ORIGINAL ARTICLE

Neurological Manifestations of Children with Systemic Lupus Erythematosus

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Summary

In a cross-sectional study of 21 children with Systemic Lupus Erythematosus, 15 (71%) were found to have neuropsychiatric manifestations. The most common finding was generalised seizures (42.8%) followed by encephalopathy (19%) and hallucinations (19%). One child (4.76%) had hemichorea. In 3 children neurological manifestations were the first symptom of SLE. Computerised Axial Tomograms (CAT scans) showed cerebral atrophy in 7 of 12 scans available for review. Ten children had abnormal EEGs. Although none of the children had clinical evidence of a peripheral neuropathy, 8 had neurophysiological evidence of a neuropathy. One child died of intracranial haemorrhage. Six children had residual neuropsychiatric sequalae.

Key Words: Neuropsychiatric Lupus, Childhood

Introduction

Systemic Lupus Erythematosus (SLE) is a multi-system disorder which has been shown to cause neuropsychiatric manifestations in 9% to 45% of affected children [1-4]. The diversity in the reporting of neuropsychiatric lupus (NPSLE) stems from the fact that there is a wide array of manifestations but no accepted classification or diagnostic criteria. Diagnosis is primarily clinical, as there is as yet no laboratory marker nor imaging modalities that can serve as the gold standard for NPSLE [5]. Although SLE is relatively common in Malaysia, there is as yet no comprehensive study on neuropsychiatric lupus in Malaysian children. We undertook a study in the Paediatric Institute of Hospital Kuala Lumpur to determine the frequency and spectrum of childhood NPSLE in our patient population.

Materials and Methods

We studied 21 children with active SLE who were undergoing treatment or follow-up at the Paediatric Institute, Hospital Kuala Lumpur from April 1996 to August 1996. All patients fulfilled at least 4 out of the 11 criteria set out by the American Rheumatism Association's classification of SLE [6]. Patients with neuropsychiatric manifestations attributable to intracranial infections or uraemia were excluded.

The medical records of the patients were reviewed to determine the nature of their neuropsychiatric presentation where present. The neurological findings during a neuropsychiatric episode were noted and a reassessment of the neurological status was performed during the study period.

Results of relevant laboratory investigations, including renal profile, full blood count, erythrocyte sedimentation rate, serum C3 and C4, LE cell

phenomenon, anti-double-stranded DNA and antinuclear antibody titres (ANA) were reviewed to confirm the presence of disease or to exclude uraemia.

Computerised Axial Tomograms (CT) scans of the brain were done during an acute episode of neuropsychiatric manifestation. Nerve conduction studies of both median (sensory and motor components), both tibial and both sural nerves were performed on those children whose parents consented to the procedure. An electroencephalogram (EEG) was performed on children with neuropsychiatric manifestation during their acute illness. Other children had an EEG done during the study period.

The study protocol was approved by the research committee of the Ministry of Health.

Results

Nineteen girls and two boys between 9 and 16 years of age (mean 11.6 years) were studied. There were 11 Malays, 8 Chinese, 1 Indian and 1 Iban. The patients had been followed-up for a period of 5 to 58 months with a mean duration of 29.5 months. The main neuropsychiatric manifestations in the 15 patients with clinically overt neuropsychiatric lupus are outlined in Table I. Seizure was the most common manifestation, occurring in 9 (42.8%) of these patients. Four patients (19%) had hallucinations, 4 had encephalopathy, while one (4.76%) patient presented with hemichorea. In three patients, 2 with encephalopathy and 1 with chorea, the first manifestation of SLE was neurological. The child with chorea was diagnosed as having Sydenham's chorea and responded promptly to steroids. She subsequently developed nephrotic syndrome and serological investigations confirmed SLE. Both the cases with encephalopathy were treated as meningoencephalitis initially. One developed proteinuria during the acute illness and a collagen screen lead to the diagnosis of SLE. Interestingly he also had a high titer of Mycoplasma antibody. The other child recovered from the acute illness possibly because steroids were given to treat raised intracranial pressure and was diagnosed later when she had other manifestations of lupus. The radiological findings in the 13 patients who had a CT scan are summarised in Table I. Unfortunately, only 12 scans were available for review at the time of the study. Cerebral atrophy was the most common finding, seen in 7 patients. One had basal ganglia calcifications as well. Patient 20, who had a normal CAT scan initially was subsequently admitted with fits, fundal haemorrhages and hypertension. The BP was 180/140 and a repeat CAT showed intraparenchymal and intraventricular hemorrhages. She passed away the same night, and was the only mortality during the study period. The family had earlier opted for traditional treatment.

Abnormal EEGs were found in 10 patients as shown in Table I. Patient 6, whose only neurological complaint was headache was classified as a case of cerebral lupus based on her EEG.

Nerve conduction tests were done in 17 (81%) of the 21 patients during the study period. The detailed analysis will be reported elsewhere. Eight children all of whom had no clinical evidence of a peripheral neuropathy, had neurophysiological features consistent with a mononeuropathy or multiple mononeuropathies. None were uraemic at the time of the nerve conduction studies.

All the surviving patients were followed-up and were able to attend school. Only one patient had a residual hemiparesis. Two patients, (patients 2 & 5 Table I) developed epilepsy requiring long term anticonvulsants, but the fits were easily controlled. One child, (patient 19 Table I) needed long term psychiatric medication, whilst another had deterioration in school performance. One patient developed optic atrophy. The child who presented with hemichorea (patient 9 Table I) needed haloperidol for a relapse of here chorea.

Discussion

In our small study of 21 children with SLE, 15 (71%) had evidence of neuropsychiatric involvement. Seizures were the most common neurological manifestations, followed by psychiatric disturbances, encephalopathy and headache. This is in keeping with other studies [1,2].

The most common finding in the brain CT scan of our patients was cortical and perisulcal atrophy. In the past

Table I

Summary of Clinical, Neurophysiological and Radiological Findings

No	Age(d)	Sex	Race	C.N.S. Manifestations	Electroencephalogram	Nerve conduction	C.T. Scan	Treatment
1	12(13)	F	Chinese	Coma *Gen.fits	L focal sharp waves	Both Tibails & surals dcv	Cerebral atrophy	Pred. Cyclo
2	11(4)	F	Malay	S.E. Cognitive/Mood swings	Bilateral post. Sharp waves	Normal	Cerebral atrophy	Pred. Cyclo. Valproate
3	8(14)	F	Malay	R. Hemiplegia, Gen fits	R focal sharp waves	R Tibial dcv & amplitude	Atrophy, multiple infarcts	Methyl Pred CBZ
4	12(36)	F	Dayak	Nil	Normal	Both surals absent	Not done	Pred. Cyclo
5	12(18)	F	Malay	Encephlopathy, Gen fits	Normal	R Tibial reduced amplitude	Atrophy, posterior infarcts	Pred. Valproate
6	13(20)	F	Chinese	Headache	Bil.central sharp waves	R Tibail dcv	N.D.	Pred
7	10(27)	F	Malay	Gen. & focal fits	Normal	Normal	NA	Pred.Cyclo.Azathioprine
8	9(22)	F	Malay	R. Hemiplegia, R local fits Psychosis*	Low voltage background	Normal	Cerebral atrophy	Pred
9	11(24)	F	Chinese	R Hemichorea *2episodes	Normal	Normal	Normal	Pred.Cyclo Haloperidol
10	13(25)	F	Malay	Nil	Normal	Normal	N.D.	Pred.Cyclo
11	15(62)	F	Chinese	Encephiopathy	Normal(ND in acute state)	Normal	Normal	Pred.
12	13(12)	F	Chinese	Flaccid paraparesis Psychosis, incontinence	L parieto-occipital sharp waves, N background	Both Tibias dcv	Atrophy, basal ganglia calcification. MRI spine N	Pred.
13	10(8)	F	Malay	Nil (mood swings)	Normal	R Tibial dcv & amp	N.D.	Pred.Cyclo
14	9(24)	F	Chinese	Nil	Normal	Both Tibials dec. amp	N.D.	Pred.Cyclo
15	9(35)	M	Chinese	Encephalopathy, Gen.fits*	Diffuse delta, R centro-temporal discharge	Normal	Cerebral Atrophy	Pred.Cyclo
16	10(26)	F	Malay	Nil	Normal	Normal	N.D.	Pred.Cyclo
17	14(47)	F	Chinese	Nil	Normal	Normal	N.D.	Pred.Cyclo
18	13(26)	F	Indian	Encephalopathy, Gen.fits Psychosis	Bilateral epileptic discharges, focal slow	N.D.	Multiple infarcts	Pred.Cyclo
19	11(4)	F	Malay	Psychosis, dystonic posture, UMN signs	Normal	N.D.	MRI Normal	Methyl Pred. Haloperidol
20	10(13)	F	Malay	Gen. Tonic-clonic fit	Diffuse slow	N.D.	Normal	Pred
21	10(37)	F	Malay	Delirium, Gen. Fits, transient L.lower limb weakness	Focal sharps	N.D	Multiple infarcts	Pred

Legend: (d): duration in months, F: female, M: male, R: right, L: left, Gen: generalised, Bil: bilateral, N.D.: not done, dcv: decreased conduction velocity, amp: amplitude, UMN: upper motor neuron, CNS: central nervous system, CPE: complex partial epilepsy, LL: lower limbs, N: normal, CT: computed tomograms, NA: not available PRED: Prednisolone, Cyclo: Cyclophosphamide

there was some controversy concerning the aetiology of cerebral atrophy in cerebral lupus. Bilaniuk et al [7] attributed microinfarcts as the cause of the perisulcal atrophy found in 50% of their patients with neuropsychiatric manifestations in 1977. Bentson et al [8] challenged their conclusion by demonstrating varying degrees of apparent cerebral atrophy in 15 patients on long term steroids in 1978. It was unclear whether the cerebral atrophy seen in SLE was due to ongoing lupus cerebritis and infarction, the effects of long-term steroid use or a combination of both. However, the current position is that cerebral lupus per se is the cause of the cerebral atrophy seen in this patients [9]. Three of our patients had neuropsychiatric involvement at the onset of SLE. The CT brain of these patients prior to administration of steroids showed both infarcts and cerebral atrophy.

One patient had both cerebral atrophy and basal ganglia calcifications. Basal ganglia calcification is a recently recognised complication in patients with NPSLE reported by Raymond et al [9]. The pathogenesis of the calcification is still uncertain. There was only one death due to massive acute intracranial bleed probably due to hypertensive encephalopathy. Dubois et al [10] reported a 26% mortality during the 1950's and Yancey et al [1] reported an improvement in mortality rates of 12% in their study done between 1968 and 1978. The duration of our study is too short to draw any conclusion about mortality rates in our children.

The actual pathogenesis of cerebral lupus is uncertain. The clinical manifestations can be divided into diffuse and focal. Diffuse manifestations including psychosis and seizures are thought to be mediated by antineuronal antibodies. Focal manifestations such as strokes are due to vascular occlusions. There are many theories about the pathogenesis of these vascular lesions. However, vasculitis which was originally proposed by Osler, and is still believed to account for the peripheral neuropathy seen in SLE [11], is probably rare in cerebral lupus. Postmortem findings demonstrate a non-inflammatory vasculopathy with endothelial proliferation, intimal fibrosis, thrombosis and perivascular lymphocytes. It is thought that antiphospholipid antibodies bind to endothelial cells and platelet membranes. This binding leads to endothelial injury and platelet hypercoagulability leading to local thrombosis. Another possible mechanism for vascular occlusion are emboli from Libman-Sacks endocarditis [12].

Conclusion

In this study of 21 children with SLE, 15 (71%) had NPSLE. Hence NPSLE is a common manifestation in childhood SLE and should be actively looked for in children with this condition. The short-term prognosis is good with only a few children developing residual neurological disease. However this group of children should be followed up to determine their ultimate neuropsychiatric outcome.

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References

1. Yancey CL, Doughty RA, Athreya BH. Central nervous system involvement in childhood systemic lupus erythematosus. Arthritis Rheum 1981; 24: 1389-395.
2. Cassidy JT, Sullivan DB, Petty RE, Ragsdale C. Lupus nephritis and encephalopathy: prognosis in 58 children. Arthiritis Rheum 1977; 20: 315-22.
3. Peterson RDA, Vernier RL, Good RA. Lupus erythematosus. Ped Clin N Am 1963; 10: 941-78.
4. Zetterstom R, Berglund G. Systemic lupus erythematosus: a clinical study. Acta Ped Scand 1956; 45: 189-204.
5. Kovacs JAJ, Urowitz MB, Gladman DD. Dilemmas in neuropsychiatric lupus. Rheum Dis Clin N Am 1993; 19: 795-813.
6. Tan EM, Cohen AS, Gries JF et al. The 1982 revised criteria for the classification of systemic lupus

erythematosus. Arthritris Rheum 1994; 37: 1609-1913.

7. Bilaniuk LT, Patel S, Zimmerman RA. CNS disease in systemic lupus erythematosus. Radiology 1977; 124: 197-121.

8. Bentson J Reza M Winter J et al. Steroids and apparent cerebral atrophy on computerised tomography scans. J Comput Asset Tomogr 1978;2 : 16-23.

9. Raymond AA, Zariah AA, Samad SA. Et al. Brain Calcification in patients with cerebral lupus. Lupus 1996; 5: 123-28.

10. Dubois EL, Tuffanelli DL. Clinical manifestations of SLE: Computer analysis of 520 cases. JAMA 1964; 190: 104-11.

11. Fathers E, Fuller G. Vasculitic neuropathy Brit Journ of Hosp Med 1996; 10: 643-47.

12. Sterling G. West. Neuropsychiatric Lupus. Rheumatic Disease Clinics of North America. 1994; 20: 129-57.