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UNUSUAL NEUROLOGIC COMPLICATIONS OF TYPHOID FEVER (APHASIA, MONONEURITIS MULTIPLEX, AND GUILLAIN-BARRÉ SYNDROME): A REPORT OF TWO CASES*

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Although typhoid fever can frequently lead to such neurological manifestations as confusion, delirium, and encephalopathy, Guillain-Barré syndrome, aphasia and mononeuritis multiplex occur very rarely. In this report, we describe two patients with typhoid fever who developed these unusual complications. *Key words: typhoid fever, aphasia, Guillain-Barré syndrome, mononeuritis multiplex.*

Neurological complications are seen in 5-35 percent of patients with typhoid fever[1]. Frequent signs and symptoms include confusion, delirium, convulsions, and meningism, which mostly result from encephalitis and/or encephalopathy. However, aphasia, peripheral neuropathy and Guillain-Barré syndrome are rarely seen, especially as complications of typhoid fever[1-7] in children. We present two patients with typhoid fever, one who developed aphasia and mononeuritis multiplex and the other, ataxia and Guillain-Barré syndrome.

Case Reports

Case 1

A thirteen-year-old boy was admitted to the Hacettepe University Children's Hospital because he had difficulty in walking and talking. He had a 15-day history of malaise, fever, headache, and somnolence and a seven-day history of progressive speech impairment resulting in aphasia. He also had progressive weakness of the extremites and was unable to walk unaided for the last three days prior to admission.

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Physical examination revealed a well developed child with normal vital signs. Neurological examination disclosed a conscious well-oriented child. Deep tendon reflexes were reduced in all extremities. The patient suffered a 60 percent loss of muscle strength in the lower extremities and a 20 percent loss in the upper extremities. He developed motor aphasia. All other physical findings were within normal limits.

Laboratory studies revealed a hemoglobin of 11.65 g/dl, white blood cell count 5000/mm^3, with a differential count of 2% band forms, 56% polymorphonuclear leukocytes (PMNL), and 42% lymphocytes. Erythrocyte sedimentation rate was 85 mm/hr. SGOT was 80 IU/L, SGPT 61 IU/L, alkaline phosphatase 132 IU/L, ammonia 248 μg/dl (normal = 20-120 μg/dl), HBsAg (−), anti-HBs antibody (−), LE cell (−), C3 170 mg/dl (normal = 60-120 mg/dl), C4 36 mg/dl (normal = 20-40 mg/dl), and ANA (−). The lumbar puncture revealed 7 PMNL/mm^3. Protein content was 48 mg/dl, glucose 80 mg/dl and viral and bacterial cultures were negative.

Cranial CT, visual and auditory evoked potentials were normal. An EEG disclosed moderately severe irregularity in bioelectrical activity, especially in the left hemisphere. Electromyographic examination was consistent with mononeuritis multiplex.

Salmonella group D "O" antigen was positive in 1/320 titer, and Salmonella group B, H and O antigens in 1/320 titer.

A rapid recovery of the patient was noted after the administration of oral trimethoprim sulfamethoxasole. On the tenth day of therapy, the patient was able to walk unaided and spoke clearly. He was discharged on the 13th day of hospitalization.

Case 2

A nine-year-old boy was admitted to the Hacettepe University Children's Hospital because he had difficulty in walking. He had a 40-day history of fever, headache, arthralgia, nausea, vomiting, and anorexia and an 18-day history of diplopia and weakness of the legs which spread to the arms. Deep tendon reflexes in the lower extremities could not be elicited. Ten days later, the weakness of the extremities and the diplopia diminished, but the patient still had difficulty in walking.

Physical examination revealed an axillary temperature of 36.5 °C, pulse rate 96/min. and respiratory rate 22/min. His general condition was satisfactory. Neurological examination disclosed a child who was conscious and who had no sensory or motor dysfunction. The cranial nerves were intact, deep tendon reflexes were normoactive and cerebellar tests revealed normal results except for an ataxic gate. The results of the funduscopic examination were within normal limits.

Laboratory studies revealed hemoglobin 12 g/dl and white blood cell count 6800/mm^3. Examination of the peripheral blood smear revealed 66 percent neutrophils, 2% eosinophils, and 32% lymphocytes. The urine analysis, and liver and kidney function tests were all within normal limits. Lumbar puncture revealed no white blood cells, protein was 120 mg/dl, glucose 63 mg/dl, and simultaneous blood glucose 106 mg/dl. Group D salmonella was isolated from the stool culture. Results of serologic tests showed Salmonella group D "H" and "O" antigens positive at 1/160 titer.

Electromyography revealed impeded nerve conduction velocity consistent with Guillain-Barré syndrome. The cranial CT was normal.

Ampicillin was administered intravenously. The patient recovered completely and was discharged.

Discussion

From five to thirty-five percent of typhoid fever cases present with neuropsychiatric manifestations such as peripheral neuritis, facial palsy, aphasia, intracerebral bleeding, encephalopathy, meningitis, meningismus, delirium, coma, hemiplegia, convulsions, parkinsonism, schizophrenia, ataxia or Guillain-Barré syndrome[1-4]. Among the neurological findings, meningismus, convulsions, confusion and delirium are quite frequent, while mononeuritis multiplex, aphasia and Guillain-Barré syndrome are rarely seen[1-7].

An evaluation of 959 patients with typhoid fever in Nigeria in 1972[2] revealed that 57% developed delirium, 5% meningism, 0.2% meningitis, 1% parkinsonism, 0.7% sensorimotor neuropathy without albuminocytologic dissociation, 1.7% convulsions, 0.3% mononeuritis multiplex, 2.6% were in a semicoma, and 1% were in a coma.

In 1968, Scragg and associates[3] showed that out of 316 patients with typhoid fever, nine (2.8%) had aphasia and that only one also had hemiplegia. All patients recovered completely within eight weeks. The etiopathogenesis of aphasia in typhoid fever is still unclear, but it is thought to be caused by Salmonella encephalitis.

Although it was not possible to isolate salmonella in the cultures obtained from Case 1, clinical presentation, history and the serologic tests were consistent with typhoid fever[8]. The fact that the patient recovered shortly after the initiation of antibiotic therapy supports the hypothesis that aphasia and mononeuritis multiplex most likely resulted from typhoid fever.

Peripheral neuritis in typhoid fever may be manifested as sensory motor peripheral neuritis, mononeuritis multiplex or Guillain-Barré syndrome[1].
Isolated cerebellar ataxia in typhoid fever is the second most common

neurological symptom after delirium. In 1985, Wadia and associates[4] demonstrated that in 718 patients with typhoid fever, the incidence of neurologic disturbance was 5 percent and that about 50 percent of them (2.3% of the total) had cerebellar ataxia. The cerebellar ataxia was mostly an isolated entity which abated within a mean of 9.4 days and a maximum of six weeks.

In Case 2, in addition to the albuminocytologic dissociation in CSF, the history, physical findings and electromyographic findings were also consistent with Guillain-Barré syndrome. The patient developed ataxia, but had no other finding of cerebellar dysfunction. Group D Salmonella was isolated in the stool culture, and antibody titers were found to be high in the serum. This patient also made a complete recovery in a short time following intravenous ampicillin treatment.

It should be emphasized that the classical findings of typhoid fever encountered in adults may not be observed in children. The child with typhoid fever may be afebrile and present only with aphasia, ataxia, Guillan-Barré syndrome, mononeuritis multiplex, schizophrenia, or parkinsonism. Thus, if a patient has unexplained neurological findings, salmonellosis should definitely be suspected.

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