A CASE OF WESTPHAL-STRÜMPPELL PSEUDOSCLEROSIS FOLLOWING ERYSIPELAS, WITH A DISCUSSION OF ALLIED CONDITIONS.*

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Of recent years the interest of neurologists has been specially attracted to those forms of brain disease in which the symptoms depend to a large extent on involvement of the basal ganglia. Epidemic encephalitis has played the rôle of experimental physiologist and, by producing acutely a variety of clinical syndromes, has thrown much light on hitherto obscure disorders. At the same time the detailed analysis by many workers of the clinical symptoms and of the histopathological changes in other types of disorder involving the basal ganglia is gradually clarifying our views. Important landmarks in our knowledge of these matters are the histopathological analysis by Alzheimer (1912) ¹ of a case of Westphal-Strümpell pseudosclerosis, the important work by Wilson (1912) on progressive lenticular degeneration,² the condition which now bears his name, the demonstration by Spielmeyer (1920) ³ of the apparent underlying kinship of Westphal-Strümpell pseudosclerosis with Wilson's disease, the emphasis laid by A. Westphal and Sioli (1922) ⁴ on the presence of inflammatory elements in a case anatomically belonging to this group, with a clinical history suggesting an infective origin of the disorder.

The case to be reported here is of special interest in regard to the problem of etiology. The first nervous symptoms (prolonged sleep) appeared with an attack of facial erysipelas; a second attack of erysipelas was associated with a period of stupor; the patient died during a fourth attack of erysipelas.

It is for the general pathologist to explain in detail the relationship between the infection, the cirrhosis of the liver, and the histopathological changes in the brain; the clinical evolution of the case certainly suggests a connection between the neurological symptoms and some underlying toxic process.

SUMMARY OF CASE.

Printer, age forty-seven. March 1, 1922. Erysipelas with prolonged sleep (thirty-six hours) and dazed behaviour; after one week

* From the Boston Psychopathic Hospital, Boston, Massachusetts, U.S.A.
disappearance of erysipelas, residual condition of restlessness and over-
activity; after one further week reappearance of erysipelas with stupor for
days.

April to September. Rather restless, irritable, explosive with occasional brief periods of somnolence, general weakness, special weak-
ess of the left side of the face, facile laughter and crying, defective
speech, yellowish tint of skin and sclera.

September 23. Behaviour more disturbed; excitement alternating with dazed or somnolent condition.

September 30 (Boston Psychopathic Hospital). Alternation of somnolence with restlessness, confabulation, disorientation, general
impairment of intellectual functions. Jaundiced appearance; tremor
of hands and head; plantar reflexes with tendency to extension; defec-
tive articulation.

October 7. Left hospital.

October–December. Restless and difficult to manage with periods
of somnolence; variable tremor.

January 1, 1923 (readmitted). Excited delirium of brief duration.

January to March. Variable mental condition; episodes of stupor and
of excitement, with tendency to perseveration of utterance; general
impairment of intellectual functions.

Variable tremor; bilateral sign of Babinski; slow and slurring
speech; left-sided facial weakness; gait slow and stiff. Jaundiced
appearance.

On February 1. Third attack of facial erysipelas.

On March 3 fourth attack of facial erysipelas: March 4, death.

James M. Forty-seven years. Admitted to the Boston Psychopathic
Hospital September 30, 1922.

Complaint.—The patient is lethargic, falls asleep frequently; has visual
hallucinations.

Family History.—Negative.

Personal History.—The patient was born in 1874. His early develop-
ment and school history were uneventful. He had the usual exanthemata;
Neisser infection several times; lues denied. For many years previous to
his admission he had been assistant superintendent of the printing room
of a daily paper, and only stopped work April, 1922. He used tobacco in
moderation; in the past a fairly heavy drinker, he had not taken any alcohol
during the year previous to admission. The patient was a married man, had
three children living and well.

Onset of Symptoms.—The following account was given by his wife. On
March 1, 1922, the patient, who had previously been in his usual health,
returned from work and slept for thirty-six hours. At the end of this time he
got up, dressed and came into the room where his wife and friend were. He
sat there looking straight ahead of him without saying a word. There was
an erysipelatous area on the left side of his face, which disappeared after one week. At the end of this week the patient was bright and alert, but restless and continually on the move. He kept his wife going from one entertainment to another. After one week of this condition the erysipelatous condition reappeared and the patient went to bed. For three days the patient was stuporous and could only be roused with difficulty and for a short time; he was incontinent. On regaining consciousness after these three days he was restless and extremely irritable. After two weeks in bed, on trying to rise, he fell. At this time his wife noticed asymmetry of the face, "a drawing up of the right side of the face." The patient went off for a vacation but continued to be restless, irritable and explosive. He would talk continually to any one who would listen. One day during this period he was drowsy and was roused with difficulty. The patient returned from vacation on May 29, and remained at home for the next two weeks. His condition during this period was characterized by generalized weakness, facile laughing and crying, marked irritability and one period of somnolence lasting twenty-four hours. The patient was in a general hospital from June 15 to June 23, 1922. It was noted that his skin had a pale yellowish cast and that the sclerae were subicteric. No abnormalities of the reflexes were recorded. "Speech defect, slowed circulation, memory defect; may be due to cerebral arterial changes from over-indulgence in alcohol." The Wassermann reaction of the blood and of the cerebrospinal fluid was negative. The cerebrospinal fluid gave a negative goldsol reaction, normal proteins, two cells. The renal function was 50 per cent. in two hours. The urine showed no albumin, but rare hyalin casts and a few red blood cells. The white count was 5,000; hæmoglobin, 90 per cent. The examination of the abdomen showed the liver dulness at the upper border of the fifth rib.

During the rest of the summer the patient remained at home, doing no work and becoming progressively weaker. He was very sleepless; he frequently complained of pain in his head and would say that he felt sick all over. At times he was very irritable with his family, but usually apologized for this. During the month of September he had three periods of loss of consciousness, lasting from twenty-four to thirty-six hours. The onset and disappearance of the unconsciousness was sudden. During the unconsciousness his breathing was heavy, there was some twitching of the feet, and incontinence of urine and faeces. The patient showed some difficulty in going up and down the stairs, and in the middle of September he fell down some steps. On September 23 he was extremely irritable and kept repeating, "What's the difference between a cup and a mug?" On September 24 he was extremely talkative and "his face dropped"; he was restless and irritable, walking the floor and complaining of members of the family. On September 25 he appeared more normal and apologized for his outbreak of the day before. In the evening he became very hilarious over his sister-in-law's description of a comic film. He was so restless that night that his wife had to walk the floor with him for several hours. On September 26 he talked in a rambling way about moving pictures and thought he was an actor. At night he shouted wildly after going to bed; he cried out, "They have got
me, they have got me, they are killing me!" On September 27 he wandered about the house in a dazed condition, repeating the question, "Am I a boy or a girl?" At night after going to bed he was very restless and whenever his wife came near his bed, he screamed, "They are going to cut you up; they will get your spine!" This continued all the night. During the following two days he seemed dazed, and on September 29 he wandered about the house continually, and talked much of a moving picture, in which he and his family and the policeman next door were the actors. At night he became drowsy, and continued so during the morning of the next day. When left alone he would go to sleep and snore loudly. On September 30 he was admitted to the Boston Psychopathic Hospital.

**Mental Status on Admission.**—In the receiving office the patient was lethargic and fell asleep frequently; upon being aroused he answered questions in a rambling, unsatisfactory way; he seemed to be confused. He talked about his work and stated that he was making a film at the present time.

On admission to the ward the patient wandered constantly about in a restless way with a look of inquiry on his face. He did not talk much spontaneously but, when questioned, talked freely. The following is a sample of his talk and shows the perseveration of the topic of moving pictures: "They were taking the film. We came here on the picture. A policeman, his wife, my wife, my daughter and myself at my house. A young girl was getting married on Beach Street. He lay flat. You'll know when you get married. The policeman had things on his arms, you know, made of steel. We all came here on the picture. It was going to be a clean-up. No, I'm not a movie actor."

The patient had a worried expression, but questioning did not elicit any topic of worry. He sat in a corner and did not seem to notice much of what was going on about him; he seemed preoccupied and was roused from his preoccupation with difficulty. The patient said that he had been having his picture taken for the moving pictures, and gave numerous poorly elaborated statements about this picture. The film started in his house; he did not know who was taking it. The picture showed the patient and a policeman with locked arms and with their respective wives holding on to them. It was started because a young girl on Beach Street had got married, and they wanted "to start off big." The patient had no idea where he was; he gave the date as November, 1922. He answered questions as to his past history after repeating the questions several times; he was able to give some of the dates of the main episodes of his life. He was quite unable to give an account of the happenings of the past twenty-four hours. He said that he had come on business related to his picture. In naming objects shown him, there was considerable hesitation; with the Marie three-paper test he failed on the first attempt, and on the second attempt he was only two-thirds successful. His general information showed very serious gaps, but he had some grasp of current events. He was unable to get the gist of a simple story; he did not attempt a test in simple subtraction.

**Physical Status.**—A well-nourished man with mildly jaundiced appearance
of the scleræ; deep reflexes active. The plantar reflex showed a tendency
to the sign of Babinski, more marked on the left side than on the right. The
abdominal reflexes were present. The pupils reacted on accommodation, but
somewhat sluggishly to light. Ophthalmoscopic examination negative.
There was some generalized weakness, but no definite paralysis of any limb.
The gait was described as normal. Marked coarse tremor of the hands and
head. Slight difficulty in articulation of the test phrases. Lungs negative;
heart, slight systolic murmur; P.R., 68; B.P., 145/100. The urine showed
no albumin, sugar or bile; sp. gr., 1,020. Blood, W.B.C., 10,700; poly-
morphs, 61 per cent.; lymphocytes, 30 per cent. Wassermann reaction of
blood and cerebrospinal fluid negative. X-ray of skull negative.

Shortly after his admission to the hospital the patient realized that
his ideas about the moving picture were absurd, but still showed some
confusion. On October 3, during a psychometric examination, he wept
constantly. His reactions were very slow; he failed in two simple tests
in the eight-year group. October 7, the patient left the hospital without
any definite diagnosis having been made of the process underlying the
mental confusion.

History of the Interval.—For one week after discharge, the patient,
according to his wife, seemed quite normal. From that time till his readmis-
sion to the hospital he was very difficult to manage at home. Almost every
night he would become very much excited, refuse to stay in bed and cry,
"Let them come! They will get me!" He would continue this for several
hours, shouting and trying to get out of bed. He would sleep till ten o'clock
in the morning, after which he would be rather somnolent for several hours.
He would then become apparently quite rational, would remember his
behaviour of the previous night and show great remorse for it. The following
description of his behaviour on December 28 gives an idea of his condition
during this period. During this day he was restless, wandered about the
house, asked what he was going to do. If anything were suggested to him,
he was extremely irritable, but in a few moments he would apologize for what
he had said. He kept repeating questions over and over during the day,
disregarding the fact that he had been answered many times. He would cry
if all his demands were not attended to. The tremor of his extremities was
more marked than it had been for a number of days. The face was drawn
over to the right side. At 7 p.m. he lay down and apparently fell asleep,
snoring loudly for four hours. His wife noticed some blood on the pillow.
After this period he attempted to get out of bed, could be persuaded to
return, but soon renewed the attempt. He would fall back in bed and start
snoring, only to wake and try to get out again. There were alternating
periods of somnolence and restlessness for twenty-four hours. After this he
became apparently clearly oriented and rational, realized that he had been
causing trouble, and was very sorry for it.

January 1, 1923, the patient was readmitted to the Boston Psychopathic
Hospital. On readmission he was excited, violent and completely disoriented.
When seen in his room he was agitated, he shouted, cried, moaned and
pounded his abdomen. He paid no attention to anybody in the room, he
walked past them as if they were non-existent. He answered no question addressed to him, but talked and mumbled to himself in an unintelligible manner. The only phrases understood were "Get away!" and "They will get me!" (as if in response to hallucinations).

On January 2 the patient had an air of perplexity and 'anxiety,' and showed little interest in the surroundings; he was able to talk with the physician and remembered the name of the latter from his previous admission. He knew where he was, but had no idea of the date. He thought it was only a week since his first admission (three months). He had no memory of the hallucinations of the previous day. He was able to give a general account of his life; he had considerable difficulty in answering simple questions on general information. He could not read a simple story of a few paragraphs, and did not grasp it when it was read to him. He had no insight at all into his mental impairment.

January 6. The physician had commented on the patient's unilateral deafness and on his feminine figure. The patient said: "Do you find doctors all perfect in shape and form; in physiques I mean? Do you require them all? Aren't there a good many doctors that become sick, poor, deaf in one ear? I mean that they had one ear that could not hear well. I imagine that is common all over the world." He repeated all questions; he named large objects shown in a picture; he called a bedspread a 'bed-pannel.' "It's a four-wooden bed, it's a four-post bed. You have seen them with a comforter on it." When asked to subtract serial seven from 100, he repeated the question. He said, "What do you mean?" Finally he answered, "Ninety-three. Seven from ninety-three; is it eighty-three or seventy-three? No, eighty-six. Seven from eighty-six is sixty-three." He stated that his vision was failing and that he could not see to tell the time on a watch. His mood was somewhat explosive; he would become irritable and again jocular. During the examination, he would fall asleep and snore and then again wake up and be clear for a few minutes.

The physical note made at this interview was: Transverse pubescence, scant pubic hair; previously over weight, he has lost 40 lbs. in the last year; carious teeth. Right knee jerk much more active than left. Sign of Babinski more marked on right side than on left. Abdominal reflexes much diminished. Marked impairment of hearing on left side. Weakness of left side of face. No special tremor noted during the interview. Difficulty in rapid alternation of movement (adiadochokinesis). The patient was too weak to walk much. Speech was slurring with some distortions. "Methodist Episcopable; no, medico-episcopable" (Methodist Episcopal). He said "begrade" for brigade.

January 9. (Examination by Dr. Percival Bailey). The speech was slow, monotonous and scanning; the facies was rather expressionless. Some incoordination of the upper extremities, especially the left; no very marked tremor at the present time. Deep reflexes exaggerated. Bilateral Babinski response. Gait slow and stiff like that of an early Parkinsonian.

On January 16 the patient became stuporous, the stupor alternating with periods of restlessness and violence. He showed marked perseveration,
repeating one phrase for an hour at a time. At this time, there was very marked coarse tremor of head, tongue, arms and legs.

January 25. The patient had become much more childish; he was tearful and petulant. He continued all day to ask the same questions of every one who passed through the ward. Very marked coarse tremor of the extremities. Mask-like expression of the face with mouth open; some asymmetry of the face.

January 27. In the morning he was rolling about on the mattress, repeating, "I won't get up, you see." He repeated this for two hours, then suddenly became clear. During the restless period the generalized tremor became very pronounced but quieted down suddenly after half an hour.

January 31. During the past four days the patient has been quiet, oriented, gives the exact date, names the physicians correctly, talks rationally with his wife during a visit. Since his readmission the urine on repeated examination had shown no abnormal constituents; W.B.C. 7,800, with normal differential blood count.

On February 1 the patient showed an erysipelatous condition of the face, spreading on each side of the nose. T., 101° F., W.B.C., 11,000. At this time there was more difficulty in articulation and swallowing than on previous visits. By February 4 the temperature had returned to normal and remained so during the rest of the month with the exception of a sudden rise on February 17 to 101° F., after which it immediately returned to normal. The urine at no time during the month showed abnormal constituents; the blood serum gave a positive reaction for bile (February 17). The non-protein nitrogen content of the blood was within normal limits. During February the patient showed the same alternation in his condition as has been already described. At times he was restless and noisy. On February 19 he was unconscious with incontinence of urine; at noon he was conscious and able to take his dinner, and later in the day walked about as usual. Blood cultures (February 2, March 1) were negative. On March 2 he was drowsy and quiet during the day, but later became noisy and restless; temperature was normal. March 3: in the morning he was bright and able to be up, but in the forenoon it was observed that the facial erysipelas had recurred. T., 108° F., W.B.C., 6,900. Injections of polyvalent anti-streptococccic serum were given. At 3 p.m. the patient was sleeping heavily; he later became noisy. March 4, death.

Pathological Report.

The autopsy was performed two hours after death (Dr. M. M. Canavan). An abstract of the findings is as follows:

The body is that of a well-built, well-developed and well-nourished white man, 172 cm. long. The skin is yellowish-white. There is scaling over the forearms and pigmentation and scaling over the lower part of the legs. The body hair is scant. There are no edema and no palpable lymph nodes. The peritoneum and the abdominal fat are injected. The edge of the liver is at the costal border. The mesenteric lymph nodes are not enlarged.

Heart.—Weight, 400 grm. The myocardium has an unusually brown
colour, but it is firm to the touch. In one of the aortic cusps are several firm yellow plaques about 0·6 cm. in diameter. The edges of the mitral valve are thickened. In the left coronary artery, one centimetre from its origin, is a small calcareous patch, which does not occlude the lumen.

Lungs.—Weight of right, 370 grm.; of left, 320 grm. The pleura over the right lung is thickened. Both lungs show a superficial congestion, but apart from this are normal, as are also the bronchi.

Thyroid.—Weight, 20 grm.

Spleen.—Is enlarged, weighing 280 grm. and measuring 18 by 10 by 15 cm. The surface is free from adhesions. The colour is bluish-red, and on section the trabeculae are broad and prominent. The consistence is firm. The splenic vein is engorged and tortuous.

Kidneys.—Weight of right, 280 grm.; of left, 250 grm. The capsule is thin and strips easily. The cortex measures 0·9 cm. in depth, is injected and poorly differentiated from the pyramids, which have white lines at their bases.

Liver.—Is moderately diminished in size, weighing 1,300 grm., and measuring 28 by 17 by 8 cm. The surface is covered with 'bosses,' most of them 0·5 or less in diameter, a few to 1·0 cm. The colour of the exterior is yellowish-brown, and the consistence of the organ is firm. On section, irregular islands of yellowish-brown parenchyma project from the cut surface, separated by large areas of translucent grey connective tissue. The diameter of the masses of liver tissue ranges from about 0·5 to 0·1 cm. The proportion of connective tissue is large. Its arrangement and distribution vary; in some places it separates the islands of liver tissue by broad bands, while over considerable areas it has entirely replaced the parenchyma.

The gall bladder is distended, but contains no stones.

Pancreas.—Weight, 190 grm. It appears normal.

Gastrointestinal Tract.—The stomach is of moderate size. The mucosa near the cardiac end is injected. The pylorus is relatively stenosed, allowing the passage of the little finger only. The lower duodenum contains some blood in the lumen, as does also the lower third of the ileum. The mucosa of the ileum is thickened. The colon appears normal.

The inferior mesenteric artery is enlarged and the inferior mesenteric vein and the portal vein are engorged.

Bladder and Prostate.—Normal.

Testicles.—The right measures 3·7 by 2·8 by 1·5 cm. The capsule is thickened. They thread well.

Aorta.—Is thin and elastic throughout. There is one plaque near the arch.

The retroperitoneal lymph nodes are enlarged and injected.

Head.—The calvarium measures 0·5 cm. in the frontal, 0·4 cm. in the parietal, and 0·6 cm. in the occipital region. The dura is adherent to the calvarium over the frontal region, and the under surface of the dura over the right hemisphere shows a brown staining (the remains of an old hemorrhagic pachymeningitis). The middle ears and the sinuses are normal.

The pituitary is plump.
**Brain.**—Weight, 1,430 grm. The pia is faintly cloudy over the central regions of the hemispheres, where there is also moderate subpial oedema. The base of the brain shows nothing abnormal. The basal vessels are delicate and appear unusually small. On horizontal section at intervals of 1 cm. the cerebrum shows no gross lesions. The vessels in the central white matter and in the basal ganglia are injected. The midbrain, pons, medulla and cerebellum similarly appear normal on section.

**Spinal Cord.**—In the dorsal and lumbar regions there is a suggestion of degeneration in the lateral columns. Otherwise the cord is not remarkable.

**Microscopic Examination of the Nervous System.**

The pia over the frontal regions is thickened and oedematous and contains large mononuclear cells, scattered lymphocytes, free red corpuscles, and macrophages filled with green pigment. In the other cortical regions and over the cerebellum the changes are similar but less marked.

Sections from the various cortical areas show the following: As to lamination, there are small foci of cell loss in all layers of the frontal cortex. These are not definitely perivascular, and there is no reaction in or around them. In other regions lamination is normal and there is a good representation of nerve cells.

Many of the nerve cells stain poorly with cresyl violet. Some are shrunken, take a dark, diffuse colour, and have indistinct nuclei. Others contain no Nissl bodies, and have a frayed, washed-out appearance. The Bielschowsky method, however, shows that the neurofibrils are distinct. The affected cells are scattered among normal ones in all layers. They are most numerous in the frontal and temporal regions, and are infrequent in the calcarine cortex. The Betz cells are normal. The involvement of the nerve cells nowhere goes beyond a moderate grade.

The cortical arterioles in all sections are moderately thickened by an increase of connective tissue in the outer coat. They are tortuous and frequently show much variation in calibre. An occasional vessel is markedly affected. The capillaries are injected. The endothelium is swollen and re-duplicated, and with Achúcarro’s tannin-silver stain there is evidence of capillary proliferation.

The most striking feature in all cortical regions is, however, the presence of very numerous large, pale glia nuclei (Fig. 1). These are three or four times as large as the nucleus of an ordinary glia cell, and are round, oval or bean-shaped, occasionally lobulated. By the Alzheimer method for amoeboïd glia they sometimes show nodular protrusions or bosses. The nuclei contain several particles of chromatin, but aside from these they stain very faintly. Mallory’s neuroglia stain demonstrates neither cell body nor fibrils, but Alzheimer’s method for amoeboïd glia brings out a small amount of cytoplasm, which contains no inclusions. These large nuclei are scattered irregularly through the cortex, both singly and in groups. They usually bear no special relation to the nerve cells, although they are occasionally situated close to a process, like a satellite. They sometimes lie along the course of the vessels.
Fig. 1.—Frontal cortex, showing the large glia nuclei. In the centre of the field they are situated in an area of oedema containing colloid droplets and shrunken nerve cells. Swelling of the endothelium.

Fig. 2.—Large glia nuclei in the putamen.
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One or more of these nuclei may be surrounded by clusters of small glia cells. Granules of green pigment are sometimes present in the vicinity of the nuclei. These cells are present also in the white matter, although less abundantly than in the cortex. They are most numerous in the precentral area, where they are found in profusion. The next most frequent site is the frontal region, but they are abundant in all the cortical areas.

The behaviour of the ordinary glia is as follows: Clusters of glia nuclei, some forming rosettes, are frequent in the various cortical areas. There is considerable satellitosis in the precentral regions. The superficial fibrillar glia is increased generally over the hemispheres and there is an increase of glia nuclei in the white matter and occasionally some perivascular gliosis.

Degeneration products are present in the form of small deposits of fat along some of the cortical vessels, also green lipid pigment and pigmented phagocytes around the vessels in the white matter.

There is an infiltration of lymphocytes around isolated vessels in the temporal cortex.

Hippocampus.—The nerve cells of Ammon’s horn appear normal, and very few large glia nuclei are present either there or in the hippocampal cortex.

Corpus Striatum.—The nerve cells of the globus pallidus, putamen and the caudate nucleus are present in good numbers, and, in general, stain normally. Large glia nuclei are very abundant (Fig. 2). In the putamen capillary proliferation is marked. The large vessels are not thickened. The perivascular spaces are distended with serous exudate and there is an active gliosis around a number of the large vessels.

The putamen contains an area of beginning disintegration in the tissue at the side of a small vessel. Small glia nuclei and large mononuclear cells are present in the focus, but there is no increase in the Alzheimer glia.

A degeneration product is present in considerable amount in the perivascular spaces of the globus pallidus. It stains a deep metachromatic blue with cresyl violet and a bright blue with Mallory’s connective tissue stain. This substance fills the perivascular spaces of a number of arteries and veins in a solid mass, and where it is less dense it appears as droplets of various sizes both in the perivascular spaces and among the neuroglia fibres just outside them. There is also considerable green pigment scattered diffusely through the tissue of the globus pallidus, some of it in phagocytes. Clusters of fat droplets are numerous among the nerve fibres of the putamen and globus pallidus. The caudate nucleus contains no fat.

Thalamus.—The nerve cells appear normal and the neurofibrils are distinct. Alzheimer glia nuclei are very numerous. The vessels are moderately thickened and a few are surrounded by considerable fibrillar gliosis. The tannin-silver preparation shows some capillary proliferation. The walls of several vessels contain masses of a non-calcareous substance which stains intensely with haematoxylin. This material extends also into the lumen and partially fills it. Green perivascular pigment is present in moderate amount, and there are collections of pigmented phagocytes and small numbers of lymphocytes around a few vessels. Clusters of fat droplets are occasionally present among the fibre bundles.
Hypothalamus.—The nerve cells are pale and satellitosis is prominent. Large glia nuclei are as abundant as in previous sections. Hyaline droplets are present in great numbers, and there are a few lymphocytes and much green pigment around the vessels.

Midbrain.—A number of nerve cells in the red nucleus and around the aqueduct are shrunken, stain deeply and diffusely, and contain no Nissl bodies. The Bielschowsky preparation shows that the neurofibrils are indistinct and the cell contours distorted. The majority of the nerve cells, however, stain well. The cells of the substantia nigra are normal. The Alzheimer glia nuclei are present in large numbers, particularly around the aqueduct. Some of the vessels are tortuous and thickened. Some are filled with polymorphonuclear leucocytes and their endothelium is swollen. In the midbrain perivascular lymphocytes are more in evidence than in previous sections, although they are not prominent. The tannin-silver preparation shows a proliferation of the capillaries. The superficial glia is increased. Hyaline droplets are very abundant among the fibre bundles of the pes.

Cerebellum.—The cells of the dentate nucleus stain normally except for an occasional one with a shrunken nucleus. They are, however, unevenly distributed and appear to be thinned out in some areas. The vessels show an increase of cells in their walls and the capillaries are proliferated. Vesicular nuclei are numerous in the dentate nucleus and the granular layer. They are not found in the central white matter, but are present in the white matter of the folia. There is a slight increase of fibrillar glia in the central white matter.

Pons.—There are considerable numbers of shrunken and darkly staining nerve cells below the ventricle. Large numbers of vesicular glia nuclei are present. There is no tract degeneration. Below the locus ceruleus on one side is a considerable collection of small glia cells in connection with a thickened artery. The vessels in general are only slightly thickened. There is a small area of fresh haemorrhage in the locus ceruleus. The ependyma is normal.

Medulla.—The nerve cells appear normal. Large glia nuclei are found in moderate numbers, although less frequently than in the preceding regions.

Spinal Cord.—The nerve cells throughout the cord stain excellently. The vessels are not notably thickened. Some Alzheimer glia nuclei are present in the grey matter, but they are infrequent in comparison with the previous sections. A marked fibrillar gliosis extends inward from the periphery and in the lumbar cord there is also a gliosis radiating from the grey matter. Tract involvement is revealed as follows in the Weigert sections: At the level of the cervical enlargement there is no degeneration. In the lower cervical cord there is some diffuse bilateral thinning in the lateral columns, more extensive on the right side. In the dorsal region there is a suggestion of thinning in both pyramidal tracts, which in the lumbar cord becomes a definite degeneration. There are no glial overgrowth and no adventitious cells in the affected tracts. The nerve roots are normal, as is also one of the lumbar nerves examined.

The optic nerves and the Gasserian ganglia are normal.
Fig. 3.—Liver, showing increase of interlobular connective tissue and focal necroses.

Fig. 4.—Proliferation of the bile ducts and infiltration of the interlobular connective tissue.
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SUMMARY

Moderate diffuse degenerative changes in the nerve cells of the cortex, midbrain and pons. Small foci of cell loss in the frontal cortex.

An abundant development of large, vesicular polymorphous glia nuclei in the cortex, corpus striatum, thalamus, hypothalamus, midbrain, cerebellum and pons.

A moderate general thickening of the arterioles. Moderate proliferation of the capillaries in the cortex, corpus striatum and midbrain; most marked in the putamen. Swelling and reduplication of the capillary endothelium in the cortex and midbrain.

A small focus of disintegration in the putamen.

Diffuse deposits of lipoid pigment and small amounts of fat. Very abundant hyaline droplets in the hypothalamus and midbrain.

Thickening of the superficial fibrillar glia over the cerebrum, brain-stem and cord, and occasional perivascular gliosis in the cortex.

Slight lymphocytic infiltration around isolated vessels in the cortex, thalamus, hypothalamus, and midbrain.

A small area of fresh hæmorrhage in the pons.

Mild diffuse pial changes.

In the lower cervical region of the cord a diffuse thinning in the lateral columns; a partial degeneration in the pyramidal tracts of the dorsal and lumbar regions, more advanced in the latter.

MICROSCOPIC EXAMINATION OF THE TRUNK ORGANS.

Myocardium.—The nuclei are indistinct. Cross striation is invisible and the cytoplasm has a granular appearance.

Lung.—Marked capillary congestion. Otherwise normal.

Liver.—The general picture shows a separation of the lobules by broad bands of connective tissue. The architecture of the organ is, however, preserved and over considerable areas in the sections there is no increase in fibrous tissue and the general appearance is normal. There are a number of foci (Fig. 3), situated in the mid-zone of lobules, in which the cell cords are broken up and the cells isolated and surrounded by débris. Some of the cells are swollen, others are shrunked. Their cytoplasm is granular and stains intensely with eosin, and the nuclei are small and pyknotic. In small areas the liver cells have entirely disappeared, leaving the meshes of the framework filled with granular débris and scattered polymorphonuclear leucocytes. These are evidently focal necroses. The sinusoids and bile capillaries are everywhere dilated, and the liver cells in some areas are compressed. Except in the areas of necrosis and of compression, the liver cells appear to be in good condition. At the edges of a few lobules are groups of three or four large cells of indefinite outline. Their cytoplasm stains intensely. The nuclei are large and rich in chromatin and frequently the cells are multinuclear. Their appearance is that of regenerating liver cells.
Mallory's connective tissue stain shows that, although the greater part of the connective tissue is interlobular, there is also considerable intralobular increase. The connective tissue is cellular and in some areas it forms large masses in which remnants of liver cells are visible. Branching columns of cells, evidently new bile ducts, are very numerous (Fig. 4). There appear to be transitional stages from the epithelium of the newly formed bile ducts to liver cells. As the cell columns penetrate into the periphery of the lobules, the nuclei grow larger and become round, and the amount of cytoplasm increases. These transitional cells sometimes occur in clumps, and in other places they take on an acinar arrangement. The connective tissue is thickly infiltrated with lymphocytes and the vessels are congested. The fat content of the tissue, as shown by the scharlach red stain, is small.

Spleen.—Lymphoid tissue is present in considerable amount. The venules of the pulp are distended. Polymorphonuclears are present in large numbers, and eosinophiles and plasma cells are also abundant. The connective tissue of the pulp and the endothelial cells lining the venules stand out prominently, and Mallory's connective tissue stain shows the former to be increased.

Pancreas.—Shows a slight increase of interlobular connective tissue.

Small Intestine.—Normal.

Kidney.—The pyramids are injected. Otherwise the kidney is not remarkable.

Adrenal.—There are areas of extreme congestion in the deeper parts of the cortex, extending into the medulla, and an area of hemorrhage in the former. The cells of the cortex stain well and contain considerable lipoid.

Testicle.—The hyaline membrane is greatly thickened. The tubular epithelium is atrophic and spermatogenesis is absent. Pigmented interstitial cells are numerous. There is no increase in connective tissue and no cellular infiltration.

Thyroid.—The section shows chiefly resting colloid gland. There are a few acini filled with large phagocytes containing masses of yellowish-green pigment. Similar pigment is frequently present in the epithelial cells.

Anatomical Diagnoses.—Cloudy swelling of the myocardium.

Interlobular cirrhosis of the liver.

Fibrosis of the spleen.

Hæmorrhage into the adrenal cortex.

Atrophy of the testicle.

Congestion of the lungs, spleen, kidney, and adrenal.

DISCUSSION.

From the anatomo-pathological standpoint this case is characterized as pseudosclerosis by the presence of large, vesicular, polymorphous glia nuclei, together with lesions of the nerve cells; the diffuse distribution of these changes in the cortex, basal ganglia and midbrain, and to a less degree in the cerebellum and pons; the absence of gross lesions in the brain; a partial degeneration of the pyramidal tracts in the cord;
and the combination of these lesions in the nervous system with a nodular cirrhosis of the liver. It is the combination and distribution of the neuropathological changes which are significant, rather than any one lesion. Even the polymorphous glia, which has been the most constant finding and has been considered (wrongly) almost pathognomonic of pseudosclerosis, is found in various toxic and infectious processes, although not in such abundance as in pseudosclerosis; transitions have also been described between it and the ordinary reactive forms of glia cells in intoxications and infections.

The pathological picture of pseudosclerosis is less clearly defined than that of Wilson's disease. The findings in the reported cases have been quite variable and in individual cases different features are in the foreground, in one the lesions of the nerve cells, in another the Alzheimer glia or capillary proliferation.

The most prominent feature of the present case is the polymorphous glia. The affection of the nerve cells is decidedly less conspicuous than in some of the reported cases, in which there was an extensive and advanced degeneration with areas of devastation. The proliferative changes in the vessels are also very moderate.

The single small focus of beginning disintegration in the putamen is of interest and importance as apparently connecting the process in this case with that of Wilson's disease.

A partial degeneration of the pyramidal tracts, such as was present in our case, has been found quite frequently in pseudosclerosis; in fact, in one of the early reports, before the characteristic glia was discovered, it was described as the only pathological finding.

A feature not usually mentioned in pseudosclerosis but present in our case is the scanty infiltration of lymphocytes around occasional vessels. It is generally stated that inflammatory lesions are absent in pseudosclerosis, but the scattered lymphocytes, taken in connection with the swelling of the endothelium, thickening of the adventitia, capillary proliferation, and changes in the pia, may easily be interpreted as of infectious origin. They are similar to the lesions of chronic epidemic encephalitis, in which proliferation of capillaries and adventitial thickening are often prominent, while the exudate may be limited to a few lymphocytes around isolated vessels. In the present case the recurrent erysipelas, with which the progress of the pseudosclerotic syndrome was associated, would suggest an infective basis.

A. Westphal and Sioli have recently brought forward evidence for the infective origin of the pseudosclerotic process. In their case the syndrome followed what was probably an attack of epidemic encephalitis, and pathological examination showed, together with cirrhosis of the liver and Alzheimer glia, marked proliferative changes in the vessels and collections of small round cells both in the nerve tissue and about
the vessels. The present case is of interest in connection with theirs. The infiltrative changes were much less marked in our case.

In the clinical picture of this case, which corresponds with that described by C. Westphal,5 Strümpell 6 and others, one may note the general mental impairment, the instability of mood with irritable outbursts, the tendency to facile laughter, the sluggishness of mimetic movements, the tremor, the monotonous speech, the episodes of terrified excitement with hallucinations. Of still greater theoretical importance are the episodes of somnolence and stupor, which have to be considered in the light of the somnolence or lethargy which has given a special name to epidemic encephalitis. The association of the pseudosclerotic syndrome with the somnolence brings up the same considerations as in the case of A. Westphal-Sioli, where the pseudosclerotic clinical picture was associated with eye-symptoms probably of encephalitic origin, and where the histopathological examination demonstrated the presence of both a pseudosclerotic and an encephalitic process. As the encephalitic process is undoubtedly exogenous, the conclusion suggested is that the pseudosclerosis is of similar origin.

The simultaneous occurrence of the erysipelas with profound somnolence in the present case would tend to reinforce this argument.

Another point of interest in the case here reported is the type of intellectual involvement. In addition to the general impairment of memory and of the grasp of general information, there were periods of vacuity or intellectual torpor when questions took a long time to penetrate, and would have to be repeated by the patient before being grasped. The same "stickiness" of the intellectual processes was seen in the tendency to perseveration on words or phrases or topics, a tendency noted as well in the original communication of C. Westphal as in the more recent case of A. Westphal-Sioli.

The abrupt transition from a condition of stupor or blind stereotyped excitement to one of comparative clearness suggests some process of rapid onset and subsidence, such as an edema.

It is obvious that in this case, as in the cases of the other authors referred to, the clinical picture with its special evolution can only be understood in the light of special localization and of a special morbid process, and it is especially in regard to the latter problem that the above case furnishes a document of interest.

REFERENCES.


PSEUDOSCLEROSIS FOLLOWING ERYSIPelas

A CASE OF WESTPHAL-STRÜMPELL PSEUDOSCLEROSIS FOLLOWING ERYSIPELAS, WITH A DISCUSSION OF ALLIED CONDITIONS

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