone (IV) Antibiotics	Oxygen (intermittent) Prednisolone (oral)	Prednisolone (oral)
Biochemistry								Reference
C-reactive protein	148	255	304	305	286	145	61-14	<8 mg/L
Procalcitonin	0.7		22	>50	>50	22		<0.5 µg/L
Ferritin				920				22-355 µg/L
Leucocyte count	11.8	9.9	6.0	15.0	10.5	8.6		4.4-10.5
Haemoglobin	8.7				6.4		7.8-9.1	6.6-9.9 mmol/L
Platelets	189	169	101	126	108	141		165-435
INR	1.3		1.2	1.2	1.2	1.2		<1.2

APTT	41		53	51	46	34		22-38 s
Fibrinogen	12		16	15	15	13		5.0-11 µmol/L
D-dimer	1.3		4,4	6.4	4.4	3.7		<0.7 mg/IFEU
Antithrombin	0.91		0.58	0.65	0.50	0.56		0.85-1.2 x 10^3
ALAT	29		33		318	278		10-50 U/L
Creatinine	108	127	136	256	164	122	99-75	52-93 µmol/L
eGFR/1.73 m^2	86	71	65	30	52	75		>60 ml/min.
Creatinine Kinase	114				402			30-370 U/L
CK-MB	<1.0			68.9	10.3			<7 µg/L
Troponin I	<3		12	10507	5886			< 7ng/L
Troponin T					219		189	<14 ng/L
ProBNP	162			17844	16638		9796	<300 ng/L

[§]The patient developed the first symptoms two days before hospitalisation (five days after the second vaccine).

ALAT, alanine aminotransferase; APTT, activated partial thromboplastin time; CK-MB, creatinine kinase myocardial band; CSF, cerebrospinal fluid; CT, computerized tomography; ICU, intensive care unit; IV, intravenous; IVIG, intravenous immunoglobulin; LV, left ventricular; proBNP, pro b-type natriuretic peptide; TTE, transthoracic echocardiogram