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ATYPICAL FORM OF ARTERIOSCLEROTIC PSYCHOSIS. A REPORT OF A CASE¹

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In recent years a number of atypical forms of arteriosclerotic brain disease have been reported. In addition to hemorrhagic areas and softenings caused by sclerotic arteries, there are several different forms of pathological changes due to a sclerotic condition of the cerebral arteries. The clinical symptoms differ considerably from the typical forms and at times make a correct diagnosis almost impossible. There have been a number of these cases reported by various observers. Jacobson reported a case of arteriosclerosis which showed bulbar symptoms and Alzheimer described perivascular gliosis, claiming it to be the result of the arteriosclerosis. Buchholz found wedge-formed arteriosclerotic degeneration of the cortex. The encephalitis corticalis of Binswanger and the vacuole formation in subcortical white matter as described by Buchholz, are also of arteriosclerotic origin. Rossbach described another peculiar alteration in the cortex of the brain due to arteriosclerosis, to which he gave the name, "état vermoulu Pierre Maries." Schob reported similar pathological changes, which clinically showed paralytic symptoms. Still later Alzheimer reported a pathological condition of the cortex of the brain, showing a spongy degeneration

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due to arteriosclerosis, but which could not be diagnosed clinically. He named this form of arteriosclerosis "*atypical*," to distinguish it from the typical, just as Lissauer's paralysis is called atypical to distinguish it from the typical form.

But how can this number of different forms be explained? The alterations are no doubt due to the sclerosis of the cerebral arteries. But the different locations, the different grades of sclerosis and perhaps the different durations of the disease, probably explain the various changes. When, for instance, pial vessels show a greater involvement than other vessels, it may cause the anatomical picture of "*état vermoulu* of Pierre Maries," when on the other hand, superficial vessels of the cortex are more attacked, it may result in the formation of the wedge-shaped degeneration of Buchholz or the spongy degeneration as reported by Alzheimer. Encephalitis subcorticalis of Binswanger and the vacuole formation in the subcortical region described by Buchholz, may also be the effect of arteriosclerosis of the medullary vessels. In the same manner, the involvement of the different stems of the brain arteries may cause different clinical symptoms; for instance, sclerosis of the basilar artery showing the bulbar symptoms as reported by Jacobson. Sclerosis of the anterior and middle cerebral arteries showing the paralytic symptoms as reported by Schob and Alzheimer, changes in the cerebellar arteries showing the cerebellar symptoms, etc.

The following is a report of a case, which was clinically diagnosed, "probably brain tumor," but pathologically showed an atypical form of arteriosclerotic degeneration.

CLINICAL OBSERVATIONS

Family History.—Mother died at the age of sixty-eight; cause of death unknown. Father died of stomach trouble. Two sisters died during childhood; one of intestinal trouble and the other of diphtheria. Another sister died of pulmonary tuberculosis at the age of twenty-four. One brother died of pulmonary tuberculosis at the age of twenty. Three brothers and one sister living and well.

Personal History.—Early development normal. Patient attended the public school and graduated from the grammar school. At the age of eighteen she came to the United States from Canada and entered the employ of the General Electric Company. She later worked in a shoe factory. At the age of twenty-one she married and her life was uneventful until the onset of her present condition. No history of venereal disease. At the age of forty the patient began to have difficulty in doing her work as well as she formerly did. She also complained of headaches which were very constant and gradually became

more severe. A year before her admission to the hospital she showed considerable memory loss. Following the death of her mother which occurred about the same time as the loss of memory, her mental condition became much worse. She became more forgetful and kept repeating, "Oh, I wish Ma was alive." She gradually grew worse and, when spoken to, repeated this sentence many times. Her memory became still more impaired for both recent and remote events. Later she began to walk with a great deal of difficulty and finally became bedridden, not being able to stand. Occasionally she was untidy. A tremor of the hands developed and it was necessary to feed, dress and care for her. She was admitted to this hospital October 5, 1918.

Physical Examination.—General Appearance: Patient was a very well nourished individual. Complexion was very muddy and colorless. Muscles were very well developed but of poor tone. Skin, moist. No jaundice. There was a mottled condition of the arms, back, legs and feet. No bruise marks. No syphilitic evidences.

Thoracic, Respiratory and Circulatory Organs: Chest, broad and well developed. Respirations, 18 per minute. Lungs negative on percussion and auscultation. Heart: Apex beat was palpable in the 5th interspace about an inch to the left of the mid-clavicular line. Radial pulse was very poor quality, at times irregular. There was no sclerosis of the peripheral arteries. Blood pressure, 160-80.

Digestive and Abdominal Organs: There was considerable fetor oris. Tongue coated. Abdomen large but showed nothing on palpation. Liver and spleen were not palpable. Digestion, good. Bowel movements, normal.

Genito-urinary Organs: Negative.

Urine: Negative.

Wassermann: 10-12-18. Reaction in blood serum negative.

Spinal Fluid: 10-9-'18. Wassermann reaction negative. Globulin slight ring. Albumin 2 in 20. Cells, 96. Gold, 1233421000.

Nervous System.—General Sensations: Patient had a feeling of exhaustion; was unable to express herself very clearly.

Eyes: Expression dull, listless. No nystagmus present. Pupils irregular and unequal, the right being widely dilated. They reacted very slowly to light and not at all to accommodation. Ophthalmoscopic examination was very unsatisfactory on account of the patient's inability to coöperate, but so far as could be ascertained the fundi were normal.

Ears: No discharge. Hearing good.

Taste and Smell: Test could not be performed as the patient would not coöperate.

Cutaneous Sensibility: Tactile appreciation was slightly impaired, although it was rather difficult to say whether she realized when she was touched by a pin or a pencil. She was unable to localize readily for touch or space. Responded to pin pricks by wincing.

Deep Sensibility: There was no sensibility over the nerve trunks.

Stereognostic Sense: Patient was unable to tell the objects which were put in her hands with her eyes closed.

Vasomotor Conditions: Dermographia was present and there was much mottling of the skin of the arms, shoulders, legs and feet.

Reflexes: Knee jerks were exaggerated. Ankle clonus was present on the right side but not present on the left. No Babinski. Gordon and Oppenheim not present.

Involuntary movements: There was a marked tremor of the hands, tongue and lips.

Sleep: Patient was somewhat restless in the hospital but as a rule slept fairly well.

Mental Examination.—Patient was in bed during her entire residence in the hospital. She was very restless, frequently pulled out handfuls of her hair, gathered up the bedclothing and threw them off, and picked at her face. All motions were meaningless and performed with considerable effort. Her movements were slow, deliberate and lacked coördination.

Speech: Patient's speech was retarded, slurring and at times showed elision of whole syllables.

Consciousness and Orientation: Patient was not oriented for persons, place or time. She did not realize where she was, nor recognize anyone about her.

School Knowledge: It was impossible to gain any knowledge from the patient. Could not give the names of the New England States and could not give any information about her school work whatever.

Calculation Ability: Could not be tested.

Handwriting: Could not be tested, her hand shook so badly.

Hallucinations: Apparently she did not react to any hallucinations.

Memory: There was marked memory loss. She was unable to recall recent events, did not know how long she had been here nor where she came from. She was unable to state even a few facts concerning her remote past. She usually answered by repeating the questions that were asked her.

Association of Ideas: There was marked retardation and looseness of thought connection. Her attention wanders so that it is almost impossible for her to concentrate for over an instant.

Judgment and Conclusion: There was no apparent delusion formation although at times she seemed a little apprehensive and suspicious, attempting to strike the examiner when approached. Had no insight whatever.

Emotions: Patient showed no increased emotional excitability. At times she was somewhat irritable but was usually dull, seclusive and listless.

Social Relations: Patient was untidy. At times aggressive, scratch-

ing the nurse and pulling her hair. It was necessary to spoon-feed her, as she was unable to help herself in any way.

Course of the Disease.—October 8, 1918. *Untidy. Helpless.*

Patient remained in bed unable to help herself in any way. Plaited the bedclothes or picked or pulled at her teeth and hair. Had no grasp on her surroundings and did not appear to comprehend what was said to her. Conversation was a repetition of what she heard. When an attempt was made to induce patient to stand, her legs could not support her and she would have sunk to the floor if not assisted. Was spoon-fed and seemed to have a very good appetite.

October 15, 1919: *Weak. Unable to articulate distinctly. Untidy.*

Last night about nine o'clock patient had an attack of syncope. Seemed very weak, dripping with perspiration; pulse feeble, rapid and irregular, 150 per minute. There was visible pulsation of vessels of neck. Was given a stimulant and revived, but since then she seemed dazed and practically inaccessible. Lay on her back with her mouth open, right leg drawn up. The mottling of the skin on the right foot was much more pronounced. She would not straighten her leg out and when attempts were made to do so for her she resisted and cried out. When questioned she kept repeating what was said to her, seldom giving an intelligent reply. Was constipated. Very untidy. Had a very good appetite.

October 20, 1918: *Died to-day.*

Patient has been unconscious for the past twenty-four hours and died to-day at 12:30 P.M. Cause of death was given as organic brain disease.

POSTMORTEM OBSERVATIONS

The autopsy was performed ten hours after death by Dr. Canavan and Dr. Uyematsu. The anatomical diagnoses were as follows: Beginning gangrene of fingers and toes; claw-like position of hands, especially the right; sclerosis of coronaries; beginning sclerosis of aorta; cirrhosis of liver; chronic diffuse nephritis; fatty replacement of pancreas; submucous hemorrhage of stomach; chronic perioöphoritis; a small fibroid in uterus; bony elevations of inner table of the calvarium; chronic pachymeningitis; chronic leptomeningitis; external hydrocephalus; universal atrophy of the convolutions (first and second convolutions of temporal lobes, orbital portion of frontal lobes and pyriform lobes are relatively in good condition); brain sclerotic; brain weight, 970 grams.

Macroscopic Observation of the Calvarium and Brain.—*Calvarium* was rather thin with no diploë. Measurements: F. 0.4—T. 0.3—O. 0.6 cm. Inner table showed small bony elevations. Grooves for middle meningeal arteries were shallow. Base of skull showed nothing notable.

Brain weighed 970 grams. Dura mater was thickened and particularly adherent over the frontal region. By pleating back the dura

mater, the pia mater could be seen lifted from the cortex by a marked quantity of clear fluid; 5 c.c. could be easily collected between any two convolutions. Pia mater was slightly opaque over the vertex and congested, especially over the occipital lobes. The atrophy was very marked over the vertex, involving the posterior part of the frontal, entire parietal and occipital lobes. The anterior inferior cerebellar artery on the right side was missing. The vertebral arteries, basilar

FIG. 1. The superior surface of the brain, showing the atrophic convolutions and the softening.

artery, internal carotid arteries and major arteries of the cerebrum and cerebellum were all very markedly sclerotic. There was marked excess of cerebrospinal fluid at the base as well as the vertex of the brain. Cranial nerves were negative.

Spinal Cord.—The dura mater was slightly thickened. There was an excess of cerebrospinal fluid. Otherwise nothing of note.

The brain was put into a 10 per cent. solution of formalin for fixing. The following is the description after two weeks' hardening: The pia

FIG. 2. Base of the brain, showing sclerosed arteries, thickened pia mater and atrophic convolutions of both cerebrum and cerebellum.

FIG. 3. The right hemisphere of the brain. The anterior part of the superior frontal, superior and middle temporal are apparently normal.

FIG. 4. The left hemisphere. The anterior part of the superior frontal, the superior and middle temporal, the lower part of the posterior central and the anterior lip of the supramarginal convolutions show apparently normal appearance.

FIG. 5. The median aspect of the right hemisphere. The gyrus fornicatus, the neighboring convolutions and the uncus are not atrophied.

mater stripped easily, except over occipital lobes, where it was firmly adherent to the cortex, the vessels were markedly congested. The convolutions of both hemispheres were extremely atrophic, as may be seen by pictures (Fig. 1-6). It is well to note that the atrophy of both hemispheres is almost symmetrical. The atrophic convolutions over both hemispheres were as follows:

Right:	Left:
Anterior central,	Anterior central,
Posterior central,	Posterior central,
Posterior one third of superior frontal,	Posterior one third of superior frontal,
Middle frontal,	Middle frontal,
Inferior frontal,	Inferior frontal except the opercular portion,
Superior parietal lobule, <i>Softening,</i>	Superior parietal lobule,
Inferior parietal,	Inferior parietal,
Posterior portion of supramarginal gyrus,	Anterior portion of the supramarginal gyrus,
Angular gyrus,	Angular gyrus,
Inferior temporal,	Posterior part of middle temporal.
Occipital convolutions,	Inferior temporal,
Paracentral lobule,	Occipital convolutions,
Precuneus,	Paracentral lobule,
Cuneus,	Precuneus,
Isthmic part of gyrus fornicatus,	Cuneus,
Lingual gyrus,	Posterior one third of gyrus fornicatus,
Fusiform gyrus,	Lingual gyrus,
Posterior part of hippocampal gyrus.	Fusiform gyrus,
	Posterior part of hippocampal gyrus.

FIG. 6. The median aspect of the left hemisphere. The superior frontal convolution, the anterior part of the fornicatus and the uncus are apparently healthy in appearance.

The only portions of the brain that did not show this curious atrophy, were the orbital portions of the frontal lobes, the anterior part of superior frontal convolutions, the anterior part of gyrus fornicatus, superior and middle temporal convolutions, opercular portion of the left hemisphere, the convolutions of the island of Reil and both uncii. At the points of the greatest atrophy in the cortex there was a process showing a moth-eaten appearance and some speculation as to the causation of this widespread atrophy might be interesting.

Those who are well acquainted with the anatomy of the cerebral arteries will know how closely the healthy portions of the brain are related to certain regions of arterial blood supply. The anterior part of the superior frontal convolution, a larger part of gyrus fornicatus, a part of paracentralis and precuneus, gyrus rectus and the bulbous and the tractus olfactorius remained relatively healthy in this case. These portions of the brain are a zone nourished by the anterior cerebral artery. This artery suffered much less from the pathological processes than the other large arteries, *i. e.*, the middle cerebral and the posterior cerebral arteries. The other healthy portions of the cortex were all located in the course of the middle cerebral. Each healthy portion was closely associated to certain branches of this artery. The uncus and the island are nourished by special arterial branches, according to Duret. The superior and middle temporal convolutions are supplied by the fourth branch of the middle cerebral artery. Though the opercular portion and the supramarginal convolution belong to regions of other branches, they are all in the neighborhood of the above mentioned healthy parts and this condition can readily be understood by an assumption of anastomosis.

Although the atrophy of the convolutions seem to correspond to certain regions of arterial supply, the alteration of the brain is so peculiar that at first it was difficult to associate the disease with an arterio-sclerotic process.

Vertical sections of the brain were made according to Dalton's method.

The cut surfaces showed atrophy of the cortex corresponding to the atrophic convolutions. In the highly atrophic parts, the surface of the cortex presented a moth-eaten appearance. The width of the cortex over the atrophic parts was noticeably narrow. Where the atrophy was pronounced the markings of the cortex and the medulla had entirely disappeared. The lateral ventricles were somewhat dilated. The centrum semiovale seemed to be atrophied on both sides, and was smaller than normal so that the entire cut surface of the vertex appeared strikingly smaller than that of the basilar portion. The corpus callosum seemed almost thinner than normal.

In the left hemisphere there was an old hemorrhage, occupying the head of the striate nucleus, internal capsule, globus pallidus and puta-

men, extending from the cut surface "through the corpus callosum and lenticular nuclei, and in front of the anterior commissure" (Dalton's ventral section, Plate VI) to the cut surface "through the corpus callosum, optic thalamus and crura cerebri" (Dalton's ventral section, Plate X). This hemorrhage destroyed the knee and the larger part of the crus posterior of the internal capsule which is supplied by the lenticulo-striate artery. This artery is considered to be the most common seat of arterio hemorrhage in the brain. There was no history of cerebral hemorrhage in this case, however, her inability to walk, the exaggerated knee reflex, the ankle clonus of the right side and the claw-like position of the hands indicate a hemorrhage, previous to the admission.

The cut surface of the parietal and occipital lobes show congestion of the vessels both in the gray and the white matter. There were also tiny hemorrhagic areas in the white matter around the posterior horn of the lateral ventricles.

Where the atrophy of the parietal convolutions was most marked there were areas of softening.

The systematic atrophy of the convolutions, the hemorrhage and the softenings point to arteriosclerotic brain disease. The question is, is this curious atrophy so extreme in character, so universal in distention due to arteriosclerosis, only? or are there other diseases which show such atrophy? Wassermann reaction being negative both in the blood and spinal fluid, these changes do not correspond to general paralysis. The patient was 48 years old at the onset of the diseases and it could hardly be a senile atrophy.

MICROSCOPICAL EXAMINATION

The Cerebrum.—Sections derived from several convolutions of both hemispheres were stained by thionin, Bielschowski's method of silver impregnation, Mallory's glia method, Weigert Pal's modification for myelin-sheath staining, Sudan III, Marchi method, hematoxylin-eosin staining, Van Gieson's method and Dabrowski's modification of Mann's method for demonstrating perivascular connective tissue. Although the cornu ammonis, Heschl's transverse convolution and anterior part of frontal convolution appeared relatively healthy, the atrophic parts showed a peculiar process of degeneration.

This peculiar process of degeneration although appearing in various forms of alteration, seemed to be related to the diseased vessels. The pia mater was irregularly thickened over the posterior part of the brain and over the cerebellum it was adherent to the cortex by brush-like glia fibers which arose from the surface of the cortex where the glia fibers were thickly interwoven. The vessels of the pia mater were sclerotic, partly calcified and partly degenerated. Fat corpuscle cells were seen around these vessels.

In atrophic parts the surface glia layer was remarkably thickened. Spider cells with large protoplasmatic body and thick fibers were numerous. The body of these spider cells contained fat corpuscles which stained both by the Sudan and Marchi methods.

FIG. 7. The cut surface of the brain, showing contrast between atrophic and healthy convolutions and the hemorrhage of the internal capsule.

The degeneration of the cortex was not uniform but varied in its appearance. It could be divided roughly into four forms.

1. *Cystic Degeneration of the Cortex* (Fig. 8 and Fig. 9).—There

were a large number of small cystic areas immediately under the glial surface. Most of them were triangular or wedge-shaped, while others were quadrangular or irregular, but in all cases the base or the broader part of the cyst was against the surface. The smaller number of these cystic areas were, however, situated in the deeper part of the cortex, generally under the valley between two convolutions. These cysts

FIG. 8. The cystic degeneration of the cortex. Paraffin section. Hematoxylin-eosin staining.

were surrounded by a luxuriant growth of glia cells and glia fibers. The inside of the cyst was not of empty space but was occupied by net-like structure. This structure was made of capillaries, perivascular connective tissue, glia fibers and a small number of cellular elements. The cells were glia cells and fat corpuscle cells, the protoplasm of

which contained waste products which were stained brownish red by Sudan, a muddy color by the Marchi method and metachromatic by methylen blue. The cysts were under the glial surface which was densely interwoven by newly formed, thick fibers, but in certain parts of the cortex was connected with the subarachnoidal space (Fig. 8).

FIG. 9 "Spongioser Rindenschwund." Mallory's glia staining. Paraffin section.

This latter condition is the same as described by Pierre Marie as "*etat vermoulu*" and reported as such by Rossbach in a case of arteriosclerosis. The cystic cavity with net formation corresponds to the second stage of the "spongioser Rindenschwund" which was described by Fischer. But in his case the areas of spongy degeneration were

situated mostly corresponding to certain cell layers of the cortex and were not absolutely associated with the sclerotic vessels. In the present case vessels of the pia mater and those of the inside and the direct neighborhood of the cysts show marked sclerosis and arterio-fibrosis. The characteristic localization and specific form of the cysts in this case are also different from Fischer's "spongioser Rindenschwund." But as the "spongioser Rindenschwund" is the name given to a certain appearance of the degeneration and is not the name of a specific disease, there is no reason why this term should not apply in the present case.

FIG. 10. The packet formation of the vessels. Bielschowsky's silver impregnation method.

2. *Packet Formation of the Vessels* (Fig. 10).—Accompanying the arteriosclerosis of the larger vessels of the brain, the microscopic examination showed a remarkable alteration in the smaller vessels of the cortex, such as proliferative elements, fatty degeneration of the adventitia, splitting of the elastica and arterio-fibrosis of Friedmann. These smaller vessels showed here and there packet formation, usually in the upper part of the cortex and including the first, second and third

layers of Brodmann but rarely extending down to the white matter. The surface of the cortex over these areas was sunken below the normal level, as was the case of the cyst formation. In the focus of the packet formation the nerve cells and myelin sheath have entirely dis-

FIG. 11. The scar tissue formation. Frozen section. Weigert's glia method.

appeared and instead of these, the place is occupied by proliferated larger and smaller vessels with connective tissue elements which consisted of glia fibers and perivascular connective tissue fibers. This kind of change is not described in the cases of Rossbach and Schob or Fischer. The packet formation could hardly be seen, as the relative increase of the vessels in consequence of the atrophy of the nerve elements.

3. *Scar Tissue Formation* (Fig. 11).—This variety of alteration was also found in the cortex where the surface was sunken below the normal level. The form of the scar tissue was usually wedge-shaped and was situated principally in the upper layers of the cortex and perpendicularly to the surface. But some of these were further down in the cortex or even in the white matter but were always situated according to the course of the vessels. The scar tissue was formed by increased vessels, glia cells and fibers. The glia cells were spider cells having large protoplasmic bodies and thick fibers. The protoplasmic bodies contained waste products. The thick fibers of the glia formed a network which was denser around the vessels than any other parts and gave a characteristic spongy appearance. This condition corresponds exactly to the third stage of Fischer's "spongioser Rindenschwund." This scar tissue was found side by side with cystic areas suggesting the same etiological factor. Yet the former seems to take place where the wasting of the brain matter is not complete enough to allow regeneration of the glia tissue.

FIG. 12. The cell island in the atrophic part of the cortex showing sclerotic changes. Paraffin section stained by thionin.

4. *Changes Pertaining to Ganglion Cells* (Fig. 12).—Excepting the general changes of the ganglion cells which consisted mostly in sclerosis and granular changes, there were small circumscribed areas where the ganglion cells had entirely disappeared. By thionin staining this condition was plainly observed. The cells about these areas showed marked

fatty degeneration combined with sclerotic changes. Fat corpuscle cells and increased numbers of glia cells were seen inside and around the focus. The ganglion cells of the healthy parts were relatively in good condition, so at Heschl's transverse convolution, cornu ammonis and

FIG. 13. The cyst formation in a lamella of the cerebellum. Paraffin section. Mallory's glia method.

orbital part and anterior part of the superior frontal convolution. Betz's cells had partly disappeared and partly remained with more or less marked degeneration. The posterior central convolutions and parietal convolutions were most heavily damaged.

The myelin sheath showed a secondary degeneration running from the degenerated parts down to the white matter and also perivascular degeneration according to the course of the long medullary vessels.

FIG. 14. The scar formation in the granular layer, the cyst formation in the molecular layer and arterio-fibrosis of the vessels. Bielschowsky's method.

There was perivascular gliosis in the white matter as well as in the cortex, but there was no perivascular infiltration of lymphocytes or plasma cells as is the case in a chronic inflammatory process.

The Cerebellum.—Pieces were taken from several parts of the worm

and hemispheres and examined by the same staining methods as for the cerebrum. The lamellæ of the lobulus quadrangularis and superior lobulus semircularis were found most atrophied. Alterations in the

FIG. 15. Disappearance of the Purkinje cells and the ganglion cells of the granular layer. Thionin staining.

cerebellum differed a great deal in appearance. The most marked and extreme one was the cyst formation (Fig. 13). These cysts were located principally in the molecular layer but also in the granular layer

and in the medulla. They were not particularly wedge-shaped but rather of irregular form and were found usually in the summit of the lamellæ. The inside of the cysts were not empty but showed a very peculiar appearance. Where the cysts lay in the molecular layer the nerve elements were entirely gone, and the remains of Bergmann's fibers running across the molecular layer reaching the thickened glial surface, gave a remarkable resemblance to a slat fence. When the cysts were in the granular layer they formed a loose network of glia fibers with very few cellular elements. They had the same appearance as the cysts in the cerebrum. The glia fibers around these cysts were thinner and denser than those in the cerebrum and the cell elements in the glial wall were not as numerous as in the cerebrum. The cell body contained fewer waste products. These conditions indicate that the degeneration of the cerebellum had taken place probably more or less earlier than in the cerebrum.

The next remarkable change was the scar-formation which was however somewhat different from that of the cerebrum. The molecular layer, where the scar was formed, was very much narrower than the healthy part, and showed no more nerve elements, such as tangential fibers, basket fibers, basket cells and dendrites of Purkinje cells. The glia fibers grew densely in this place in the form of Bergmann's fibers, *i. e.*, running in parallel order, perpendicularly to the surface and further into the pia mater in the form of a brush. The scar formation in the granular layer and medulla was practically the same as found in the cerebrum except that the glia fibers were thinner and more densely interwoven.

The third kind of alternation was the disappearance of the cell element, especially Purkinje cells and the small round ganglion cells of the granular layer (Fig. 15). In the highly degenerated parts no Purkinje cells were observed. The degeneration of the ganglion cells of the granular layer was found focally, as is seen by illustration.

The smaller vessels of the cortex were as sclerotic as those of the cerebrum. In general, the Purkinje cells were more or less sclerotic; the cell body was emaciated; the endocellular and epicellular network was not well defined; by thionin staining the protoplasm and nucleus stained dark showed no Nissl's bodies; dendrites had for the greater part disappeared. The axis cylinder of Purkinje cells was thickened; in certain parts, mostly in the neighborhood of the cyst formation or scar formation, the peculiar swelling of the axon was observed. Fatty degeneration of the Purkinje cell were not marked, except in those near the degenerated focus. Fat corpuscles were found around the thickened vessels in the Purkinje cell layer and around the area of disappearance of the nerve elements.

Spinal Cord.—By myeline-sheath staining, the left anterior pyramidal tract and the left lateral pyramidal tract were stained considerably

paler than in any other places. The glia fibers seemed to be increased in these areas, but no lipoid matter, either by Sudan III or by the Marchi method, could be demonstrated. The secondary change resulting from cerebral hemorrhage, should, therefore, be considered fairly old as the lipoid matter had been completely resolved and had permitted the glia tissue to grow in its place. Abundant amyloid corpuscles were found about the posterior root and in the degenerated pyramidal tracts.

COMMENT

The patient began to fail seven or eight years ago and could not do her work as well as she formerly did. She complained of constant headache, which gradually became more severe, especially during the past year. At this time her mental condition became much worse; memory was very much impaired; she became demented, disoriented, showed stereotyped conversation and echolalia. Physical examination revealed irregular, unequal pupils, which reacted very slowly to light and not at all to accommodation. She also showed exaggerated knee jerks, ankle clonus of the right side, tremor of the hands, tongue and lips, impaired stereognostic sense and disturbance of tactile appreciation. Her speech was retarded, slurring and at times showed elision of whole syllables. Although there is no history of any dizzy spells or hemorrhage, she has been unable to walk for the past year and at the time of her admission she was not even able to stand. The hands, especially the right, showed a claw-like contraction and there was beginning gangrene of the fingers and toes at the time of her death.

The whole history, physical and mental examination show, therefore, much likeness to general paralysis with focal symptoms, *i.e.*, the Lissauer's paralysis. But the course of the disease is perhaps a little too long for the general paralysis and the negative Wassermann of blood and spinal fluid are also against the presumption of this diagnosis. So the case was left undiagnosed, being probably a case of cerebral tumor, because of the constantly increasing headache and more or less conspicuous focal symptoms.

Autopsy showed sclerosis of the coronary vessels, beginning sclerosis of the aorta, cirrhosis of the liver, chronic perioöphoritis, chronic diffuse nephritis, etc. The brain was found extremely atrophic and at the point of greatest atrophy there was evident a process resembling moth-eaten result in the cortex. A careful examination indicated that the atrophy of the convolutions was intimately related to the sclerotic brain arteries which occurred mostly in the basilar, posterior and middle cerebral arteries. In addition

to small areas of softening, there was an old hemorrhage occupying the internal capsule of the left side. So this curious atrophy of the brain seemed to be related to arteriosclerosis of cerebral vessels.

The microscopical examination showed arteriosclerosis, especially of small vessels of cortex, such as proliferative changes in endothelium, regressive processes in proliferated elements, fatty degeneration of adventitia, splitting of elastica and marked arteriofibrosis. The degenerative process of the cortex which seems to be a result of arteriosclerosis, was exactly the same as described by Fischer as "spongioeser Rindenschwund." He observed this special alteration of the brain, most commonly in general paralysis and less so in senile dementia, tabes and presenile psychosis. He assumed it to be an independent specific disease due to some unknown toxic agent. He divided this alteration into three different stages: first, disappearance of the ganglion cells in circumscribed areas; second, loosening of the tissue of these areas, and third, growth of the glia fibers in the loosened tissue. He took also great pains to explain that this kind of alteration has nothing to do with the sclerotic vessels. But the "spongioeser Rindenschwund" is the name given to a certain appearance of the degeneration and not to etiological factors or symptoms of the disease, so that we could reasonably apply this term in the present case. In fact, Alzheimer reported a peculiar degeneration of the brain due to arteriosclerosis and in which the histological findings were described as "spongioeser Rindenschwund."

In the present case the alteration is divided into four different forms. I do not mean that they are different stages of one and the same process, as were explained by Fischer, although they are found side by side in the same convolution. They must, at least in this case, depend upon the occlusion of the vessels. If this occlusion is sudden and complete, a cystic cavity may be formed, showing a reactive growth of neuroglia on its peripheral portion. If on the other hand the occluding is slow and progressive, it might show various stages of reactive growth of neuroglia and removing process of the wasted products, according to the grades of the destruction. In the same way the budding of the vessels or the packet formation in the different parts of the same convolution might be explained.

The brain alteration due to arteriosclerosis, as was already mentioned in the introduction, may have occurred in various ways. But the spongy degeneration of the cortex is one of the rarest findings of this nature. So far as I have been able to find, the case of Schob

(1911) and the case of Alzheimer (1913) have been the only two which have been reported as such. The former was not described as spongy degeneration, but the findings are almost exactly the same as Alzheimer's and this case should readily be classified into this form. Strictly speaking, his case showed also the condition which was called by Pierre Marie "etat vermoulu" and was described as such in a case of arteriosclerotic brain degeneration by Rossbach. "Etat vermoulu" and "spongioeser Rindenschwund" due to arteriosclerosis are considered as the same process, the former involving the surface of the cortex, the latter somewhat deeper part, *i.e.*, beneath the glial surface.

The clinical symptoms of the two reported cases were similar to the present case, that is, general paralysis with more or less apparent focal symptoms. In Schob's case the patient was 26 years of age at the onset of the disease and showed progressive dementia, marked disturbance of speech and handwriting, disturbance of gait and later epileptiform seizures. The patient died at the age of forty-one. In Alzheimer's case the patient was 55 years of age when he showed the first symptoms, which consisted of loss of memory, stereotyped conversation, disturbance of speech such as stumble of syllables and scanning speech, amnesic aphasia, handwriting with many paragraphs, retarded pupillary reaction, exaggerated knee reflex, etc. This patient died at the age of 60. In both of these cases Wassermann's reaction in the blood serum was positive, while the reaction in the spinal fluid was negative. Schob's case was diagnosed as a demented form of general paralysis, while Alzheimer's case was diagnosed general paralysis or presenile dementia. But in both of these cases the negative findings of the spinal fluid made the diagnosis very uncertain.

The question is: why should the arteriosclerotic psychosis not have been considered in these cases as well as in the present one? Are there no characteristic symptoms which would lead one to suspect an arteriosclerotic process?

Let us first consider what symptoms may be attributed to arteriosclerosis. According to Alzheimer the onset of the disease is usually in the sixth decade. In the beginning there are headaches, dizziness, loss of memory, listlessness, irritability, and later more and more increasing dementia, which requires a longer period of time to develop than in the case of general paralysis. Active symptoms of mental disturbances such as delusions and hallucinations are always transitory in character and are not even frequent in this form. One of the most remarkable symptoms is the insight into the

condition which is kept even in the later stages. Loss of accommodation to light, disturbances of speech, handwriting and gait, tremor of the hands, lips and tongue and other symptoms are described as less common.

In the present case, the headaches in the beginning of the disease, which constantly became worse, loss of memory, gradually increasing dementia, listlessness and irritability are quite typical of cerebral arteriosclerosis. The relatively young age of the patient (40 years at the onset of the disease), stereotyped conversation, echolalia, disturbances of speech, slow reaction of pupils to the light, tremor of the hands, lips and tongue, impaired stereognostic sense, disturbance of tactile appreciation, etc., are rather unusual for arteriosclerosis, if not absolutely against it. Disturbance of gait especially with ankle clonus of one side and the claw-like position of the hand, especially of the right, would rather point more to hemorrhage than tumor. Insight was absent when she was admitted and the history is not accurate enough to judge on this point, previous to her admission. The case is very similar to the two cases reported by Rossbach and Alzheimer.

But in this case and perhaps in Rossbach's case, the relatively younger age of the patient and the normal blood pressure would account for the diagnosis being made without the consideration of arteriosclerosis. Sclerosis of the cerebral arteries, as is well known, is not always parallel with that of the peripheral arteries. Advanced arteriosclerotic changes may be present in the vessels of the brain when the condition is not marked in the radial arteries. The gangrene of the fingers and toes must signify circulatory disturbance of the peripheral arteries. At the autopsy the coronaries showed sclerotic changes, the aorta very slight change, but all of these suggest only beginning arteriosclerosis. So it may be impossible to judge the condition of the cerebral arteries by the condition of those of the peripheral arteries or even by the blood pressure. This makes accurate diagnosis in arteriosclerotic condition of the cerebral arteries very difficult and at times impossible.

In the reported cases and in the present case the disease occurred at a relatively young age and lasted for many years—Rossbach's case fifteen years, Alzheimer's case five years, and the present case seven to eight years.

The etiology of arteriosclerosis occurring in the cerebral arteries of relatively young persons is very obscure and cannot be explained. In the two reported cases the Wassermann reaction of the blood serum was positive, but the sclerotic changes of the arteries were

quite different from those as a result of syphilis. The microscopical examination of the thyroid, ovaries and other organs of internal secretion, which are sometimes supposed to be the cause of the early occurrence of senility, showed nothing to account for the arteriosclerotic changes.

Finally we have to explain the correlation between the clinical symptoms and the anatomical findings. The reader may have already recognized the striking similarity of the process of destruction in this case and those already reported to that of general paralysis. The progressive and extreme wasting of the brain in this case must have given the same clinical features as in cases of general paralysis. The disturbance of the speech, the tremor of the hands, lips and tongue, the dementia, the diminution of tactile appreciation, can all be attributed to the extreme degeneration of the areas of the cortex, which are associated with these functions. The ankle clonus of the right side and the claw-like position of the right hand must be the effect of the hemorrhage in the knee and anterior two thirds of the crus posterior of the internal capsule.

CONCLUSION

1. The presented case is one which showed clinically paralytic symptoms, but with a negative Wassermann's reaction both in the blood and spinal fluid.
2. Constantly increasing headaches and focal symptoms made one suspect brain tumor.
3. By autopsy the brain was found extremely atrophic, giving a moth-eaten appearance.
4. Major arteries of the brain were found markedly sclerotic.
5. The microscopic examination revealed a peculiar alteration of the cortex, which is called by Fischer "spongioser Rindenschwund." (The writer attributes this peculiar alteration to the result of malnutrition caused by sclerotic brain arteries.)
6. An old hemorrhage was found in the left internal capsule, which also points to the arteriosclerotic nature of this peculiar atrophy.
7. The paralytic symptoms are believed to be the expression of the progressive and profound wasting of the cortex, which resembles the wasting process of general paralysis.
8. As for the etiology of the sclerosis of the brain arteries the writer is not able to give any satisfactory explanation.

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