TREATMENT OF TUBERCULOUS MENINGITIS

BY

JOHN G. KERR, M.B., M.Ch.Orth.

Senior Orthopaedic Physician, Lakeville State Sanatorium,
Middleboro, Mass., U.S.A.

The appearance of the article by Russell and MacArthur (1953) on the treatment of tuberculous meningitis with intrathecal streptomycin, and the results reported therein, prompts one to wonder whether this is a very good method of treatment. As so often in the past, one wonders how many of the after-effects are due to the disease and how many to the treatment. Clark, Elmendorf, Cawthon, Muschenheim, and McDermott (1952) have reported the use of isoniazid in the treatment of miliary and meningeal tuberculosis. They expressed the hope that the use of isoniazid orally and streptomycin by the intramuscular route might permit the elimination of the intrathecal use of streptomycin without sacrificing the maximal obtainable antimicrobial activity within the central nervous system. A similar hope led to the use of this regime in three cases of tuberculous meningitis. Although it is obviously too early for final assessment, it is felt that the quite remarkable improvement obtained and maintained should be reported even at the risk of prematurity.

Case 1

A coloured female child aged 3 was admitted on March 12, 1952. On January 1 a diagnosis of tuberculous meningitis had been made and proved elsewhere. Initially intramuscular and intrathecal streptomycin were given for 49 days. A right sixth-nerve paralysis was noted and her general condition was described as apathetic and listless. As she did not respond to this therapy, increasing doses of intrathecal purified protein derivative were given in addition to streptomycin, with some slight improvement. She received 50 mg. of streptomycin and 5 µg. of purified protein derivative every other day intrathecally, together with 1 g. of streptomycin intramuscularly daily. Her cell count varied between 280 and 350 per c.mm. At the time of her admission to this hospital she was found to be apathetic and almost completely blind. She had paralysis of the sixth nerve on the right and a probable defect in associated ocular movement. The optic disk showed evidence of early primary optic atrophy. A spastic paralysis on the right and a flaccid paralysis on the left affected the lower limbs almost entirely. There was paralysis of the left sternomastoid muscle. She was incontinent of urine and faeces. Examination of the spinal fluid showed 366 cells per c.mm. and a total protein of 230 mg. per 100 ml. Intrathecal therapy was continued, but her general condition did not improve. The cell count rose to 490 per c.mm.

On April 1 it was decided to discontinue intrathecal therapy, to persevere with the intramuscular streptomycin and oral P.A.S., and to give, in addition, 50 mg. of isonicotinic acid daily. The improvement was remarkable. Two weeks after discontinuation of the intrathecal therapy the cell count of the cerebrospinal fluid was 88 per c.mm. and the protein estimation was 75 mg. per 100 ml. One month after starting isoniazid therapy the child was up in a wheelchair. After a further two weeks the cell count was 9 per c.mm., all lymphocytes. On July 16 her sight was regarded as normal. There was no paralysis and her gait was good. At the time of writing, one year after the commencement of isoniazid therapy, she was a normal child.

Case 2

A coloured woman aged 23 was admitted on November 18, 1952. Ten weeks previously the diagnosis of tuberculous

meningitis had been proved and treatment instituted elsewhere. Her treatment consisted of daily intrathecal and intramuscular streptomycin together with P.A.S. A flaccid paralysis of the lower extremities appeared and showed no signs of improvement. At the time of her admission to this hospital she was found to be well developed. She was having some difficulty with speech and was slightly disorientated. The abdominal muscles showed spasm and tenderness, with hyperactivity of the abdominal reflexes. The upper extremities were grossly normal. The lower extremities showed an extensive flaccid paralysis with hyperaesthesia. Examination of the cerebrospinal fluid showed 348 cells per c.mm. (96% lymphocytes, 4% polymorphs).

In the light of the previous case and with the knowledge that intrathecal therapy had not already effected any great improvement, it was decided to give the patient no further intrathecal medication, but to rely on intramuscular streptomycin, 1 g. twice a week, P.A.S., 12 g. daily by mouth, and 6 mg. of isonicotinic acid derivate per kg. daily. Within two weeks her condition had greatly improved both objectively and subjectively. She became completely orientated and had no complaints. Her legs were no longer painful, and they increased in strength daily. Three weeks after the beginning of the treatment the cell count was 88 per c.mm. Two months later it was 2 per c.mm. At this date examination rated all the leg and abdominal muscles as either good or normal. In March, 1953, a cerebrospinal fluid examination showed a normal cell count, there was normal power in the lower extremities, and she was asymptomatic.

Case 3

A white male aged 30, with a long history of extrapulmonary tuberculosis involving the spine and the sternum, was operated on for fusion of the spine from D 10 to L 1 on July 3, 1952. The post-operative course was uneventful and progress to fusion steady. In December he became fully active wearing a brace, and was asymptomatic. On January 5, 1953, he first developed extremely severe headaches. Lumbar puncture was done and fluid was found to be under a pressure of 200 mg. of water. A cell count showed 239 cells (98% lymphocytes); total protein was 55 mg. per 100 ml. The cerebrospinal fluid was negative for tuberculosis by guinea-pig test and by culture, but the tuberculous nature of the meningitis was assumed. The patient had been under treatment with streptomycin intramuscularly and P.A.S. orally for one year until December 23, 1952.

X-ray examination showed disease well below the spinal fusion. The fusion was solid from the tenth dorsal vertebra to the first lumbar. The second lumbar vertebral body was diseased, with thinning of the intervertebral disk between the second and third lumbar vertebrae. Streptomycin intramuscularly, 1 g. three times a week, P.A.S., 12 g. daily, and ditubin, 400 mg. daily, were started on January 5, 1953. Two weeks later the patient was virtually asymptomatic and the cell count had fallen to 16 per c.mm. The total protein was 30 mg. per 100 ml. At the time of writing, three months after his acute episode, he was completely asymptomatic.

Conclusion

These three cases are obviously too few in number and of too limited duration to be the subject of dogmatism. However, they do indicate that intrathecal streptomycin is potentially dangerous and is apparently no more beneficial than the combination of intramuscular streptomycin and oral isonicotinic hydrazide and P.A.S. No trial has been made of isonicotinic hydrazide alone, as most workers have felt that the optimum effect is obtained by using all three drugs. Further findings will be reported when a greater number of cases have been treated for a longer period.

REFERENCES

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