This group of infants developed a transient rise in intracranial pressure without evidence of central nervous system infection. Discussion with colleagues leads us to believe that this condition is much more common than has previously been recognised.

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Cerebral systemic lupus erythematosus

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SUMMARY Cerebral systemic lupus erythematosus is uncommon in childhood. Three further cases are presented to draw attention to the unusual and varied clinical manifestations of this condition.

The diagnosis of cerebral systemic lupus erythematosus (SLE), even in adults, is easily overlooked in the absence of more widespread systemic involvement by the disease. In children there is an even greater likelihood of misdiagnosis because of the rarity of the disorder in this age group.¹ The present report of three children who presented with cerebral manifestations of SLE emphasises not only the varied features of such neurological involvement but also the need to investigate any obscure neurological illness in children by immunological tests.

Case reports

Case 1. A boy aged 6 years presented with writhing movements of the left arm followed several weeks later by sudden flexion and extension movements of the left leg. These worsened over the next three months and were accompanied by the evolution of dystonia of the left eyelid and episodic deviation of the eyes to the left. Six months later he developed focal tonic clonic seizures affecting the left side which were difficult to control, despite the use of phenytoin, sodium valproate, clonazepam, and phenobarbitone.

Over the next two years he followed a fluctuating course, with variation in his dystonia and mobility. Attention span, behaviour, and both reading and writing all deteriorated. Investigations, including biochemical screening of plasma and urine for inherited or acquired metabolic disorders, a computed tomogram of the brain and nuclear magnetic resonance brain scan, carotid angiography, and brain biopsy all failed to give a diagnosis. An area of atrophy in the head of the left caudate nucleus was the only finding of note. At the age of 9 years he developed a 'lupus syndrome' characterised by arthralgia, lymphadenopathy, and a morbilliform rash, which was initially thought to due to his anticonvulsant treatment. The presence of changes pathognomonic for SLE on immunohistology of a skin biopsy specimen, together with the presence of characteristically high titre antibodies to double stranded DNA (table), however, suggested that the whole illness, including the presenting neurological features, was the result of SLE. Treatment with prednisolone (40 mg/1.73 m²/day) was introduced with a dramatic improvement not only in the lupus syndrome but also in behaviour and intellectual function. Gradual withdrawal of the prednisolone over a period of a month was followed by a deterioration which, however, responded once more to the reintroduction of steroids and a small supplement of azathioprine. These measures were followed by an appreciable improvement in behaviour, speech, and in school performance. Control

Table Investigation and immunological findings in three children with neurological manifestations of systemic lupus erythematosus

	Case 1	Case 2	Case 3
Erythrocyte sedimentation rate (mm in the first hour)	16	81	4
Total leucocyte count ($\times 10^9/l$)	5.0	8.8	8.2
Total lymphocyte count ($\times 10^9/l$)	1.2	1.94	3.69
Antinuclear antibody (reciprocal of titre)	500	300	100
Antidouble stranded DNA antibody (reciprocal of titre)	640	160	Negative
Antilymphocyte antibody	Positive	Positive	Negative
C3 (g/l)*	0.86	1.73	0.80
C4 (g/l)†	0.10	0.38	0.28
Urea (mmol/l)	3.2	0.5	5.7
Skin biopsy specimen immunohistology	Granular deposits of IgG/IgM at dermoepidermal junction	Granular deposits of IgG/C3 at dermoepidermal junction	Vasculitis with IgM/C3 in dermal vessels and deposits of C3 at dermoepidermal junction

*Reference range 0.20–0.65 g/l; †reference range 0.15–0.45 g/l.

of the epilepsy has remained variable on continuing anticonvulsant treatment and there has been no improvement in the dystonia, despite the performance of stereotactic surgery.

Case 2. A 6 year old girl developed headaches and blurred vision, which resolved spontaneously over a five week period. A computed tomogram of the brain and a cerebral angiogram were both normal. Two months later she developed fever and meningism with a pleocytosis in the cerebrospinal fluid (270 leucocytes $\times 10^6/l$; 75% polymorphonuclear leucocytes). Bacteriological studies, however, gave negative results and she failed to respond to antimicrobial chemotherapy. Her illness progressed with the development of ptosis, nystagmus, intention tremor, a left VII nerve palsy, and bilateral extensor plantar responses. Recent experience with case 1 prompted further immunological investigations (table), which suggested a diagnosis of cerebral SLE on the basis of high titre antinuclear antibodies coupled, once more, with pathognomonic changes on immunohistology of a skin biopsy specimen. She made a dramatic response to high dosage prednisolone (60 mg/1.73 m²/day) with resolution of fever and all neurological signs and has continued to make excellent progress physically and educationally on a gradually reducing alternate day regime of prednisolone. It proved possible to wean her off steroids after some 12 months' treatment with no evidence, as yet, of any relapse.

Case 3. A 7 year old girl presented with a one week history of ocular flutter and intention tremor. A computed tomogram of the brain was normal and a diagnosis of cerebral SLE was again established

by immunological screening (table) which, again, showed the presence of high titre antinuclear antibodies and vasculitic changes in immunohistology of a skin biopsy specimen. Her symptoms disappeared after 10 days treatment with high dosage prednisolone (60 mg/1.73 m²/day) while further progress has been satisfactory on a continuing low dose alternate day regime of prednisolone.

Discussion

SLE is an uncommon disease in childhood with a very variable incidence of involvement of the central nervous system, which ranges from 20% to 44% in two recently published series.^{1 2} The most often observed manifestations include seizures, cranial nerve palsies, ataxia, nystagmus, papilloedema, meningitis, tremor, cortical blindness, and coma.^{2 3} Neuropsychiatric manifestations including psychosis and personality disorder may also occur. In the present report, the child with hemidystonia is, we believe, the first described case of this syndrome occurring as a result of cerebral SLE. In the series of Yancey *et al* involvement of the central nervous system occurred at the onset of the disorder in 13 of the 16 cases with neurological disease,² and this tendency for the central nervous system involvement to be an early feature is evident in the present small group as well.

Our cases also show clearly the value of early immunological investigations in children with obscure neurological manifestations. All three children had high titre antinuclear antibodies associated with characteristic changes on immunohistology of skin biopsy specimens, which proved particularly valuable in confirming the diagnosis in the two

patients who did not have any other systemic features of the disease.

The high titre antibody to double stranded DNA in case 1 was also helpful in excluding a drug induced lupus syndrome while additional screening for both precipitating antibodies to extractable nuclear antigens^{4 5} (such as anti-RNP, anti-Ro, anti-La and anti-Sm) and anticardiolipin antibodies might also have been useful. These additional autoantibodies can help to define subsets of the disease (such as the thrombotic tendency associated with anticardiolipin antibodies⁶) as well as occasionally being positive when conventional testing for antinuclear antibodies produces negative results.

The improved survival reported in recent series of cerebral SLE has been attributed to earlier diagnosis, more aggressive treatment, and appropriate follow up as well as to the recognition of milder cases.^{1 2} In our series, although the diagnosis in the first case was delayed for three years, increasing awareness and early immunological screening led to a prompt diagnosis in the other two cases who responded well to vigorous steroid treatment and were left without any residual neurological deficit.

We present these cases to show the varied neurological presentations of cerebral lupus erythematosus and to draw further attention to this

condition in childhood. In view of its rarity, we feel it would be useful to set up a national register of cases to monitor progress and treatment of the disorder.

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Copper in urine and hair in Indian childhood cirrhosis

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SUMMARY In advanced Indian childhood cirrhosis (ICC) urine copper concentration was higher (range 416–103 448 mg/g creatinine) than in other hepatic diseases (range 67–10 303 mg/g creatinine). In early ICC urine copper concentration was more modestly raised (1188–9470 mg/g creatinine), but rose to high values (2222–42 819 mg/g creatinine) after a single dose of penicillamine 20 mg/kg. A post-penicillamine urinary copper:creatinine ratio >10 000 mg/g supports a diagnosis of ICC. The concentration of copper in the hair, while increased in advanced ICC, is of no diagnostic value in early cases.

The clinical diagnosis of Indian childhood cirrhosis (ICC) is easy in the late presenting case but is unreliable at an earlier stage. Liver biopsy is therefore necessary.¹ We sought a robust non-

invasive diagnostic method and we have therefore evaluated copper concentrations in urine and hair. To obviate the need for 24 hour urine collections, which would not be feasible if the method was to become of value in the field, the copper:creatinine ratio was measured in random samples of urine. The cupriuretic effect of a single dose of penicillamine is of diagnostic value in Wilson's disease,² and was studied in ICC and other hepatic disorders.

Hair is painless to collect, easy to store and transport, and provides a historical measure of intracellular copper. Despite well described limitations of hair trace metal analysis,³ previous workers have suggested that copper concentration in hair is raised in ICC.^{4 5}

Methods

Urine was collected from 57 children with ICC and