# NEUROLOGICAL MANIFESTATIONS OF INFECTIOUS HEPATITIS

## A CASE REPORT

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Infectious hepatitis is today regarded as being a fairly mild disease with a good prognosis. It must, however, be remembered that there can be fatalities—2% in a series of 1,200 cases reported by Stokes and Miller[1]—and that complications do occur.

Most of us are familiar with the neurological manifestations of hepatic precoma, or with portal systemic encephalopathy; it is far less common, however, to find neurological changes in cases of acute infectious hepatitis, and a further case is reported here.

### CASE REPORT

B.G., a 19-year-old telephone technician, was admitted to this hospital on 9 October 1960, with a 2-day history of upper abdominal pain and nausea. For about 5 days he had noticed that his urine had been dark in colour, and his stools somewhat lighter than usual. On examination he was jaundiced, and the liver was barely palpable and tender. There was no lymphatic-gland enlargement.

*Laboratory Investigations (10 October 1960)*

*Urine:* Urobilinogen, present (trace); urobilin, present (trace); bilirubin, present (++++); and bile acid, present (++).

*Blood:* Haemoglobin, 17·1 G. per 100 ml.; white-cell count, 4,500 per c.mm.; neutrophils, 61%; monocytes, 7%; lymphocytes, 32%; and erythrocyte sedimentation rate, 18 mm. in first hour.

*Liver-function tests:* Total protein, 7·3 G. per 100 ml.; albumin, 3·6 G. per 100 ml.; globulin, 3·7 G. per 100 ml.; bilirubin (direct), 4·5 mg. per 100 ml.; bilirubin (total), 5·8 mg. per 100 ml.; alkaline phosphatase, 18 King-Armstrong units; thymol turbidity, 8·8 units; thymol flocculation, positive (+++); Takata-Ara reaction, positive (+); and serum G-0 transaminase, 475 units per 100 ml.

*Course of Illness*

On 12 October the patient started complaining of cramps in the abdomen and also spasm of the neck. These spasms were intensely painful and accompanied by profuse sweating. During the course of the day he had a number of attacks, as follows: there was a period of hyperventilation followed by a cry, the head turned to the right, right arm and leg rigid, pupils widely dilated, patient conscious throughout and responding to questioning. This attack lasted about 30 seconds.

During this attack blood was taken for chemical studies, with the following results: Blood sugar, 146 mg. per 100 ml.; blood urea, 29 mg. per 100 ml.; chlorides, 106 mEq. per litre; sodium, 137 mEq. per litre; potassium, 4·9 mEq. per litre; and calcium, 4·9 mEq. per litre. A lumbar puncture was performed. The pressure was 140 mm. $H_2O$. The cerebrospinal-fluid (CSF) chemistry was normal.

The patient was heavily sedated, mainly with paraldehyde,

but despite the liver disease it was found necessary to add barbiturates as well. He remained reasonably free of attacks, but on 13 October started having similar attacks again; this time, however, they were left-sided. These attacks were once again controlled by sedation, but, since his general condition appeared poor, it was decided to add cortisone, 25 mg. 6-hourly, to the regimen of high carbohydrate diet and oral neomycin. Neomycin was given to 'sterilize the bowel', since there was the suggestion of hepatic precoma.

On 15 October he developed a fine, almost Parkinsonian tremor of both hands, excessive salivation and mask-like facies. There was also a ptosis of the right eye; pupillary reactions were normal. This stage was the worst reached by the patient, and from this time on there was a rapid improvement in his condition.

The dose of cortisone was reduced and, since he was so well, he was allowed to go home on 27 October, with the injunction not to exert himself and to return for follow-up studies.

He was last seen on 5 November, when he was feeling very well. On this date his liver-function tests were as follows: Total protein, 8·3 G. per 100 ml.; albumin, 4·8 G. per 100 ml.; globulin, 3·5 G. per 100 ml.; bilirubin (direct), 0·4 mg. per 100 ml.; bilirubin (total), 0·8 mg. per 100 ml.; alkaline phosphatase, 8·8 King-Armstrong units; thymol turbidity, 4·9 units; thymol flocculation, negative; and Takata-Ara reaction, negative.

Other investigations of interest which were performed were: Paul-Bunnell test, negative; leptospiral agglutinations, negative; and viral studies of blood and CSF, negative. There was no increase in urinary amino acids.

## DISCUSSION

We were faced in this case with a triple problem: (1) Did this patient show neurological manifestations as an unusual presentation of infectious hepatitis? (2) Was this infectious hepatitis with coincident encephalitis? (3) Was this epilepsy precipitated by infectious hepatitis?

In their series of 1,200 cases, Stokes and Miller[1] reported involuntary movements in 6 patients, ankle clonus was present in 8, and facial palsy, external rectus palsy and external strabismus were seen in single patients. McMath[2] stated that neurological complications of infective hepatitis were rare. The incidence varied from 2 of 170 cases in one series, to 32 of 151 cases in another.

Himsworth[3] described limbs with a peculiar clasp-knife rigidity not unlike that in Parkinson's disease; occasionally fine tremors and spasmodic movements are present, rarely do convulsive attacks occur. There may also be drenching sweats, and both these and the convulsive attacks may sometimes be caused by hypoglycaemia consequent on impairment of the glycogenic functions of the liver.

Stokes, Owen and Holmes[4] classified the neurological findings in infectious hepatitis into 4 main groups:

1. Coma, convulsions, delirium, and incontinence.

2. Generalized or localized muscular rigidity with increased tendon jerks, with or without a Babinski sign, choreiform movements, and in one case a Parkinsonian tremor.

3. Large focal haemorrhages into the nervous system, which may or may not produce focal signs.

4. Peripheral neuritis.

The same authors make the following suggestions to account for the occurrence of the pyramidal and striatal signs: (*a*) Mutation of the infectious hepatitis virus giving it a neurotropic character, (*b*) specific attack on basal ganglia and pyramidal tracts by products of autolysed liver cells, and (*c*) toxins from the bowel passing through an incompetent liver.

In the case reported here the signs were a mixture of pyramidal and basal-ganglion involvement. The cerebrospinal-fluid findings were normal, and this bears out the finding of Stokes, Owen and Holmes,[4] although Sherlock[5] stated that 'an increase in protein and lymphocytes of CSF has led to the suggestion that the hepatitis virus may have neurotropic properties'.

The drenching sweats which occurred in this patient have already been referred to, but the normal blood sugar does not bear out the contention of hypoglycaemia.

Despite the apparent severity of this patient's condition and the initial alarm occasioned by his bizarre symptomatology, his response was good. Before the steroid era, Lescher[6] had stated that the general prognosis of nervous complications seemed to be good, even though the patient may be profoundly ill.[7] Steroid therapy in this case may, however, have accelerated the resolution of the disease as shown by the rapid return to normality of liver-function tests, since it is known that cortisone and ACTH cause a rapid fall and a lower peak in the serum-bilirubin concentration, and more rapid reversion to normal of the thymol and cephalin-cholesterol tests.[5]

In view of the normality of the CSF findings, and the normal viral, leptospiral and rickettsial studies, and also the virtually spontaneous response and complete resolution of the condition, it seems that this was a neurological manifestation of infectious hepatitis rather than a concomitant encephalitic process.

## SUMMARY

A case of infectious hepatitis with neurological manifestations is described. Recovery was complete. The literature on the subject is briefly reviewed.

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