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Is It or Is It Not Vaccine-associated Paralytic Poliomyelitis: A Case Report of Acute Flaccid Paralysis after Oral Polio Vaccine Booster Dose

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Abstract Poliovirus spread has been described as a "Public Health Emergency of International Concern" despite effective immunisation programmes. With the rare but serious adverse effect of vaccine-associated paralytic poliomyelitis after oral polio vaccination, the target for global eradication has evolved to include both endemic and vaccine-related poliomyelitis. Until oral vaccines are completely withdrawn, the risks of vaccine-associated paralysis continue to exist, requiring a high index of suspicion and timely investigations to evaluate the etiology of acute flaccid paralysis. Here we present a four year old boy with acute paralysis one month after oral polio booster dose. This case illustrates how vaccine-associated paralytic poliomyelitis should be queried as a possible differential during the work-up for acute flaccid paralysis, especially after excluding all other causes and in the context of a positive immunisation history.

Key words Oral poliomyelitis vaccine; Poliomyelitis; Vaccine-associated paralytic poliomyelitis

Introduction

Live oral polio vaccines (OPV) were introduced to the Childhood Immunisation Programme in Hong Kong in 1963, prompting marked reduction in paralytic poliomyelitis, from peak incidences of 11 per 100,000 people in 1962 to zero cases since 1984.[1] The last case was notified in 1983, proving the effectiveness of induced herd immunity through spread of live vaccine polioviruses.[1] Given Hong Kong's polio-free status since 2000, and the acute flaccid paralysis (AFP) surveillance system established in 1997, focus has shifted towards surveillance of imported cases.[1] China likewise became polio-free in 2000 after its last local and imported case in 1994 and 1999 respectively.[2] However, imported wild-type poliovirus from Pakistan led to an outbreak in 2011, reinforcing the importance of global eradication as imported cases still threaten polio-free regions.

Despite significant benefits of OPV, many countries have switched to inactivated polio vaccines (IPV) due to vaccine-associated paralytic poliomyelitis (VAPP). VAPP occurs in approximately 1 in 1.4 million doses in England or 1 in 2.5 million doses in US.[3] Hong Kong reported two cases in 1985 and 1995, with Sabin strains type 3 and 1 isolated respectively.[1] Since 2007, Hong Kong's vaccination programme also changed to IPV combined with diphtheria, tetanus, and acellular pertussis vaccines – the "DTaP-IPV" vaccine.[3] China recommends continuing OPV as imported IPV is limited and self-financed. OPV is given at two, three and four months, with booster at four years old. This regular mass administration has resulted in persistent occurrence of local VAPP cases.

Given Hong Kong's proximity to China, vigilance for VAPP should not be lowered. Until global OPV cessation, prompt recognition of VAPP during AFP evaluation is important. Here we report a child presenting with acute generalised limb weakness one month after OPV booster dose.

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Case Report

Our patient is a four-year-old boy born at full term by normal delivery in Hong Kong, with up-to-date vaccinations in China, most recently the 4th OPV dose on 30th September 2014. Contact history was negative with no record of adverse effects after vaccination or immunodeficiency since birth. He developed fever and cough on 28th October 2014, one month after vaccination, with bilateral hand tremor on exertion the following day due to inability to sustain active movement. This progressed to frank upper limb proximal muscle weakness over the next three days. By day 32 post-vaccination, weakness was generalised over all limbs but more prominent over the left with upper limbs more affected; fever was resolved. Independent gait was retained despite frequent falling and poor muscle strength on rising. He was admitted to a hospital in Zhejiang on 4th November 2014. Initial electrophysiology studies suggested motor neuron disease. Subsequent magnetic resonance imaging (MRI) showed no cord swelling but suspicious hyper-intense T2 signals over the cervical region suggested acute myelitis. Steroids were prescribed with improvement of gait noted. No lumbar puncture was performed. By day 20 of weakness onset, normal gait had resumed but both arms still could not be raised. The child was discharged and referred for rehabilitation. Due to persistent upper limb weakness, he attended our hospital on 20th November 2014, 23 days after weakness onset, and almost two months post-vaccination.

On examination, the child was afebrile with normal tone and sensation over all limbs, and no muscle atrophy or tongue fasciculations. Asymmetrical proximal muscle weakness was noted over bilateral upper limbs and the left lower limb (Medical Research Council Grade 4-/5), with full power over the right proximal lower limb and all distal muscles. The left lower limb and bilateral upper limbs were hypo-reflexive. He could walk independently with small steps and decreased arm swing.

Laboratory evaluation, autoimmune markers, immunoglobulin levels and lymphocyte subset profile were normal (Table 1). Serology for anti-HIV 1 and 2, anti-tetanus and anti-polio 1, 2 and 3 were negative. Contrast MRI spine was normal with no suspicious findings over the cervical region despite ongoing limb weakness. Cerebrospinal fluid (CSF) results were unremarkable with no cytoalbumin dissociation or culture growth. Heavy metal and porphyria screening was negative. Stool cultures yielded no virus or organisms.

Nerve conduction studies confirmed normal conduction velocities and F-wave latencies. Needle electromyography of left biceps, left semimembranosus and left quadriceps showed fibrillation potentials at rest and decreased recruitment pattern on exertion; motor unit action potentials size was normal as remodeling had not occurred yet (Figure 1). Overall findings suggest motor neuron disease with anterior horn cell involvement.

Discussion

WHO recommends that poliomyelitis be considered in anyone younger than fifteen presenting with AFP.[4] Investigations include two stool samples within 14 days of paralysis, collected 24-48 hours apart.[4] Despite no universal definition, VAPP is defined when paralysis occurs 4-40 days post-OPV or if vaccine-related poliovirus is isolated; isolated wild poliovirus is considered confirmed polio.[4] Diagnostic barriers are twofold: suspicion thresholds are high as VAPP is rare and clinically indistinguishable from wild-type poliomyelitis.[5] Furthermore, isolated vaccine-derived strains do not equate to VAPP since infection may result from exposure to recent OPV recipients. Thus adequate contact and vaccination history is as essential as good quality stool specimens within the recommended period. Even in cases presenting beyond two weeks of weakness, like our patient, stool samples are still advocated as vaccine enteroviruses may shed up to two months post-exposure.[5]

Incubation time between OPV and VAPP is 4-40 days, requiring vigilant history tracing.[5] It is postulated that increased replication time in immune-naïve hosts allows vaccine viruses greater opportunity to revert into neurovirulent strains, thus the first dose carries highest VAPP risk: 1 in 1.4 million versus 1 in 27.2 million for subsequent doses.[6] Despite onset within the incubation period, VAPP after the fourth OPV dose is unusual, especially when prior vaccinations were well tolerated in our patient. Failure to isolate the causative strain increases diagnostic difficulties; negative results may be associated with stool collection beyond the shedding period, as our patient was admitted almost two months post-vaccination.

Like wild-type poliomyelitis, VAPP characteristics include fever at onset; asymmetrical weakness within 24-48 hours with proximal muscle predominance; rapid progression till fever resolution, typically after 72 hours; unaffected sensory function; and residual paralysis 60 days post-onset.[7,8] Our patient developed weakness within 24 hours of fever, progressed over 72 hours and plateaued upon fever convalescence, compatible with a poliomyelitis-like

presentation. He was discharged with residual upper limb and mild left proximal lower limb paresis on day 31 of weakness; paralysis beyond 60 days is unknown due to no follow up.

Despite high VAPP suspicion, other AFP differentials must be investigated. In Hong Kong, Guillain-Barre syndrome (GBS) is most common (25.9%) with myelitis in second place (13.4%).[1] GBS is unlikely in our patient given the normal conduction velocities and F-wave latencies; no CSF cytoalbumin dissociation; and negative anti-ganglioside antibodies.[7] Spinal cord imaging is crucial for diagnosing myelitis whilst simultaneously excluding space-occupying lesions like spinal abscesses, tumors and haematomas that can also present as AFP.[7] At weakness onset in China, our

Table 1 Laboratory results of the patient since admission

Laboratory tests	22/11/14	23/11/14	25/11/14	26/11/14	28/11/14	Reference
Infection workup						
Antibody titres						
Influenza A	<10				<10	–
Influenza B	<10				<10	–
M. pneumoniae	20				20	–
Mumps	<10				<10	–
VZV	<10				<10	–
Enterovirus	NSP*				NSP*	–
HSV	<10				<10	–
Anti-Polio 1, 2, 3	Negative					–
Anti-Tetanus	Negative					–
Stool viral studies						
Enterovirus	Negative	Negative				–
Salmonella	Negative					–
Aeromas	Negative					–
Campylobacter	Negative					–
Plesiomonas	Negative					–
Immunological evaluation						
Lymphocyte subset[#]						
B-cells (CD19) %				37.4 (H)		18.5-28%
B-cells (CD19) no.				1877 (H)		500-1200/uL
T-cells (CD3) %				56.1		56-68%
T-cells (CD3)				2808		1500-2900/uL
Th (CD4) %				31.9		29-40%
Th (CD4) no.				1596		1000-2100/uL
Ts/c (CD8) %				19.2		19-25%
Ts/c (CD8) no.				961		700-1100/uL
CD4 : CD8				1.66		1.1-2
NK cells (CD16/56) %				6.5 (L)		9-19%
NK cells (CD16/56) no.				328		300-600/uL
Anti-HIV 1, 2	Negative					–
CSF workup						
Glucose			3.4			2.2-3.9 mmol/L
Protein			0.36			0.12-0.60 g/L
Total cell count			3 x 10^6/L			–
Red cell			Absent			Absent
Oligoclonal proteins			Negative			–
CSF IgG			3.6			<5.5 mg/dl
Serum IgG			777.0			617-1349 mg/dl
Enterovirus				Negative		–
HSV 1, 2				Negative		–
VZV				Negative		–

*Non-specific reaction; [#]Normal values for subjects younger than 18 years of age are for Singaporean Asians.

VZV=varicella zoster virus; HSV=Herpes simplex virus; CSF=cerebrospinal fluid; IgG=Immunoglobulin G

patient's MRI showed suspicious findings in the cervical region with clinical response to steroids, strongly indicative of transverse myelitis. Furthermore, OPV has a causal relationship with vaccine-associated transverse myelitis, a probable diagnosis in this context.[9] However, the second MRI taken on day 30 of weakness onset with persistent upper limb paresis, diverges from expectation as normal imaging in the setting of transverse myelitis is associated with clinical recovery. In this regard, one may suspect co-existing OPV-associated transverse myelitis and VAPP, with the former showing clinical resolution through return of independent gait after steroid treatment and subsequent normal imaging. VAPP is the likely cause of residual upper limb weakness, with the needle electromyography studies performed in China and Hong Kong confirming anterior horn cell involvement.

Other differentials include polio-like paralysis due to non-polio enteroviruses such as coxsackievirus and echovirus.[7] Negative stool cultures in our patient exclude these infections although sampling beyond shedding periods may confound results. Normal CSF studies on cell count, glucose, protein, and bacterial and viral cultures also exclude infectious etiologies of the central nervous system.[7]

Whilst VAPP can indicate immunodeficiency, normal immunoglobulin and lymphocyte subset with negative HIV status confirmed immunocompetence in our patient.[5] Normal antinuclear antibodies and autoimmune markers exclude autoimmune disorders such as systemic lupus erythematosus and polymyositis.[7] Normal creatine kinase levels and electromyography findings further confirm no acute myopathic involvement.[7] Normal electrolytes, thyroid function, ceruloplasmin levels, urine porphyrins and heavy metals screening exclude channelopathies such as hypokalaemic periodic paralysis; hyperthyroidism associated with thyrotoxic periodic paralysis; Wilson's disease; acute porphyria; and poisoning due to heavy metals inclusive of lead, arsenic and thallium.[7] Although uncommon, comprehensive electrolyte, metabolic and endocrine workup is necessary during AFP evaluation to exclude these differentials before considering VAPP.

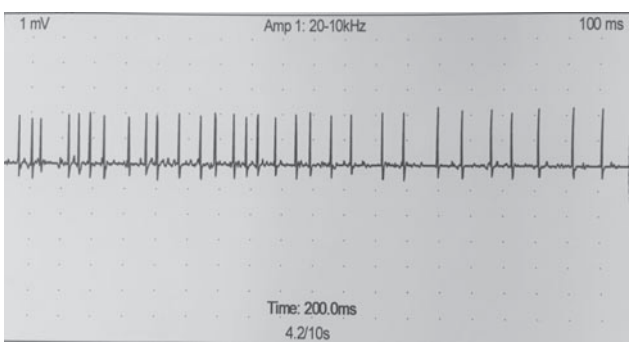

Figure 1 Needle electromyography of the left quadriceps during exertion showing decrease recruitment with incomplete interference pattern. The motor unit potentials are of normal amplitude of up to 2.5 mV.

In summary, we report a case of suspected VAPP presenting one month post-OPV booster dose. Of the 247 AFP cases in Hong Kong since 2011, all were classified as non-poliomyelitis AFP, indicating the rarity of poliomyelitis.[1] Therefore despite VAPP suspicions, the aim should be to exclude other causes whilst seeking confirmation. Given our patient's static limb weakness and negative stool cultures, he was discharged with follow up in China for rehabilitation.

Conflicts of Interest

Ms. Iris Chung was an MBBS V student when she wrote this case report as part of her assignment in the Specialty Paediatrics Clerkship in the University of Hong Kong.

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