rological deterioration and most of the children die by 10 years after the onset of neurological deficit.

REFERENCES

1. Menkes JH. Hallervorden-Spatz disease. *In:* Text Book of Child Neurology, 3rd edn. Philadelphia, Lea and Febiger, 1985, pp 130-131.
2. Vakili S, Drew AL, Von Schuching S, Becker D, Zeman W. Hallervorden-Spatz syndrome. Arch Neurol 1977, 34: 729-738.
3. Swisher CN, Prensky AL, Devivo DE. Co-existence of Hallervorden-Spatz disease with acanthocytosis. Trans Am Neurol Assoc 1972, 97: 212-214.
4. Sethi KD, Adams RJ, Loring DW, el Gammal T. Hallervorden-Spatz syndrome: Clinical and magnetic resonance imaging correlations. Ann NeuroU 988, 24:692-694.

Oral Acyclovir in Treatment of Suspected Herpes Simplex Encephalitis

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Herpes simplex encephalitis (HSE) is **a** relatively frequent cause of sporadic acute encephalitis associated with progressive neurologic signs(l). It is the most common cause of fatal sporadic encephalitis and it accounts for 33-57% of cases of encephalitis with focal localizing signs. In survivors, it frequently produces severe sequelae(2). Intravenous acyclovir is currently the drug of choice for HSE and it substantially reduces the mortality and morbidity(2). We could* not come across any reports of trials of oral acyclovir in the treatment of HSE.

We report here, a case of suspected herpes simplex encephalitis, which responded dramatically to oral acyclovir therapy. The cost of 10 days treatment of a 25 Kg child with intravenous therapy drug is Rs. 21,000/-, while it is only Rs. 750 with oral therapy.

Case Report

A 2 year 10 months old girl was admitted with complaints of sudden onset of altered sensorium, fever and left sided recurrent focal seizures for the past 7 hours. There were no overt manifestations of herpes simplex infection in the patient or in her contacts and no local outbreaks of similar illness. There was no history of head injury, ear discharge, local infection, and dog bite.

On admission, the patient was

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Received for publication: August 9,1994; Accepted: November 1,1994

semicomatosed, pyrexic, normotensive and had recurrent left sided focal seizures. On examination there was left sided upper motor neuron hemiparesis and ipsilateral supranuclear facial nerve palsy. The pupils were normal in size and reaction and fundus examination revealed bilateral hyperemic discs.

From the above findings, a possibility of focal brain inflammatory pathology, either bacterial or viral was entertained. Since the child's parents could not afford the cost of intravenous acyclovir therapy an informed consent was taken for withholding it.

Relevant investigations done during hospital stay were: hemoglobin 8.5 g/dl; total leukocyte count—9,500 cu/mm; differential leukocyte count $P_{67}L_{33}$; cerebrospinal fluid examination-normal; and bacterial culture-sterile. Anti Herpes simplex virus (lgM) titre was 70.35 Eu/ml (convalescent sera by Elisa method) and antiherpes simplex igG titres, in both acute and convalescent sera, were 1:160. Acute and convalescent sera were negative for Japanese encephalitis. The CT Scan Head on third day of hospitalization revealed findings consistent with cerebritis in right temporal, parietal and occipital lobes. Cerebritis was diagnosed by CT scan on visualizing focal irregular mass of low attenuation in the white matter which had irregular enhancement with contrast, without any significant edema around it or any pressure effect on the ventricles. A repeat CT scan three weeks later showed findings consistent with post encephalitic atrophy (generalized) with exaggerated atrophy in the right temporal, parietal and occipital lobes. Electro-encephalography (on the 4th week of hospitalization) showed generalized slow wave activity, more prominent on right side.

There was initially improvement in sensorium, and on the 6th day, the patient became conscious and seizure free. However, 48 hours later the child showed increasing irritability with deterioration in her sensorium and loss of vision. We suspected cortical blindness, since the pupils were of normal size and reaction and the repeat fundus evaluation was within normal limits. At this juncture, keeping in mind the possibility of HSE and its association with vacillations in mentation and relentless progression we began oral acyclovir, 30 mg/kg/day divided in 8 hourly doses, for 10 days.

At the time of discharge, after completion of 10 days oral acyclovir therapy, she had normal vision and neurologic sequelae consisted of left hemiparesis (grade 3/5) in both upper and lower limbs. On 4 weeks follow up, she was seizure free, had normal vision and the power on the left side had further improved to grade 4/5.

Discussion

HSE was suspected in our patient on the basis of the clinical triad of fever, altered consciousness, and focal neurologic involvement and development of neutralizing antibody titres. We also ruled out Japanese encephalitis, this being another common focal encephalitis in our area.

Herpes simplex is known to cause sporadic, often focal acute encephalitis(l-3). There is a bimodal age distribution, with a significant group of patients in the pediatric age group(4). The diag-

nosis of HS infection is based on any two of the following: (i) a compatible clinical picture; (ii) isolation of virus; *(iii)* development of specific neutralizing antibody; and *(iv)* demonstration of characteristic cells or histological changes on biopsy(3).

Acyclovir, a synthetic purine nucleoside analogue, has been established by large collaborative studies, as treatment of choice for biopsy proven HSE(5). *In vitro,* viral plaque formation is reduced by 50% by plasma drug concentration of 0.02—0.2 mg/ml for *Herpes simplex* type 1 and 0.03-0.5 mg/ml for *Herpes simplex* type 2(5) viruses. The intravenous dose of 250 mg/m^2 results in peak plasma concentration of about 10 mg/ml; these value declining to an average of about 0.7 mg/ml by 8 hours(5). Bioavailability of oral acyclovir is only 15-30%(5,7). With this value of oral bioavailability of the drug and using the same dosage as for the intravenous therapy, we derived that the peak and average concentration of the drug attained by oral administration will be within the *in vitro* 50% viral plaque reduction range from both type of *Herpes simplex* viruses.

Therefore, taking into consideration, the high mortality and morbidity associated with focal encephalitis, poor feasibility of definitive diagnostic tests, high cost of intravenous acyclovir(5), and our experience with oral acyclovir, we feel that this modality of treatment has potentials to prove beneficial. Further trials are needed to establish the usefulness and dosage of oral acyclovir in the treatment of suspected HSE.

REFERENCES

1. Corey L. *Herpes simplex* viruses. *In:* Harrison's Principles of Internal Medicine, 13th edn. Eds Braunwald, Issenlbacher KJ, Wilson JD, Martin JB, Fauci AS, Rasper DL. New York, McGraw Hill Book Company, 1994, pp 781-787.
2. Kohl S. Herpes simplex virus encephalitis in children. Pediatr Clin North Am 1988, 35: 465-483.
3. Phillips CF. *Herpes simplex* virus. *In:* Nelson Textbook of Pediatrics, 14th edn. Eds. Behrman RE, Kliegman RM, Nelson WE, Vaughan VC. Philadel phia, WB Saunders Co, 1992, pp 797-800.
4. Olson LC, Buescher EC, Artenstein MS, *et ah* Herpes virus infection of the human nervous system. N Eng J Med 1967,277:1277-1277.
5. Douglas RG (Jr.). Antimicrobial agents; Antiviral agents. *In:* The Pharmacological Basis of Therapeutics, 8th edn. Eds. Cilman AG, Theodore WR, Nies AS, Taylor P. New York, Pergamon Press, 1991, pp 1182-1201.
6. Whitley RJ, Alford CA, Hirsch MS, *et al.* Vidarabine *versus* acyclovir therapy in HSE. New Engl J Med 1986, 314: 144-149.
7. Dharnidhaika VR, Agarwal M, Dandge VP. Acyclovir. Indian Pediatr 1993,30: 553-558.