SHORT REPORT

Live viral vaccines in a DiGeorge syndrome patient

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We report a case of pneumonia in a 13 month old male child with partial DiGeorge syndrome who died after inadvertently receiving live viral vaccines. Although live viral vaccines have been used safely in some children with DiGeorge syndrome, there are insufficient data to recommend their routine use in those with severe immunodeficiency.

Although live viral vaccines have been safely administered to some patients with partial DiGeorge syndrome,^{1,2} no published guidelines exist for their use in this patient population. This report describes a 13 month old boy with partial DiGeorge syndrome and complex congenital heart disease who developed pneumonia following administration of live viral vaccines.

CASE REPORT

A 13 month old male child with DiGeorge syndrome and complex congenital heart disease was admitted to our hospital with a 1 week history of decreased oral intake, lethargy, vomiting, and one episode of haematemesis.

He was a full term infant diagnosed at 5 days of age with tetralogy of Fallot. At 10.5 months of age, a Rastelli procedure was performed. Genetic testing at birth demonstrated a hemizygous 22q11.2 deletion, confirming a diagnosis of DiGeorge syndrome. During the first 3 months of life, he had recurrent oral candidiasis but had no other significant infections. At 8 months of age, he was found to be severely immunosuppressed with a total of 396 T cells/ μ l (21%) (nl: 2400–6900; 50–77%), 320 CD4 T cells/ μ l (17%) (nl: 1400–5100; 33–58%), and 57 CD8 T cells/ μ l (3%) (nl: 600–2200; 13–26%) and was placed on prophylactic trimethoprim/sulphamethoxazole. Lymphocyte response to the mitogen PHA was within normal range when analysed at 12 months of age. Despite a recommendation not to administer live vaccines, he inadvertently received MMR and live attenuated varicella vaccine at 12 months of age.

Physical examination on admission revealed a thin, pale, afebrile but irritable 13 month old child. He was well perfused but tachycardic with a grade 4 holosystolic murmur radiating to the back. Respiratory exam revealed tachypnea and sparse inspiratory crackles bilaterally. His liver was palpated 4 cm below the right costal margin. No rash was noted.

Initial laboratory examination data revealed a non-immune haemolytic anaemia and chest radiograph demonstrated worsening congestive heart failure. Treatment with packed red blood cell transfusion and aggressive diuresis with furosemide was started.

After developing a fever and increasing diffuse patchy infiltrates on chest radiographs, a bronchoscopic examination was performed on day 11 of hospitalisation and showed multiple white plaques on an erythematous base in the bronchi. Microscopic examination of the bronchoscopy specimen showed many haemosiderin-laden macrophages and few multinucleated giant cells with nuclear inclusions (fig 1), suggesting a viral pneumonia. The culture of the specimen grew

Candida tropicalis but was otherwise negative for all other infectious aetiologies including varicella by PCR. The patient was treated with 2 weeks of antifungal therapy for a possible candidal pneumonia.

The patient remained febrile, mechanically ventilated, and on medication to support his blood pressure. On day 19 of hospitalisation, 7 weeks post-immunisation, he developed five vesicular lesions on his trunk. The lesions were positive for varicella zoster virus by direct fluorescent antibody and positive for the varicella vaccine strain by PCR. Tracheal aspirates (tracheal aspirates 1–3) from the same time period also demonstrated varicella vaccine strain by PCR (fig 2). Tracheal aspirates and urine samples were negative for measles by PCR. The rash did not progress and he received 10 days of aerosolised and intravenous ribavirin as well as 14 days of intravenous acyclovir to treat possible measles and/or varicella pneumonia.

The patient died due to a pulmonary haemorrhage at 19 months of age after prolonged intubation for chronic lung disease. Autopsy showed extensive pulmonary damage and haemorrhage and generalised lymphadenopathy. No thymic tissue was evident. Specific viral immunohistochemistry stains were negative. VZV was not detected in lung or lymph node tissue by PCR. GMS stains for fungal organisms were negative.

DISCUSSION

Patients with DiGeorge syndrome have a variable degree of immunodeficiency due to an underdeveloped thymus. The majority of patients have a partial cellular defect, with a variable decrease in absolute T cell numbers and typically a mild to moderate immunodeficiency without apparent predisposition to opportunistic infections.³ Limited studies have been done on the use of live viral vaccines in the DiGeorge population. Two retrospective studies have reviewed vaccine adverse events in DiGeorge patients and found rates of side effects such as fever and rash to be no higher than those of the general population.^{1,2} In both studies, however, the total CD4 T cell counts were significantly higher than the CD4 T cell counts of our patient.

Figure 1 Papanicolaou stain of a bronchoscopy specimen showing the clustering of nuclear inclusion bodies within a giant cell.

Figure 2 M: molecular weight standard (622–67 bp); U: undigested, B: digested with Bgl-I restriction endonuclease, P: digested with Pst-I restriction endonuclease. Lanes 1–6: undigested, Bgl-I, and Pst-I restriction digestions, respectively, of control WT (1–3) and Oka isolates (4–6). Lanes 7–18: undigested, Bgl-I, and Pst-I restriction digestions, respectively, of patient samples from tracheal aspirate 1 (7–9), tracheal aspirate 2 (10–12), tracheal aspirate 3 (13–15), and skin lesion (16–18), all of which exhibit the Oka vaccine pattern (Bgl-I lanes: 350 bp undigested product, 222 bp digested to 135 bp and 87 bp fragments; Pst-I lanes: 350 bp and 222 bp undigested products).

Our patient's severely immunocompromised status placed him at risk for varicella as well as measles pneumonitis following live viral vaccination. The varicella positive tracheal aspirates likely represented mucosal involvement by the vaccine strain, although the bronchoscopic specimen was negative for varicella by PCR. Approximately 5% of immunocompetent vaccinees will develop a mild varicella-like rash about 1 month after vaccination; however, this percentage is significantly higher in patients with greater degrees of immunosuppression.⁴ As with varicella vaccine administration, the degree of immunosuppression is also important in predicting adverse reactions to MMR vaccination. Subsequent to the death of an HIV infected man due to vaccine strain measles pneumonitis, the Advisory Committee on Immunization Practices (ACIP) revised their recommendations and advised withholding MMR vaccination from severely immunocompromised persons such as our patient, defined as a CD4 T lymphocyte count of less than 750 cells/ μ l or less than 15% of total lymphocytes for children less than 1 year of age.⁵

Although tracheal aspirates and urine samples were negative for measles by PCR, the clustering of nuclear inclusion bodies within giant cells seen on the bronchoscopy specimen was suggestive of measles.

In conclusion, although live viral vaccines are likely safe in some children with partial DiGeorge syndrome, our patient's post-immunisation course suggests that caution and further study are needed in DiGeorge patients with severe immunodeficiency.

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