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BRIEF COMMUNICATION

TEMPORAL ASSOCIATION BETWEEN THE ISOLATION OF SABIN-RELATED POLIOVIRUS VACCINE STRAINS AND THE GUILLAIN-BARRÉ SYNDROME

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SUMMARY

Thirty eight paralysis cases classified as Guillain-Barré syndrome (GBS) in Brazil were analysed. In all these cases Sabin-related poliovirus vaccine strains were isolated. In most of the cases the last vaccine dose was given months or years before the onset of GBS, suggesting a persistent infection or the transmission of the Sabin-related strains to the patients. The isolation of Sabin-related strains from GBS cases some days or weeks after the onset of the disease, demonstrated a temporal association between the isolation of the strains and the disease. Although the isolates from the GBS cases may not be the etiological agent of the disease, this study strongly indicates that infections caused by Sabin-related vaccine strains can trigger the GBS in certain cases.

KEYWORDS: Sabin vaccine; Poliovirus; Guillain-Barré syndrome - vaccine-associated.

Polioviruses are known as the causative agents of poliomyelitis, a paralytic and some times fatal disease of humans [1, 15]. The attenuated strains developed by Dr. A. Sabin have been effectively used as an oral live vaccine to control the disease and the circulation of wild strains in Brazil [4]. Although a rare event, paralytic poliomyelitis cases classified as vaccine-associated occur in Brazil [6, 7, 8] and also in other countries [1, 13, 15, 18]. The isolation of Sabin-derived strains in Brazil from cases classified as Guillain-Barré syndrome (GBS) [5, 8], facial paralysis [5], and transverse myelitis [8], suggested that these paralysis could also be caused by Sabin-derived strains in certain cases. Guillain-Barré syndrome is an acute demyelinating polyneuropathy with progressive, most often ascending flaccid paralysis of the body [11, 16]. Its cause is unknown, although it is frequently preceded by infections and vaccinations [10, 11, 16, 17]. In the present study paralysis cases classified as GBS in Brazil, and from which type 1, type 2 or type 3 Sabin-related polioviruses were isolated were analysed, indicating that Sabin-derived strains could also trigger the GBS in certain cases.

Polioviruses were isolated from fecal samples from cases classified as GBS [4]. The relationship of the isolates to the P1/Sabin, P2/Sabin or P3/Sabin strains was demonstrated previously by molecular hybridization and PCR [4]. Epidemiological data of the patients is presented in table I. It can be observed in the present study and in a previous study [8] that in certain cases the onset of GBS occurred some days or weeks after a single OPV administration and Sabin-related strains were isolated from these patients. In most of these cases the last vaccine dose was given months or years before the onset of motor deficiency, and in all cases Sabin-related strains were isolated after the onset of

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TABLE 1
Epidemiological data of GBS cases from which Sabin-related strains were isolated

Patient	Age	Origin / year isolat.	Vaccination			Date of onset of motor deficiency	Collecting data of the sample	Isolated virus	t	Clinical background
			Doses	N.	Last dose					
M.C.S.	10 years	DF/90	yes	4	19/05/83	19/01/90	24/01/90 26/01/90	P3v P3v	7 years	GBS (s)
E.F.C.	6 years	PB/90	-	-	-	08/04/90	20/04/90 24/04/90	P3v P3v	-	GBS
T.P.	1 year	RS/90	yes	5	22/09/90	19/11/90	22/11/90 23/11/90	N P3v	2 months	GBS (s)
L.S.	13 years	SP/91	yes	1	-	14/11/91	23/11/91 24/11/91	P3v N	-	GBS
L.D.L.P.	5 years	MG/92	yes	8	17/10/92	17/10/92	28/10/92 02/11/92	P3v N	11 days	GBS (s)
J.V.R.	1 year	RS/92	yes	1	07/05/92	25/09/92	02/10/92 03/10/92	P3v N	5 months	GBS (s)
D.M.G.	5 years	MG/93	yes	4	27/08/91	05/06/93	09/06/93 10/06/93	P3v P3v	2 years	GBS (s)
R.S.S.	6 years	PE/93	yes	1	19/06/93	28/09/93	07/10/93 13/10/93	P3v P3v	4 months	GBS
J.S.M.	2 years	SP/93	yes	6	23/10/93	30/10/93	11/11/93 22/11/93	P3v N	19 days	GBS
V.R.S.	1 year	BA/90	yes	2	11/09/89	02/02/90	13/02/90 14/02/90	Plv+P3v Plv+P3v	5 months	GBS
D.S.S.	1 year	BA/90	yes	8	07/04/90	11/04/90	19/04/90 20/04/90	Plv+P2v Plv+P2v	12 days	GBS
J.A.S.	1 year	BA/90	-	-	-	21/09/90	17/10/90 18/10/90	Plv Plv+P3v	-	GBS
F.C.	2 years	CE/90	yes	2	18/10/88	19/08/90	20/08/90 21/08/90	N Plv	2 years	GBS
T.R.C.	6 years	MG/90	yes	4	-	30/11/90	06/12/90 11/12/90	N Plv+P2v	-	GBS
E.A.S.	7 years	MS/90	yes	8	12/08/89	26/03/90	10/04/90 11/04/90	Plv+P2v+P3v N	8 months	GBS
M.T.C.	< 1 year	RN/90	yes	5	29/09/90	09/10/90	30/10/90 31/10/90	Plv Plv	31 days	GBS (s)
F.P.	1 year	SC/90	yes	4	-	19/11/90	27/11/90 28/11/90	Plv+P2v+P3v N	-	GBS
I.C.S.	9 years	BA/91	yes	3	16/06/84	29/01/91	04/02/91 05/02/91	Plv+P2v+P3v Plv+P2v+P3v	7 years	GBS (s)
D.N.S.	3 years	RJ/91	yes	5	22/09/90	26/04/91	15/05/91 16/05/91	Plv Plv	8 months	GBS
A.M.E.	2 years	SC/91	-	-	-	01/05/91	04/05/91 06/05/91	Plv Plv	-	GBS (s)
F.P.A.	4 years	SP/91	yes	7	22/09/90	04/03/91	11/03/91 14/03/91	Plv+P3v Plv+P3v	6 months	GBS
M.A.J.	< 1 year	SP/91	yes	3	29/11/90	09/03/91	22/03/91	Plv	4 months	GBS
A.F.S.	4 years	AM/92	yes	4	22/09/90	07/05/92	20/05/92 21/05/92	Plv N	2 years	GBS (s)
R.A.S.	4 years	MS/92	yes	8	22/08/92	16/10/92	20/10/92 22/10/92	Plv+P3v N	2 months	GBS (s)
V.L.S.	4 years	SP/92	yes	8	22/09/90	08/07/92	10/08/92 11/08/92	N Plv	2 years	GBS (s)
M.S.R.S.	2 years	BA/93	yes	5	17/10/92	19/03/93	06/04/93 07/04/93	Plv Plv	6 months	GBS (s)

Patient	Age	Origin / year isolat.	Vaccination			Date of onset of motor deficiency	Collecting data of the sample	Isolated virus	t	Clinical background
			Doses	N.	Last dose					
F.S.	5 years	ES/93	yes	8	26/08/92	06/05/93	11/05/93 12/05/93	N Plv	9 months	GBS (s)
T.G.S.	1 year	GO/93	yes	3	03/09/92	17/08/93	22/08/93 23/08/93	Plv Plv	11 months	GBS
R.R.A.	12 years	RJ/93	-	-	-	19/11/93	21/11/93 22/11/93	Plv N	-	GBS (s)
J.L.S.	8 years	PB/94	-	-	-	22/08/94	29/08/94 30/08/94	Plv Plv	-	GBS
W.R.S.	< 1 year	RO/94	yes	1	16/06/94	20/06/94	23/06/94 24/06/94	Plv P2v	7 days	GBS (s)
C.C.M.	8 years	RS/94	yes	5	30/12/88	06/09/94	12/09/94 15/09/94	Plv N	6 years	GBS
G.S.	3 years	SP/94	yes	5	02/01/92	06/08/94	22/08/94 25/08/94	Plv N	2 years and a half	GBS
R.G.A.S.	3 years	GO/90	yes	1	12/08/89	17/04/90	27/04/90	P2v	8 months	GBS
A.S.B.	2 years	RS/91	yes	4	19/12/90	02/09/91	10/09/91 11/09/91	P2v N	9 months fatal case 07/10/91	GBS (s)
C.C.F.	3 years	SE/93	yes	8	17/10/92	15/03/93	18/03/93 20/03/93	P2v P2v	5 months	GBS
L.R.C.U.	3 years	GO/94	yes	5	11/06/94	08/07/94	11/07/94 12/07/94	P2v N	1 month	GBS
M.R.M.	4 years	PR/94	yes	6	13/08/94	20/12/94	27/12/94 29/12/94	N P2v	4 months	GBS

(t) approximate time delay between the last vaccine dose and the isolation of Sabin-related strains.
Plv = Pl/Sabin-related; P2v = P2/Sabin-related; P3v = P3/Sabin-related; N = Negative.
(-) not available data; (s) = sequels.
Brazilian states:
DF = Distrito Federal; PB = Paraiba; RS = Rio Grande do Sul; CE = Ceará; ES = Espirito Santo; SP = São Paulo; BA = Bahia; MG = Minas Gerais; PA = Pará; PE = Pernambuco; MS = Mato Grosso do Sul; PR = Paraná; RN = Rio Grande do Norte; SC = Santa Catarina; RJ = Rio de Janeiro; AM = Amazonas; GO = Goias; RO = Rondônia; SE = Sergipe; MG = Minas Gerais.

motor deficiency. These results demonstrate a temporal association between the isolation of these strains and the GBS, and suggest a persistent infection or the transmission of Sabin-derived strains to the patients [5, 7, 8]. Studies have demonstrated the capacity of Sabin-derived poliovirus strains to cause a persistent infection in vitro [2, 3, 14]. Other studies have demonstrated the capacity of a Theiler's virus strain, also a member of the *Picornaviridae* family, to cause a persistent infection in the central nervous system of mice, leading to demyelination [9]. This study supports the idea that poliovirus strains could also lead to demyelination of the CNS in certain cases.

Studies have demonstrated that GBS is frequently preceded by infections and vaccinations [11, 16]. A significantly increased incidence of GBS cases were observed in Finland [10, 17] in 1985 during and soon after a mass vaccination campaign against poliomyelitis with oral polio vaccine (OPV). In Finland immunization against poliomyelitis is routinely performed with inactivated polio vaccine, and the OPV use was a one time campaign in 1985. In previous studies Sabin-derived polioviruses were isolated in Brazil from cases classified as GBS [5, 8]. The possibility that the OPV triggered the GBS in these cases can not be ruled out. Enterovirus 71 has also been isolated from many GBS cases in Brazil (unpublished results), and Dr. A. Sabin also developed the GBS after working many years with enteroviruses [12]. Although the poliovirus strains isolated from GBS cases in Brazil may not be the etiological agent of the disease, this study strongly indicates that infections caused by Sabin-derived strains can trigger the GBS in certain cases.

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