

LETHARGIC ENCEPHALITIS

A REPORT OF TWO CASES, WITH THE ISOLATION OF A STREPTOCOCCUS
FROM THE BLOOD OF ONE CASE

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The term encephalitis lethargica was first applied by Von Economo¹ to a number of cases which appeared in Vienna in 1917. The chief clinical characteristics of this disease were lethargy, associated with cranial nerve involvement, manifested by ocular or facial palsy, and fever. Von Economo refers to a similar epidemic disease which occurred in 1712 and 1891, following pandemics of influenza. Numerous other writers have reviewed the literature showing the association of a "sleeping sickness" following pandemics of influenza, and it is not necessary to repeat this here. It may be mentioned that the disease was known as *nona* in Italy following the epidemic of influenza in 1890-91.

Following the observations of Von Economo in 1917, the disease was noted in France and England in the early part of 1918, while Pothier,² Neal,³ and Bassoe⁴ were the first to report this disease in this country in 1919. Numerous reports have appeared since then in the literature.

The recurrence in the past months of an epidemic of influenza in certain sections of this country, and particularly in Chicago, lends interest to the report of the present cases.

CASE 1.—A. L., aged nineteen, girl, stenographer, was seen for the first time February 3, 1920. The history obtained was rather meager. The patient was sick for about two weeks, during which time she complained of fever, chilliness, backache, and cough. She was a well nourished girl, feverish and toxic. The physical findings in the chest were negative. The temperature was 102, respiration 26, and pulse 122. No attention was paid to the reflexes except that the patellar reflexes were absent. The patient was seen again the next morning. On entering I asked how she felt and the response was slow, but she answered, "All right." On asking her other questions, I noticed a facial asymmetry, the furrow on the left

side of the face being rather distinct, while that on the right was absent. On the previous day, I had asked the patient to cough, but she whistled instead. I asked her to whistle again, which she did, but she could not say the words "five," "fifteen," or "four." In spite of the drowsiness, which was striking, she was easily aroused, and seemed to be aware of what was going on about her. A tremor of the fingers and a slight degree of rigidity of the neck was also noted. There were no ocular findings. The patient was removed to the Mt. Sinai Hospital. A spinal puncture was made on admission, the patient reacting only slightly during the puncture and scarcely realizing what was being done.

The spinal fluid was under moderately increased pressure, clear, and globulin was also present. There were 48 cells per cmm., the majority of which were lymphocytes. Cultures of the spinal fluid were made on aerobic and anaerobic media.

On February 5 the facial involvement was not as distinct as on previous day. The enunciation was not clear and the voice had a distinct nasal quality. There was no paralysis of the palate, but the uvula was directed to one side. The abdominal reflex was absent. The patient voided urine every half hour, but there was no incontinence. Clear mentally.

Feb. 6. Patient was not as irritable as on the previous day. Speech was somewhat improved. The condition of the reflexes was as follows: Patellar present, Kernig was questioned as positive. Brudzinski, negative. Babinski, negative. An ankle clonus on the left side was obtained but this was transient and was therefore questionable. The pupils were equal, but the reaction to light was slow.

Feb. 7. The appearance of the patient was not unlike that of a case of typhoid fever. The absence of enlargement of the spleen and rose spots ruled out this possibility. A mitral systolic murmur present at the apex was now observed associated with a slight enlargement of the heart to the right. A possible ulcerative endocarditis was ruled out by the absence of petechiæ, the relatively low leucocyte count and absence of chills and fever. A tuberculous meningitis was considered as a possibility, but this was eliminated by the clinical course of the case.

Feb. 8. Patient was extremely irritable and cried at periods, the cry being not unlike that of a child with meningitis. Mentally the patient was very clear. The pupils reacted to light only slightly, and then dilated again. A second spinal puncture at this time revealed a clear spinal fluid, under moderately increased pressure, showing a positive globulin reaction and 26 cells per cmm. Eighty

per cent. of these cells were lymphocytes. Following this puncture the patient became delirious for a short period.

Feb. 9. The facial involvement was very distinct. The pupils did not react to light. There was no ptosis, nystagmus, or photophobia. The other reflexes were as on previous days. A constant coarse tremor of the left arm was present at this time. The patient was clear mentally, but responded only in monosyllables, and was unable to whistle.

Feb. 10. The speech was improved to a slight degree and patient was able to say "sister," "Gertrude," "two," "three." Ophthalmoscopic examination by Dr. Lebensohn showed the fundi to be normal.

Feb. 11, 8:30 P.M. Patient suddenly became stuporous and was unable to swallow. Restlessness was also present and was accompanied with movements resembling the polishing of the hands by a manicurist. Ptosis of the left upper eyelid appeared. Urinary and fecal incontinence.

Feb. 12. A paresis of the entire left side with a complete hemianesthesia developed on this day. The Babinski was absent, as was a left ankle clonus, but a right ankle clonus was obtained. An ankle clonus appeared later in the day on the left side. Difficulty in swallowing was also noted at this time. Blood was obtained for culture on this date.

Feb. 13. Rigidity of the neck appeared, the stupor increased, also the respiratory rate, but there was no evidence of any lung involvement. The findings with reference to the reflexes were as previously. The patient had a number of attacks which were characterized chiefly by delirium. These came on in the evening about 8 P.M., were short in duration, associated with wild and uncontrollable movements, rapidity of pulse and profuse sweats.

Feb. 14. The mask-like appearance of the face, so often described, was most apparent on this day. The face was immobile and expressionless. A ptosis of the left upper lid was present. The left side of the face was now smooth. The right upper extremity was rigid and extended with difficulty. The patient was now able to move the left upper and lower extremity about and the anesthesia of the left side had disappeared also, but there was a paresis of the entire right side.

Feb. 15. The paresis on the right was now a complete paralysis, with anesthesia. An ankle clonus on the right was present but no Babinski. The patient's condition was poor. Difficulty in swallowing increased, the temperature and respiration were elevated.

Edema of the lungs was apparently developing. On the 16th the condition was unchanged and on the 17th the patient died. Necropsy was refused.

The leucocyte count on admission was 10,000 per cmm. and daily white counts showed the highest cell count as 16,000 per cmm. A differential count showed 80 per cent. polymorphonuclear leucocytes.

Cultures of the blood and spinal fluid were negative. The spinal fluid was also negative for acid fast bacilli. Blood was examined under dark field, but was negative. The urine was negative, but on the day before patient died sugar appeared.

CASE 2 was seen at the request of Dr. L. Handelsman. J. F., aged fourteen, boy, had been sick for five days with an acute infection resembling pneumonia in severity, but which showed no distinct physical signs. On the sixth day of illness Dr. Handelsman noticed a facial asymmetry, and a ptosis of the left eyelid, and suspected that he was dealing with a case of lethargic encephalitis. At the time I saw the patient he presented the following: There was a ptosis of the left eyelid and a left facial paralysis. The left pupil was contracted, and responded only slightly to light. The speech was slow, and drawn out. There was no difficulty in expression. The reflexes were normal except that a bilateral ankle clonus was obtained. The patient was clear mentally, and while unquestionably lethargic, he was not stuporous. The temperature at this time was 101. Blood was drawn for culture. Two days later a spinal puncture was made. The spinal fluid was clear, under normal pressure, negative for globulin, 5 cells per cmm. This patient made an uneventful recovery.

From the blood of this patient Dr. R. Tunnicliff and I have obtained a streptococcus, in ascitic fluid tissue media with oil. The same organism was obtained on a blood agar slant to which an excess of the patient's blood was added, the clotted blood probably acting as anaërobic media. In the first generation no growth was obtained by aerobic cultures, but the organism grew aerobically in the second generation. The colonies on blood agar plates are moist, flat, about 1 mm. in diameter. The organism is hemolytic, has a tendency to produce green on blood agar, is not bile soluble, does not ferment inulin and mannite, but does ferment salicin and lactose. Injected intravenously into two rabbits and one guinea pig the organism failed to produce any effect.

Cultures of the spinal fluid from this case were negative.

REMARKS

A review of the literature concerning the etiology of this disease shows that at the present time the exciting cause is unknown. Von Economo¹ considered food poisoning as an etiological factor but ruled it out because of the absence of gastro-intestinal symptoms. He believed that the disease was due to a specific virus resembling but not identical with that which causes poliomyelitis. In England the disease was at first considered as a form of botulism but the work of McIntosh⁵ has disproved this view. It may be remarked that at the present time there have been numerous reports of cases of botulism in this country. While the cases reported are undoubtedly due to *B. botulinus*, it is noteworthy that cases of lethargic encephalitis have prevailed in the community at the same time, and because of the similarity in the clinical manifestations errors in diagnosis are likely to occur.

The late Sir William Osler⁵ and others considered lethargic encephalitis to be a form of poliomyelitis, but the recent studies of the English investigators⁵ would seem to disprove such a view.

Sainton⁶ regards the disease as a result of the localization in the brain of the prevailing influenza, while Bassoe⁴ says that "the etiological relationship of this disease to influenza rests on the coincidence of epidemics of lethargic encephalitis and pandemics of influenza." According to Bassoe⁴ it is not common for patients to have had distinct influenza. He believes that "the encephalitis itself may be a cerebral form of influenza, or it may be caused by a separate virus which in order to become active must have come in contact at one time or other with that of influenza."⁸ Netter regards the disease as a "maladie autonome," the specific agent of which has a special affinity for the nerve centers. Bassoe⁷ and Hassin have suggested that "the similarity between the pathologic changes in African sleeping sickness and epidemic encephalitis suggests a close relationship of the etiologic factors, that is, epidemic encephalitis may be caused by a parasite allied to the trypanosome."

Von Wiessner⁹ found a gram positive diplostreptococcus post mortem in the brain of a monkey in which an encephalitis was produced by the injection of the emulsions of the brain of patients dying of lethargic encephalitis.

Hala and Smith¹⁰ found a gram negative motile bacillus, unidentified but probably belonging to some intermediate class of typhoid enteridites group. The work of Wegeforth and Ayer, J. Neal¹¹ are inconclusive. House¹² found a streptococcus post mortem.

Strauss, Hirschfeld and Loewe¹³ report the presence of a filterable virus in the nasopharyngeal mucous membrane of cases of epidemic lethargic encephalitis, which is capable of producing typical lesions in monkeys and rabbits and have cultivated globular bodies¹⁴ similar in appearance to the organism described by Flexner and Noguchi for poliomyelitis. Our own observation of a streptococcus in one case is another addition, inconclusive but of interest.

Summarizing these views, we may classify them into the following divisions: (*a*) that the disease is due to food poisoning (botulism), which has been disproved; (*b*) that it is a form of poliomyelitis, which has also been disproved; (*c*) that it is due to virus; (*d*) that it is a cerebral form of influenza; (*e*) that it is due to a parasite allied to a trypanosome, and (*f*) that it is due to a microörganism as yet unknown.

The present cases are of interest from a clinical point of view, because a careful review of the literature shows that anesthesia has not occurred in any cases reported. Anesthesia was present in our first patient, and both Dr. Bassoe and Dr. Hassin, who saw this patient in consultation, confirmed its presence. According to the English observers, transitory paralysis, the clearing of a paralysis in one area and its appearance in another region is characteristic of lethargic encephalitis. This was particularly true of our first patient, who first showed a left hemiparesis, which later disappeared only to be followed by a paralysis of the right side. Of still further interest was the early appearance of an ankle clonus opposite the paralyzed side, also the presence of a bilateral ankle clonus and negative Babinski. These findings suggest a diffuse involvement in this case not only of the nuclei at the base, but of the gray matter in the cord.

Attention is also drawn to the attacks of delirium which appeared in both cases. Bassoe described the occurrence of "crises of coarse tremor or choreiform jerkings attended with profuse perspirations and weak and rapid pulse"; while the English observers have described attacks of delirium alternating with somnolence. In my cases both delirium and coarse movements were present. McNalty explains the occurrence of delirium in a state of somnolence as attempts of the individual to cerebrate. He is of the opinion that the lethargy is due to the failure of the normal sensory impulses to reach the cerebrum because of involvement of the thalamus. When such an individual attempts to cerebrate in the absence of

normal impulses, the result is incoördinate and manifested by delirium.

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