CHOREA COMPLICATED BY SEPTICÆMIA, MENINGITIS AND CEREBRAL SYMPTOMS FOLLOWING SEROTHERAPY, WITH RECOVERY.

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Doris B., a girl aged $8\frac{1}{2}$ years, was admitted on November 22nd, 1933, under the care of Dr. Frew, with 10 days' history of stumbling, dropping things, and becoming increasingly inarticulate. She had had pains in the knees four weeks previously, and had been worrying recently over school examinations and her father's illness. There was no history of sore throats, but the tonsils had been removed two years before, following otitis media.

The mother had had acute rheumatism at the age of 10 years.

On examination the child appeared pale and thin, with active choreic movements of the face and hands; the speech was severely affected. Temperature 98° F., sleeping pulse rate 120, respirations 24 per minute. The knee jerks were equal and active. The heart was not appreciably enlarged, and no cardiac murmurs were heard. The sedimentation rate was 50 (normal value—under 10).

Course. The choreic movements, though not very severe, persisted with little change. A week after the child's admission, an apical systolic cardiac murmur was heard, and ten days subsequently an early diastolic murmur became audible in the mitral area. The knee jerks could be obtained only with difficulty.

On February 1st, 1934, there appeared a blood-stained persistent discharge from the left ear, from which a few colonies of hæmolytic streptococci and staphylococcus aureus were cultured. The general condition, however, had improved, and the sedimentation rate had fallen to normal, when on March 28th the child developed measles, and was transferred to the Fever Hospital. Recovery was uneventful until April 15th; the temperature then rose to 101° F. and the child vomited and complained of headache. The vomiting continued. On April 17th the temperature was 104° F. and choreic movements were again active. 40 cc. of anti-scarlet-fever serum were given on this day.

The following day the child was readmitted to the Hospital for Sick Children. She was then extremely ill, with furred tongue, sordes on the lips, active choreic movements, and a loud systolic cardiac murmur conducted out to the axilla. There was definite neck rigidity; Kernig's sign was not obtained. She was given continuous intravenous glucose solution (5 per cent.).

Blood Culture (19.4.34). Hæmolytic streptococci grown.

Lumbar Puncture (21.4.34) showed the presence of turbid cerebro-spinal fluid under increased pressure, and in view of the positive blood culture, 50 cc. of anti-streptococcal serum were given intrathecally and 100 cc. intramuscularly.

The following table shows the findings in the cerebro-spinal fluid obtained on this and subsequent dates.

Table showing Cerebro-spinal Findings.

Date.	Appearance of C.S.F.	Albumin grms. per cent.	Sugar	Chlorides mgs. per cent.	Cells per c.mm.	% polymorphs.	Bacteriological examination.	Anti-Streptococcal serum.
April 21st	Turbid, small clot	0.04	Nil	6.5	1,650	94	No organisms seen. Sterile	50 cc. intrathecally
April 22nd	Turbid	0.25	Nil	6.5	3,000	95	3 pairs gram negative (?) extra-cellular diplococci seen. Culture: sterile	100 cc. intramuscularly
April 23rd	Slightly turbid, yellow	0.20	Nil	6.45	5,400	95	No organisms seen: culture sterile	50 cc. intrathecally
April 24th	Turbid, yellow	0.10	Nil	6.75	650	95	" "	100 cc. intravenously
April 25th	Turbid	0.08	Delayed reduction of Fehling	6.55	980	Mainly	" "	100 cc. intravenously
April 26th	Slightly turbid	0.08	" "	6.8	850	"	" "	100 cc. intramuscularly
April 27th	Very slightly turbid	0.08	Good reduction	6.95	245	50	" "	

The clinical improvement during this time was rapid, and although the temperature was irregularly raised until May 7th the child was subsequently afebrile, with gradual return to normal of the pulse and sedimentation rates. On May 4th the child had a moderately severe anaphylactic shock following the intravenous administration of 40 cc. anti-streptococcal serum, which was given owing to the temperature still being raised. (Serum had been omitted since April 26th.) The child recovered rapidly with adrenalin.

On May 12th, she vomited several times and complained of headache. Two days later she appeared dazed and kept her head turned to the right. She was almost completely unable to use the left arm, which was flaccid and grossly incoordinate. There was marked dysdiadochokinesis of the left arm, and well marked coarse nystagmus of both eyes to the left. There was some weakness of both external recti. The abdominal and tendon reflexes were normally obtained; both plantar reflexes were doubtfully flexor. There was no demonstrable disturbance of sensation and no papilloedema. The child complained of diplopia at this time and developed a generalized serum rash.

In view of the previous history of aural discharge, a cerebellar abscess was at first suspected, but there was no development of papilloedema, and the nystagmus and ataxia of the left arm gradually disappeared. Ten days later there were no residual cerebellar signs.

The child remained in hospital until July 31st, when she was discharged home for prolonged bed-rest. When seen in March, 1935, she appeared plump and well (having gained weight steadily to 6 stone 7 lbs.). There were still slight choreic movements present, and a well compensated mitral lesion. The child was otherwise free from symptoms.

Commentary.

The early history of the case is the classical one of chorea complicated by rheumatic carditis. Whilst the rôle of streptococci in the production of rheumatic lesions remains nearly as problematical to-day as it was twenty years ago, it is well recognized that streptococcal infection of the upper respiratory passages is a frequently associated finding. In this instance hæmolytic streptococci were grown from a persistent discharge from the left ear, and six weeks later, when the child was recovering from an intercurrent infection (measles) she developed streptococcal septicæmia. At approximately the same time she presented meningeal symptoms, and lumbar puncture performed two days after hæmolytic streptococci had been grown from the blood stream showed a turbid cerebro-spinal fluid containing 1,650 cells per c.mm. of which 94 per cent. were polymorphs. In spite of the fact that the sugar content of the fluid was reduced, no organisms were seen on direct examination and cultures were sterile. Since anti-streptococcal serum was administered intrathecally, the cell-counts and albumin-content of the subsequent cerebro-spinal fluid examinations must be interpreted as being due in part to the meningeal reaction which always follows the injection of serum or any other meningeal irritant. The first examination, however (21.4.34), gives definite proof of meningitis having preceded the latter.

The nature of this meningitis is of some interest. Although the presence of streptococci in the blood stream strongly suggested at the time that the condition would prove to be a true streptococcal meningitis, it will be seen that cultures were in every instance sterile. On the second examination (22.4.34) it was thought that three pairs of gram negative extracellular diplococci were seen, but the absence of organisms on each subsequent examination and the negative results of culture make it appear probable that these were artifacts. As the term "aseptic meningitis" is usually reserved for those cases in which no infection is found either in the cerebro-spinal fluid or elsewhere, the present case may be described as a "sterile" meningitis, in which there was no evidence of organisms within the dura. It is almost certain that streptococcal infection was causally related, there being a meningeal inflammatory reaction to the organisms which were present in the blood-stream or ear.

The term "serous-meningitis," which has been used rather loosely and applied to at least two distinct conditions⁽¹⁾, is taken by some writers to imply a localized meningitis of otitic origin, which may either subside or proceed to a purulent meningitis with organisms present in the cerebro-spinal fluid. In this sense, the term would probably be applicable to the present case, though here again it is most exceptional to find the cell-count in the cerebro-spinal fluid so high whilst the latter remains sterile. In most instances, serous meningitis is characterised by considerable increase in pressure of the cerebro-spinal fluid, with a relatively slight

increase in the number of cells ; a cell-count of over a thousand will almost always imply that the condition has passed on to a streptococcal or pneumococcal meningitis. It is also unusual to find serous meningitis occurring without other evidence of mastoid infection or sinus thrombosis, and the reduced sugar-content of the cerebro-spinal fluid in the absence of organisms is another feature of the case that is anomalous.

Apart from the immediate meningeal reaction, the use of anti-streptococcal serum appears to have resulted in cerebral symptoms, a recognised though rare complication of serotherapy. Ten days after an anaphylactic reaction, the child developed a well-marked serum rash, a flaccid paralysis and inco-ordination of the left arm, and nystagmus. From the extent of the paralysis, it is perhaps more probable that the part of the nervous system principally affected was the right fronto-parietal region rather than the left cerebellar hemisphere, and from the progress of the case that the lesion was in the nature of a cerebral oedema, which subsided comparatively rapidly.

It has been said that such cerebral symptoms following serum administration are of rare occurrence. Allen⁽²⁾, who reviewed the neurological complications of serotherapy, found less than fifty examples in all, of which only six were of central type. It is impossible in the present case to insist too dogmatically on the interpretation of the cerebral symptoms, owing to the complicated clinical picture and the fact that a preceding middle-ear infection was known to exist ; but the occurrence of such symptoms in association with a typical serum-rash and their rapid remission do very strongly suggest that they owed their origin to a serum reaction affecting the central nervous system. One is tempted to speculate whether the central nervous system was rendered abnormally vulnerable first by the chorea and then by the aseptic meningeal reaction, whilst the streptococcal septicæmia may well have resulted in some local capillary damage. Such a combination of events certainly makes more understandable the fact that the central nervous system in this instance was involved in the general serum reaction.

Clinically, the most remarkable and cheerful feature of the case has been the recovery from a series of complications, any one of which might reasonably have been expected to prove fatal.

I wish to thank Dr. R. S. Frew for permission to report this case, and Dr. Russell Brain for his helpful criticism.

REFERENCES :

- (1) Brain, W. R., *Diseases of the Nervous System*, 1933, 312.
- (2) Allen, I. M., *Lancet*, 1931, 1, 1128.