NEUROVIROLOGICAL RESEARCH OF ENCEPHALITIDES IN AND AROUND KARACHI THE CLINICAL ASPECTS (INTERIM REPORT)

Pages with reference to book, From 159 To 169

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Abstract

One hundred-and-fourteen cases of encephal itides and encephalopath ies were selected from the patients admitted to the Neurology ward Civil Hospital, Karachi (CHK), during the twelve years' period from 1971 to June 1983. There were eleven cases of subacute scierosing pan encephalities (SSPE) and seven cases of chronic progressive encephalopathies (CPE).
Forty-three cases of encephalitides and encephalopathies were collected at the CHK during the eight and a half months period (July 1983 to March 1984) on which clinical and serological studies were performed.
Of these, nineteen were cases of acute encephalitides which included five cases of Japanese encephalitis and two probable and three possible cases of herpes simplex encephalitis.
In the 43, seven cases of SSPE or SSPE-like diseases were found, all of which were associated with positive antibodies against measles virus in cerebrospinal fluid (CSF).
Besides, six cases of subacute encephalitis or encephalopathy other than SSPE or SSPE or SSPE-like diseases were collected, one of which was associated with positive CSF antibodies against rubella virus, and another was a case of typhoid encephalopathy. -
Seven cases of CPE were also found in the 43, but their aetiology remains to be elucidated (JPMA 36:159, 1986).

INTRODUCTION

This Project originated from the report published in this Journal by one of the present authors in 1980[1] stating that on an average two to three cases of SSPE per year have been seen in the Civil Hospital, Karachi during eight to ten years prior to 1980, which would reflect an appreciable incidence in Karachi population. The actual activity commenced in July 1983 after one year of preparatory research. It's aim was to study the aetiology and frequency of encephalitides in Karachi.
In view of existing complete ignorance about encephalitides in Pakistan, multidisciplinary approach was adopted to study not only the cases of encephalitides but to evolve information bearing on various aspects of virus and other (inflammatory) encephalitides. These aspects include mortality patterns in Karachi, and seroepidemiological, neuro-epidemiological and entomological backgrounds.
The preliminary seroepidemiological, neuro epidemiological, and entomological aspects and backgrounds in this project are reported in this issue of the journal sepaiatély.[2-5]

MATERIALS AND METHODS

1) The series of cases

All the in-patients discharge cards at the Neurology-Ward Civil Hospital, Karachi (CHK), were reviewed to pick up the cases of encephalitides and encephalopathies. A card index .o\n the diagnosis of each patient admitted to the ward is maintained since 1971. All the diagnoses were based solely on clinical observation. Serological studies were conducted in a limited number and autopsy was not done in any of the cases. A diagnosis of "encephalitis" was made only in the presence either of cerebrospinal fluid (CSF) pleocytosis or of fever in the course of the illness or both.

2) The new series of cases

An many cases of encephalitides and encephalopathies as possible were collected during the eight and a half months' period from July 1983 to March 1984 from the Neurology, Medical and Paediatric Wards of CHK, and some from the Specialists' Clinic, and Abbassi Shaheed Hospital, Karachi. Detailed clinical history and neurological status were recorded in each case on a proforma. Clinical diagnoses were made after joint discussion among the authors.

3) Serological studies

One or more serum samples were taken from all the cases and CSF sample obtained mostly on the same day as the serum. All the specimens were kept at 20°C in aseptic airtight containers and transported at -20 C from Karachi to Tokyo, and stored at 80 C for less than ten months until examination. Some samples, specifically those transported in December 1983, were exposed to room temperature (around 10°C) for less than probably two weeks because of an accident, but there was no apparent indication of microbial proliferation in the samples examined.

The titres for antibodies against Japanese encephalities virus (JEV), West Nile virus (WNV)), Dengue-2 virus (DV), and tick-borne encephalitis virus (TBEV) were estimated by Sugamata at the Department of Hygiene, Teikyo University School of Medicine, Tokyo, Japan, with haemagglutination-inhibition test (HI). The titres for antibodies against measles viurs (MV) and rubella virus (RV) were estimated partly by Sugamata and partly at the Special Reference Laboratory (SRL), Hachioji, Tokyo, Japan, with HI. In some of these selected samples, the titres for antibodies against MV were estimated with neutralization test (NT) by Yamanouchi and Skaguchi at Department of Veterinary Pathology, the Institute of Medical Science, Tokyo University, Tokyo, Japan. The titres for antibodies against entero-virus-70 (EV 70) were estimated at SRL with NT. The titres for antibodies against JEV, MNV, DV, TBEV, MV and RV in samples were regarded as positive if the titres were not less than 10,10,10, 10, and 8 in CSF, respectively. NT antibodies against EV7O in samples were regarded as positive if the titres were not less than 4 in serum and if they were not less than 1 in CSF. NT antibodies against MV in samples were regarded as positive if the titres were not less than 10 both in serum and in CSF. Immunoglobulin-G (IgG) and immunoglobulin-M (1gM) antibodies against herpes simplex virus type 1 (HSV) were quantified separately with solidphase antigen enzyme-linked immunoadsorbent assay (ELISA) in 400 times diluted serum and in 40 times diluted' CSF and with solid phase anti-immunoglobulin ELISA in 200 times diluted serum and in 100 times diluted CSF, respectively at SRL. The quantity of antibodies against HSV were expressed in grades; as for lgG antibodies a preliminary correlation study showed that +,++,+++ and ++++ are roughly equivalent to 4, 16 (4), 64 (4), and 256 (4), of complement fixation titres, respectively; IgG antibodies against HSV were regarded as equivocal if the ELISA values were more than 0.15 and not more than 0.20 and as positive if they were more than 0.20 respectively. 1gM antibodies against HSV were regarded as equivocal if the ELISA values were more than 0.25 and not more than 0.35 and as positive if they were more than 0.35, respectively. IgG. concentration in CSF was determined at SRL with Laser immunoassay.

RESULTS

1) The clinical Diagnosis: One hundred and fourteen cases of encephalitis or encephalopathy collected

at the Neurology Ward, CHK, during the twelve years period (1971 to 1983). The definition of "encephalitis" stated in the materials and methods. "Encephalopathies" include all the diseases of the brain itself, excluding multiple sclerosis and heredodegenerative diseases and including all cases for which we have no direct proof of infectious aetiology, but we cannot entirely rule out this possibility; meningitides were excluded.
In these 114 cases (Table 1)

TABLE - I
Encephalitides and Encephalopathies of the Past Series, Neurology Ward, CHK (1971 to 1983).

Encephalitides		58	114
AE	7		
SSPE or SSPE-like	11		
SE*	3		
Others	37		
Encephalopathies		56	
SE*	5		
CPE	7		
Others	44		

*For AE, SSPE, SE, and CPE see the results section of the text.

seven, five eleven ad seven cases of AE, SE, SSPE or SSPElike diseases and CPE weke found. Distribution of these cases by age and sex is shown in Table II.

TABLE - II
Age-Sex Distribution of the Past Series, Neurology Ward, CHK (1971 to 1983).

Age (yrs)	Male		Female		?	Total	
5 >	7	13	7	10	0	11	20
5 –	6		3		0	9	
10 –	10		15		3	28	
20 –	4		7		0	11	
30 –	2		1		2	5	
40 –	2		1		0	3	
50 –	3		1		0	4	
60 –	2		2		0	4	
?	3		11		2	36	
Total	59		48		7	114	

One thing peculiar was that the sex ratio (M/F) of SSPE or SSPE-like diseases was 4/7 in contrast to the known male preponderance of this disease in U.S.A. ,Europe and Japan.

2) The neuro-virological diagnosis of the new series of cases. During the eight-and a half months' period (July 1983 to March 1984) a total of 71 new cases with a tentative diagnosis of encephalltis or encephalopathy were collected. After discussion, 43 of them were accepted as such, 15 excluded and in the remaining 13 the decision suspended (Table III).

TABLE – III

Encephalitides and Encephalophaties of the Present Series, Neurology Deptt., CHK (Jul. 1983 to Jun. 1984).

Accepted			
	Encephalitides		55
	AE[1)]	30	
	SSPE or SSPE-like[2)]	8	
	SE[3)]	6	
	Others[4)]	11	74
	Encephalopathies		19
	SE[5)]	7	
	CPE[6)]	10	
	Others[7)]	2	
Pending[8)]			16
Rejected[9)]			18
Total			108

The distribution of the 43 cases by age and sex is shown in Table IV.

TABLE - IV
Age-Sex Distribution of the Present Series, Neurology Ward, CHK (Jul. 1983 to Jun. 1984).

Age (yrs)	Male		Female		?	Total	
5 >	15	19	10	18	0	25	37
5 –	4		8		0	12	
10 –	4		11		0	15	
20 –	8		2		0	10	
30 –	2		1		0	3	
40 –	1		0		0	1	
50 –	1		2		0	3	
60 –	2		3		0	5	
?	0		0		0	0	
Total	37		37		0	74	

a) Acute encephalitides: Of 43 there were 19 cases of AE (Table III), thirteen of which were associated with some serological evidence for JE and /or some other arbo virus infection. Five of the latter were associated with very high titres for serum antibodies against JEV (640) together with a high titre for CSF antibodies against JEV (40) in one of them (Table V)

TABLE - V

Acute Encephalitis With Strong Evidence of Japanese Encephalitis and/or Some Other Arbo Virus Infection, Neurology Deptt., CHK (Jul. 1983 to Mar. 1984).

Case code	age/ sex	onset of illness	clinical diagnosis	serological data JEV	WNV	DV	TBEV	MV	RV	HSV -1gG	HSV -1gM	EV70	Sampling day of illness	aetiological diagnosis
0089	30y M	25/7/83	AE	⩾640/–	320	160/–	20/–	–/–	32/–	++/–	–/–	–/–	24th/24th	JE
0098	13m F	18/8/83	AE	⩾640/–	80/–	40/–	10/–	32/–	32/8	++/–	–/–	–/–	13th/13th	JE
0102	20y M	18/10/83	AE	⩾640/	=640/	640/–	80/–	64/–	–/–	++/–	–/–	4/–	11th/	JE prob.
0113	17y F	9/11/83	AE	⩾640/ 40	=640/ 40	=640/ 10		8/–	16/–	/–	+/–	–/–	41st/50th	JE prob.
0129	16y F	16/1/84	AE	⩾640/–	320/–	160/–		8/–	128/–	/±	–/–	8/–	9th/9th	JE
				⩾640/–	160/–	80/–		8/–	128/–	/	–/–	8/–	18th/	
				320/–	80/–	80/–		8/–	64/	/	–/	8/–	25th/	

Notes for table 5, 6, 8, 9, 10 and 11: The numerators and the denominators represent antibody titers or valuaes in serum and CSF, respectively. The figures without paranthesis are based on the results of estimation by Sugamata (H.I.); those in ( ) on those at S.R.L. (H.I. except that of Sohail Anjum in which C.F. was empolyed.), and those in [ ] on those by Yamanouchi and Sakaguchi (NT).

and a significant fall of the titres for serum antibodies against WNV and probably against JEV in the course of ifiness in another. In three of the five the aetiological diagnosis of JE was almost certain and in other two probable. The clinical history of the two of these five are briefly described towards the end of this section. Fourteen of the nineteen cases of AE were associated with serological evidence for HSV (Type 1) infection, in five of which the evidence was strong, four were associated with a very high ELISA value for serum antibodies (++++) and another with a significant rise of ELISA value for serum antibodies in the course of the illness (-to+++) (Table VI).

TABLE - VI

Acute Encephalitis With Strong Evidence of Herpes Simplex (Type–I) Infection, Neurology Department, CH (July 1983 to March 1984).

Case Code	Age/ Sex:	Onset of illness:	Clinical Diagnosis:	Serological Data: JEV	MNV	DV	TBEN	MV	RV	HSV -IgG	HSV -IgM	EV70	Sampling day of illness:	Aetiological Diagnosis:
0116	1y F	22/12/83	AE	160/	80/	20/		–/	–/	++++/	+/	4/	12th/	HSE or JE ?
0117	2½y F	18/12/83	AE	80/–	160/–	40/–		8/–	–/–	++++/++++	+/–	–/–	16th/18th	HSE
				20/	160/	–/		–/	–/	++++/	+/	–/	45th	
0127	21y F	3/1/84	AE	140/	20/	40/		32/	32/	–/	–/	4/	15th	HSE
				40/	40/	80/		32/	64/	++++/	±/	4/	37th	
0141	42y M	3/2/84	AE	–/	–/	–/		16/	1024/	++++/	±/	–/	24th	HSE or Rubella E ?
0142	38y M	26/2/84	AE	160/–	160/–	160/–		–/–	32/–	++++/–	–/–	–/–	2nd/2nd	Non viral?

* Figures in table show serum antibody titres and CSF antibody titres, respectively.

One of the afore-mentioned four cases was also associated with a very high ELISA value (++++) for CSF antibodies. In two of the five patients the aetiological diagnosis of herpes simplex encephalitis (HSE) was almost certain and in the other two it was possible. The clinical history of two cases are

described below, too.

b) SSPE: Among the 43 accepted cases seven cases were clinically diagnosed as SSPE (Table VII).

TABLE - VII
SSPE, Neurology Deptt., (July 1983 to Mar. 1984).

Case code	age/sex	history of measles	duration of the illness	preceding fever	myoclonus	EGG	Clinical diagnosis
SOHAIL ANJUM	13y M	?	5m	–	?	No PSD	SSPE or Schilder's dis.
0014	8y F	1y	8m	+	+	?	SSPE (prob.)
0086	10y F	?	2m	+ HG	±	SSPE-like	SE with SSPE-like EEG
0090	9y F	?	6m	+	+	PSD	SSPE
0126	5y F	?	1m	–	–	SSPE-like	SE with SSPE-like EEG
0130	6y F	3y	2½m	+ HG	+	SSPE-like	SSPE-like
0132	8y F	1½y (rash)	1½m	+ HG	+	PSD	SE (febrile, progressive)
0134	11y M	6m	10m	±	+	SSPE-like	SSPE

Notes: HG: High grade, PSD: periodic synchronous discharges

All had a subacute onset and their electroencephalograms showed periodic synchronous discharge (PSD) whether they were typical or somewhat atypical of SSPE.

History of measles was noted in three and in another a history of rash associated with fever. Myoclonic jerks were observed in six. One thing peculiar in these cases in Karachi was again that the sex ratio (M/F) was 2/5 and another that, in six, fever apparently preceded the onset of the neurological deterioration. The details of the clinical features of these cases will be reported separately by one of the authors (A.A.).

All these cases had a high titre for serum antibodies as well as positive CSF antibodies against MV(Table VIII)

TABLE - VIII

SSPE , Neurology Deptt., CHK (Jul. 1983 to Jun. 1984)

case code	m*	age/sex	duration of illness	clinical diagnosis	Serological Data JEV	WNV	DV	TBEV	MV	RV	HSV-IgG	HSV-IgM	EV70	CSF total protein (mg/dl)	IgG (mg/dl)	(%)	sampling date (serum/CSF)	serological diagnosis
		13y M	5m	SSPE or Schilder's disease	(−)/(−)			(−)/(−)	(≥ 256)/(32)	(32)/(−)	16/−		14/−				7/82/7/82	MV
0014	1y	8y F	8m	SSPE (prob.)	−/−	−/−	−/−	−/−	64/− (256)/(16) [>1280]/[160]	128/− (64)/(−)	±/− ±/+	−/− −/−	−/− −/−	?	10.9	?	5/7/83/5/7/83	MV
0086		10y F	2m	subacute encephalitis with SSPE-like EEG	−/−	−/−	−/−	−/−	64/− [>1280]/[80]	64/−				18	7.2	40	9/7/83/9/7/83	MV
					−/−	−/−	−/−	−/−	32/− (64)/(8) [>1280]/[240]	32/8 (−)/(−)	−/− −/−	−/− −/−	−/− −/−	18	6.3	35	9/7/83/9/7/83	
0090		9y F	6m	SSPE	20/−	10/−	−/−	−/−	32/− (256)/(16) [>1280]/[120]	32/− (−)/(−)	±/− ±/±	−/− ±/−	−/− −/−				10/8/83/10/8/83	MV
0126		5y F	1m	subacute progresive encephalopathy with SSPE-like EEG	/40 /−	/40 /−	/40 /−	/− /−	/>1024 /(32) /[480]	/(−) /(−)	/± /±	/± /−	/− /−	?	3.3	?	/15/1/84 /24/1/84	MV
0130	3y	6y M	2½m	SSPE-like	≥640/−	≥640/−	≥640/−	−/−	(1024)/(32) /[>1280]	(−)/(−)	±/±	±/−	−/−	20	3.9	19.5	25/1/84/2/2/84	MV
0132	(rash) 1½y	8y F	1½m	subacute febrile progressive panencephalitis	−/−	−/−	−/−	−/−	(256)/(16) /[1280] /[480]	(256)/(−)	±/+	±/−	−/−	36 36	9.9 4.7	27.5 13.1	29/1/84/28/1/84	MV
0134	6m	11y M	10m	SSPE	160/−	160/−	80/−	−/−	(1024)/(32) /[480] /[240]	(128)/(−)	±/±	±/−	−/−	?	7.4 3.4	? ?	30/1/84/30/1/84	MV
					160/−	160/	80/−	−/−	(512)/(−) [>1280]/[320] /[480] /[320] /[480]	(128)/(−)	±/+	±/−	−/−	?	7.2 2.2 2.0	? ? ?	17/3/84/17/3/84	
0148	3y	10y M	3m	SSPE	/−	/−	/−	/−	/(32)	/(−)	/+	/−	/−	120 50			/31/3/84	MV

Notes: See footnotes for Table 5. In this table the figures for serological data on JEV, TBEV, MV, and RV in ( ) and [ ] were determined at SRL and at Prof. Yamanouchi's laboratory, respectively, while those without parenthesis by Sugamata. The estimation of antibody titres for MV was done with HI at Sugamata's laboratory and SRL and with NT at Prof. Yamanouchi's laboratory, except for Sohail Anjum (See footnotes for Table 7), in which the estimation for MV and HSV was done with CF. All the estimations for S-A. were done at SRL. * : history of measles.

and one also had positive CSF for antibodies against RV. Moreover, in five, an abnormally high IgG content in CSF either in absolute value or in relative value to total protein was noted (Table VIII). In one (0134) brain biopsy was performed and the formalinfixed and frozen specimen were transported to Japan for detecting MV with immunofluorescence and for isolating the virus with culture, although the results were both negative. Immunofluorescence was negative probably because the site of biopsy was inappropriate and culture was negative probably because freezing was not the optimal way for preserving the virus activity.

c) Other types of SE sub-acute Encephalitis/ encephalopathy: Beside SSPE two cases of subacute encephalitis and four cases of subacute encephalopathy were found (Table IX).

TABLE - IX

Subacute Encephalitis of Encephalopathy other than SSPE, Neurology Department, CHK (Jul. 83 to Mar. 84).

Case code	Age sex	Durn of illnes	Prece ding fever	Myocl jerks	PSD in EEG	Clinical diagn	Clinical diagn	Serological data JEV	WNV	DV	TBEV	MV	RV	HSV -IgG	HSV -IgG	EV70	total protein (mg/dl)	CSF IgG (mg/dl)	IgG (%)	Sampl. date serum	Sampl. date CSF	aetiological diagnosis
0105	21y F	6w	+	– ?	–		SE(+itis or –opathy)	10/–	10/–	10/–	–/–	–/–	64/32	–/–	–/–	4/–	30	2.8 6.1 2.2	10.1 20.3 7.3	14/11/83 14/11/83		rubella E(–itis)
0110	5½y F	6w	+	– ?	?		SE(–itis)	–/–	–/–	–/–	–/–	64/–	8/–	+++/–	–/–	128/–					30/11/83 30–11/83	
0114	25y M	6w	+	– ?	–		SE(itis)	80/–	80/–	160/-		16/–	64/–	–/–	+/–	4/–	88				18/12/83 18/12/83	typhoid E(–itis)
0118	60y M	6m	– ?	–	–		CE(–opathy) + diabetes mellitus	320/–	320/–	160/–		16/	64/	+++/	+/	–/	160 (prob. traumatic)				2/1/84	
0123	6y M	5m	+	– ?	–		SE(–itis) (brainstem)	/–	/–	/–		/64	/–	/+	/–		32				11/1/84	measles E (–itis)
0137	65y F	4w	+	– ?	– ?		SE(–opathy)	640/–	320/–	40/–		64/32	256/–	++/+	–/–	–/–	26				7/2/84 5/2/84	MV or JEV ?

None of the six were associated with PDS in EEG or with myocionic jerks.

Serologically two cases were associated with positive CSF antibodies against MV, one with positive CSF antibodies against RV, one with a very high titres for serum antibodies against JEV and in another with a strongly positive Widal reaction reaction in serum. Aetiological meanings of these observation are still being discussed. The clinical history of case with positive CSF antibodies against RV is described later.

d) Chronic progressive encephalopathy:

Among the 43 accepted cases, seven cases of CPE were found (Table III). In One of these seven the results of antibody estimation were negative both in serum and in CSF and in another only in Serum for all eight viruses examined (Table X).

TABLE - X

Chronic Progressive Encephalopathies, Neurology Deptt., CHK (Jul. 1983 to Mar. 1984).

Case code	age/sex	duration of illness	clinical diagnosis	Serological Data									sampling date (Serum) (CSF)
				JEV	WNV	DV	TBEV	MV	RV	HSV -IgG	HSV -IgM	EV70	
0015	2y M	ly	CPE	–/–	–/–	–/–	–/–	–/–	–/–	–/	–/	4/	4/7/83 4/7/83
0092	13y F	2y	CPE	80/–	40/–	40/–	10/–	8/–	–/–	/±	–/–	4/–	8/83 8/83
0094	9y M	4y	CPE	–/–	–/–	–/–	–/–	–/–	64/–	/–	–/–	–/–	23/8/83 23/8/83
0099	13y F	11m	CPE with myo-clonus and abnorm. EEG	–/–	–/–	–/–	–/–	–/–	–/–	–/–	–/–	–/–	31/8/83 31/8/83
0107	2y7m M	ly	CPE	–/	–/	–/	–/	–/	–/	–/	–/	–/	13/11/83
0112	10½y M	4y	CPE with myo-clonic epi.	160/–	80/–	80/–	10/–	32/–	8/–	–/–	–/–	4/–	4/12/83 13/12/83
0115	7y	F 10m	CPE following postmeasles myelopathy at 2 years	80/–	20/–	20/–		32/–	256/–	/+	+/–	4/–	19/12/83 21/12/83

* Figures in table shows serum antibody titres and CSF antibody titres.

In the remaining five, the results were positive in serum for one or more of the eight, and in all of the five they were negative in CSF except for the two cases in which antibodies against HSV were weekly positive or equivocal.

e) Others: Four cases of diseases other than those classified into a, b), c) or d) were as shown in Table XI).

TABLE - XI

Cases of Diseases other than AE, SSPE, SSPE–like, SE and CPE, Neurology Department, CHK (July 1983 to March, 1984).

Case Code:	Age/ Sex:	Duration of illness:	Clinical Diagnosis:	Serological Data									Sampling Date
				JEV	WNV	DV	TBEV	MV	RV	HSV -IgG	HSV -IgM	EV70	Serum CSF
0096	5y F	6y	Postvacc. encephalitis?	–/–	–/–	–/–	–/–	32/–	–/–	++/–	+/–	8/–	27/8/83 27/8/83
0119	26y M	2y	Chronic progressive choreoathetosis after AE	640/–	640/–	160/–		16/–	32/–	++/–	±/–	–/–	11/1/84 21/1/84
0122	66y M	4m	Postzoster encephalitis with motor neuritis	640/–	640/–	640/–		–/–	16/	++/	±/	–/–	12/1/84
				40/	40/	10/	–/–	–/	–/	–/	+/	–/	12/1/84
0124	13m M	3m	Postinfections allergic	–/	–/	–/		1024/	–/	+/	±/	8/	16/1/84
				160/	160/	80/		8/	64/	++/	–/	16/	12/1/84

Over all, the causative agent was identified in 15 out of 43 cases (JEV 3, HSV 2, 6, RV 1, typhoid) and probable in other 3 (JEV 2, MV 1). If combined together, the rate of identification was 35%.

CASE REPORTS

Case 1 (case code : 0098) : JE

This female infant, aged 11 months, had fever and cough for three days, followed by fits prior to admission on 21/8/83, when she was found to be semicomatose and febrile (104° F). Her oculomotor function was intact. The muscle tone was generally increased. The deep tendon reflexes were normoactive, but with extensor planter responses. There were jerky movements in all four limbs but no neck rigidity or Kernigs sign. The peripheral leukocyte count was 16,000 per cmm with 80% polymorphonuclear cells. The CSF was clear, containing two cells per cmm, with negative Pandy test. On 27/8/83 the CSF was clear, containing two cells per cmm, 30 mg of protein and 66 mg of sugar per lOOmi.

On 30/8/83 (13th day of illness) the titre for serum antibodies against JEV was not less than 640, although it was less than ten in CSF, i.e. the antibodies were negative in CSF (Table V).

Although paired samples were not taken, judging from her very young age and the demonstratibn of a high titre of antibodies against JEV during the course of her AE is strongly suggestive of Japanese encephalitis (JE).

Case 2 (cases code: 0129: JE)

The girl, aged 16 years, had had headache, vomiting and fever for three days and been disoriented and drowsy for two days prior to adinission on 19/1/84. She suffered from measles at the age of 14 years. On admission she was drowsy and restless. There were neck rigidity and bilateral extensor plantar responses, but no paralysis. She had one generalized seizure. The CSF contained occasional cells, 30 mg of protein and 61 mg of sugar per 100 ml.

EEG taken on 24/1/84 (9th day of illness) was within normal limits. On the same day the titre for serum antibodies against JEV was not less than 640, although less than ten in CSF.

On 2/2/84 (18th day of the ifiness) the titre was again not less than 640, but on 9/2/84 it was 320. She completely recovered except mild headache (Table III).

In this case the significant fall of the titre for serum antibodies against JEV demonstrated with paired samples strongly suggests that her mild acute encephalities was due to JEV ‘infection.

Case 3 (case code: 0117): HSE

A female infant, aged two-and-a-half years had had fever for two days prior to admission on 20/12/83 for fits, vomiting and coma EEG showed generalized delta activities, which were not associated with any PSD. On 23/12/83 count was 13,800 per cmm with 75% of polymorphonuclear cells. CSF contained ten cells per cmm, 20 mg of protein and 69 mg of sugar per lOOmi.

On 2/1/83 (16th day of the illness) she was awake, but unable to sit, suck or eat. Her limbs were spastic with extensor planter responses. On the same day IgG antibodies against HSV were ++++ both in serum and in CSF and 1gM antibodies against the same virus was ++ in serum and negative in CSF (Table VI). On 31/1/84 (45th day of the illness) the serum antibodies against HSV were not remarkably chaiiged. On 9/2/84 she was more conscious than before but still unable to sit.

The demonstration of a very high ELISA value for IgG antibodies against HSV not only in serum but also in CSF at due time during the course of her ifiness with a significantly high value for 1gM antibodies strongly suggests that the AE in this case would probably be due to the HSV infection which occurred for the first time in her life.

Case 4 (case code: 0127): HSE

The 21-years-old young woman had had fever for five days and been drowsy for one day prior to admission on 8/1/84, when she had fever (103 F) and headache. EEG mamly showed theta activities

with a few high voltage waves mixed with occasional delta waves.
On 17/1/84 (15th day of the illness) serum antibodies against HSV were negative, but on 23/2/84 (37th day of the illness) serum anti IgG antibodies were +++. On that day she responded almost normally to verbal commands.
The SE in this case was probably caused by a reactivation of HSV infection, because the significant rise in serum IgG antibodies against HSV demonstrated in paired samples during the course of her illness without any significant rise in 1gM antibodies

Case 5 (case code: 0134): SSPE

A ten-year-old boy, who had a history of measles at the age. of 6 months, had had low-grade fever and frequent falls for ten months prior to admission. He had a grandma! seizure five months prior to admission and had had violent myoclonic jerks in bed for three months prior to admission.
On admission on 5/2/84 he was moderately demented. EEG showed high voltage sharp wave complexes, each of which was followed by delta waves; myoclonus involving neck, all four limbs, and face at each myoclonic jerk he opened his mouth, assumed opisthotonic posture, extended his arms and flexed his legs at his joints. On 4/3/84 he had eyes open and followed light. His pupil were isocoric and normoreactive to light. Snout reflex was positive, Jaw jerk was exaggerated. He responded to simple verbal commands, but did not speak. There were no meningeal signs. The muscle tone was only slightly increased. There was no forced grasping. His gripping power was good. The deep tendon reflexes were rather hypoactive in upper limbs and brisk in lower limbs. There was unsustained clonus bilaterally. The plantar responses were flexor. There was no startle reaction on sound.
Serologically the NT titre for CCE antibodies against MV was very high (Table VII).
The results of serological studies together with the clinical course, presence of mycolonic jerks and of the PSD in EEG fovoured the diagnosis of SSPE caused by MV infection, although there were some atypical features; the PSD were not composed of typical high voltage delta waves but of sharp waves and the onset of his illness was apparently preceded by low grade fever. Case 6 (case code: 0105): SE
A young man, aged 21 years, had been weaker and less active than before and lost weight for one year, had low-grade fever, sometimes with chills, and fits for one month, and been unable to walk or speak; disoriented, and incontinent of urine and had not eaten, drunk or,answered for two weeks prior to admission on 13/11/83, when he was somnolent, apathetic, having bedsores, neck rigidity, generalized spasticity and paresis of the four limbs. The deep tendon reflexes were present.
On 14/11/83 the peripheral leukocyte count was 11,000 with 70% neutrophils. The CSF contained two cells per cmm, 30 mg of protein and 60 mg of sugar per 100 ml. The titres for serum and CSF antibodies against RV were 64 and 32, respectively (Table VI). The antibodies against RV were 64 and 32 respectively (Table VI). The CSF taken on 2/12/83 contained 11.9mg of IgG per 100 ml; EEG taken on 13/12/83 showed some slow waves.
On 5/3/84 he was unable to converse or sit up and had spastic tetraparesis. 1984).
The SE in this case was probably due to RV infection of the central nervous system reflected by the presence of antibodies against RV in serum and CSF. This case might possibly be one of progressive rubella encephalitis.

DISCUSSION

A.A. one of the present authors, reported seven cases of SSPE in 1980, which were part of the more than 25 cases probably of SSPE seen by him in Karachi over the ten years upto the year 1980. Besides SSPE, cases of CPE were also encountered in Karachi. These observations were confirmed in this study, but, aetiological diagnosis of such cases needed the introduction of more sophisticated ancillary examination as in the present study.
Nearly half as many as the total cases of encephalitis or encephalopathy collected at the Neurology

Ward, CFIK during the past twelve years were gathered in this study during the eight and a half months' period. The number of SSPElike diseases and CPE in the new series was quite comparable with that of the past series.
Serological studies demonstrated that all the new SSPE cases, so diagnosed solely clinically, were associated with a significantly high titre for antibodies against MV both in serum and in CSF.
It has long been debated whether JE occurs west of India. The three case (0089, 008 and 0129) of the present series were associated with a specifically high titre for antibodies against JEV in serum, being exceedingly high over other arboviruses, so that in these three there must have been an actual JEV infection, which was almost certainly the cause of the AE in these cases. HSE also occurs in Karachi. Detection of JEV and HSV is needed to confirm the diagnosis of JE and HSE in Karachi.
In this study, the identification rate of aetiology was 35%. The rate would certainly improve if paired samples could be collected in more cases.

CONCLUSIONS

1) A number of cases of encephalitides and encephalopathies can be encountered in Karachi, and around 44% of such cases collected at the Department of Neurology CHC, from 1971 to 1984 were AE, around 16% SSPE or SSPE-like diseases, around 14% other types of SE and around 10% so collected were CPE.
2) All the SSPE or SSPE-like diseases so diagnosed clinically were associated with a high titre for antibodies against MV both in serum and in CSF.
3) One of the cases of subacute onset encephalitis was associated with positive CSF antibodies against RV.
4) Serological studies on CPE have not given any definite conclusion about their aetiology yet. Further studies are required for elucidating the aetiology of CPE in Karachi.
5) Five cases were found in which the clinicoserological correlation strongly suggests the occurrence of JE in Karachi. In three of them the diagnosis was almost certain. However, the final conclusion should await virological confIrmation.
6) Two cases were almost certainly those of HSE.
7) On the whole, the aetiology was identified in 15 out of 43 cases (35%).

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