TWO CASES OF ATYPICAL EPIDEMIC (LETHARGIC) ENCEPHALITIS WITH A HISTOPATHOLOGIC REPORT

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Epidemic encephalitis often exhibits atypical clinical syndromes which render the proper diagnosis difficult. Of the great number of atypical forms recognized by the discoverer of this disease, G. V. Economo (1), and described in this country by Tilney (2), Riley (3), Bassoe (4), Hunt (5), La Salle Archambault (6), we might mention the meningitic, hyperkinetic (myoclonia, chorea, paralysis agitans), delirious and tabetiform types which, however, have so far been recorded only clinically, that is, they were not confirmed by postmortem studies. Bassoe's case is the only American one on record in which a reliable histopathologic examination was made. To this we might add two more cases which are even more striking as to the clinical and pathologic findings.

CASE I.—A thirty-three-year old Ruthenian, bartender by occupation, entered Cook County Hospital's neurologic service on June 8th, 1920, with a history of seven days' illness. Neither the onset, nor the nature of the initial symptoms could be ascertained as the patient was delirious and unable to give intelligent answers.

Examination.—A well developed and nourished male, with a large square head, and normal bony and muscle systems. There were not deformities, signs of injuries, paralyses or atrophies. Voluntary and passive movements were carried out with ease, in spite of continuous muscular twitchings of the abdomen, thorax, face, upper and lower extremities. The twitchings were in the form of rapid

clonic jerks involving a larger or smaller portion of the muscle when they showed as fascicular contractions. Especially numerous were they in the abdominal musculature which was in a state of constant restlessness without stopping for a moment until the patient's death.

Aside from the muscle twitchings there was profuse sweating of the entire body, especially marked on the face. The cranial nerves showed no visible abnormalities, except a sluggish pupillary reaction even to a very strong light. The movements of the eye balls, eyelids, the facial expression, including mimical and voluntary movements of the face muscles, the tongue, the deglutition, all were normal. The reflexes—tendon, abdominal, cremasteric, corneal, conjunctival, nasal—were normal; there were no Babinski Oppenheim phenomena, nor clonuses.

The sensibility appeared highly blunted, the patient having failed to perceive the strongest painful irritations.

The urinary and rectum controls at the first examination were normal.

The mental condition was at times apparently normal, at times, there was marked delirium, but apathy and lethargy were absent.

The urine as well as the Lange and Wassermann tests in the blood and spinal fluid were negative. The cell count and globulin test could not be determined, as the spinal fluid was bloody. White blood cells numbered 12,400; blood pressure, 142 systolic and 68 diastolic. The abdominal and chest organs showed no abnormalities. Temperature was 100, pulse 114, and respiration, 24.

Course.—June 9th, 1920. The temperature was 101, pulse 120, respiration 30; patient perspiring profusely and very restless, noisy, irrational; tried to get out of bed, and had to be restrained. The restlessness continued the whole night; involuntary urination. June 10th, 1920. The patient is extremely noisy and restless; takes water, but is irrational; does not sleep; temperature (forenoon) 102, pulse 120, respiration 30; at noon time—temperature 99, pulse 108, respiration 24; delirious; the entire body twitches.

June 11th, 1920: Morning temperature 100 (rectal), pulse 96, respiration 24; at 4 P.M. temperature 104, pulse 120, respiration 28; perspiring profusely and stuporous. June 12th; swallows with difficulty; temperature (morning 8 A.M.) 106, pulse 96, respiration 60. At 11 A.M. rectal temperature 109, pulse 124 (?), respiration 48; death at 11:20 A.M.

Autopsy (Dr. Stangl).—The head is large; the calvarium very

thick and heavy; it is easily removed and is 19 cm. long by 16.2 cm. wide, by 10 cm. deep and 6 mm. thick. It weighs 560 grams.

The leptomeninges are close to the cortex; the convolutions are broad and flat, the corresponding sulci being narrowed and very shallow. The blood vessels in the visceral arachnoid even to the fine radicles are filled with red blood. There is an escape of abundant fluid from the region of the chiasm when the brain is removed, fluid apparently escaping from inside the ventricles. The brain is boggy, large, and weighs without the dura 1,720 gm. No further examination was made because of the limitations of this autopsy permit, since only fifteen minutes were allowed by the relatives to remove the brain. Further examination showed a marked internal hydrocephalus with distension of all the ventricles of the brain.

Microscopical Examination.—Various portions of the cortex, midbrain, cerebellum, pons, medulla were fixed in alcohol (95 per cent.), imbedded in celloidin and stained with toluidin blue. The pia especially of the base was slightly infiltrated, the subarachnoid space showed greatly distended meshes containing foci of freely scattered red cells. In some places, like the base of the brain, around the pons, the pial large vessels were markedly infiltrated chiefly with lymphocytes, very few plasma cells and an abundance of pigment granules. The cortex and other portions of the brain tissues showed no hemorrhages but a great abundance of vessels and capillaries which were mildly infiltrated chiefly with lymphocytes. The ganglion cells of the deeper cortical layers showed marked changes; they were homogeneous in appearance with densely stained processes and frequently invaded by glia cells (neurophagia) which were numerous all over the cortex and subcortical areas. All these phenomena—infiltration, ganglion and glia cell changes—were somewhat more marked in the large basal ganglia, but especially so in the pons region, midbrain (around aqueductus Sylvii) and locus niger. The infiltration in these regions was enormous, confined not only to the perivascular spaces but also invading the parenchyma itself, which was abundantly covered with plasma cells.

We must point out that the cortical regions were subject to a very careful study in view of the marked cortical symptoms presented by the patient, in whom the classical symptoms of epidemic encephalitis—apathy, lethargy, ocular palsies—were absent and replaced by delirium, restlessness, sleeplessness, muscular twitchings and profuse sweating. The sole indication of a probable midbrain involvement was a sluggish pupillary reaction to a very strong light.

Yet pathologically it proved to be a typical instance of lethargic encephalitis.

CASE II.—The history and brain of this patient were kindly furnished to one of us (Hassin) by Dr. H. Gideon Wells, Professor of Pathology at the University of Chicago. Unfortunately the clinical facts are too meager and incomplete.

History and Examination.—A thirty-four year old clerk in the army ordinance department was admitted in November, 1919, to Washington Park Hospital (the exact date could not be obtained) complaining of severe headache, weakness and fever. The temperature was .99 degrees and 102 for two or three days, after that 103 and 104 degrees. The patient was delirious and most of the time unconscious, so that an accurate history was not obtainable. Neither could his relatives furnish any information relating to the onset of the disease or the previous condition of patient's health.

The examination revealed almost rigid pupils which did not react to light; some rigidity of the neck with a negative Kernig; exaggerated tendon reflexes with negative Babinski and Chaddock phenomena. No sensory disturbances, like anesthesia or hyperesthesia; for the last thirty-eight hours, a foot drop. There were a few râles in the lower posterior part of the chest on both sides, a decreased precussion resonance in the right lung anteriorly to the axillary and posteriorly to the nipple line. There were no signs of fluid. The examination of the abdomen and of the urine was negative. Sero-logic tests and the Widal reaction were also negative. Leucocytes were 5,000 on entrance with 60 per cent. polymorphonuclears, 33 per cent. lymphocytes, 7 per cent. large mononuclears, red cells—3,500,000, hemoglobin was 80 per cent.

The patient was given an intraspinal injection of arsphenamin according to Swift-Ellis method. On the third tapping a large amount of thick bloody fluid was obtained. The autopsy performed on November 15th, 1919, by Drs. Fink and Long showed: lethargic encephalitis, slight atrophic cirrhosis (of the liver), hypostatic hyperemia and edema of the lower lobes of both lungs, beginning bronchopneumonia of the lower lobe of the right lung, postmortem digestion of the stomach with large perforations and extravasations of its contents into the lesser peritoneal cavity. The histologic examination of the viscera and chest organs, showed practically normal heart, pancreas, spleen, suprarenal bodies. *Lungs*—Hemorrhages, edema, emphysema, extreme anthracosis and a beginning bronchopneumonia.

Kidneys.—Slight increase in the round cells particularly under

the capsule, otherwise they were fairly normal. *Liver*—slight increase in the interlobular connective tissue and no increase in round cells under the capsule.

The brain tissues carefully studied in celloidin sections stained with thionin showed the same changes as in the previous case; namely very mild meningeal infiltration which consisted mostly of mesothelial cells and only on the base showed lymphocytes; interstitial and parenchymatous changes in the cortical areas, somewhat more marked changes in the large basal ganglia and an enormous perivascular infiltration of the midbrain, pons and medulla.

COMMENT

Like the previous case this one did not show any of the signs commonly found in typical epidemic encephalitis, the clinical symptoms having been delirium, rigid pupils and an acute febrile course with negative serologic findings. Yet, like the previous case this also proved to be pathologically a typical lethargic encephalitis. In other words, many cases of the latter disease may be clinically atypical, but pathologically perfectly typical. Whatever the clinical type might be the lesion is always in midbrain, especially in the region of the Sylvian aqueduct and the peduncles. The sole manifestation of this anatomic lesion is principally involvement of the third nerve which was also present in both of our cases. However, this nerve lesion did not show as ptosis or other ocular extrinsic paralysis, but rather as an intrinsic palsy in the form of sluggish or rigid pupils. The latter, therefore, should always be carefully examined in every case suspected as epidemic encephalitis, for it is inconceivable that such a wide spread lesion of the midbrain such as occurs in lethargic encephalitis, whatever its type, should run without some ocular manifestations.

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