CLINICAL CASES I.

ACUTE CONFUSIONAL EXCITEMENT, WITH THE BRAIN LESIONS OF PROGRESSIVE PARALYSIS AND CONTRACTED KIDNEY.

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A. B., widow, aet. 42, temperate, was admitted to City Asylum January 8, 1898, suffering from a confusional form of sub-acute mania.

The family history given by one of her sisters is absolutely negative as to nervous or mental diseases. The personal history of the patient's husband could not be obtained. There was no obtainable record of miscarriages. The past history of the patient showed that she had not been troubled by any previous form of alienation, and had lived in a private family until a few weeks before as a domestic. Four weeks ago she lost her only child, a son, and soon afterwards became despondent, and her physical health suffered greatly. It was soon noticed by those around her that her character was undergoing alteration, and that she was sleepless, irritable, and desirous of being left alone. The maniacal outburst, which seems to have been of a very mild nature, did not take place until three days before she was sent to the institution.

The examination on admission showed a well-built, but physically very much run-down woman of 5 feet 8 inches in height, without traces of somatic disease other than simple anæmia, with no marked cranial deformities, and no signs of syphilis. The blood examination gave a very moderate polynuclear leucocytosis. She was considerably excited, the excitement being chiefly of a motor type, such as tearing her clothing, striking the doors or interfering with the other patients, and if left alone she would

amuse herself by destroying linen or any other material which she could lay hands upon, but never injuring herself. It was with some difficulty that she could be induced to speak, but on persuasion she talked a little in a rambling, incoherent manner, but could not remember her name, age, and did not recognize her surroundings. Her only connected speech was a jargon about the Catholics (she was a member of that church), who were coming to save her from what she could not tell. She also imagined that all the patients on the ward were Catholics, and called the nurse by the name of a Sister of Charity. These lasted but a few days and were her only ascertainable delusions. Within a period of a few hours she would be mildly excited, and then as mildly depressed, but the most striking symptom at all times was an intense mental confusion, out of which she never came, a reduction entirely inconsistent with the short duration of the mental trouble. Hallucinations were watched for but were never noticed.

The physical examination showed the pupils to be equal, 2 mm., reactive to light and accommodation. The motor functions of the extrinsic muscles were also normal. The deep reflexes were exalted; those of the skin natural. Ordinary sensation was present. There was perfect, though slow, co-ordination of the facial and hand muscles; no disturbance of equilibrium on standing with closed eyes, and the special senses, as far as could be tested, were natural. Articulation was slow, drawling, but there was no actual defect. The gait was a little unsteady, which was ascribed to her very weak condition. The circulation was impaired; the pulse feeble; arteries dilated. Temperature was not elevated. The urine the day after admission gave no traces of albumen or sugar, but showed an increase above the normal of urea and uric acid. Indican and skatol were absent. The specific gravity was 1023.

After being in the house for some time she became much more talkative, the motor excitement decreasing, though not entirely subsiding. Her speech consisted of entirely disconnected words. She did regain the remembrance of her name after it had been frequently repeated to her, and retained it, but otherwise remained as mentally confused as upon admission.

Steadily her strength decreased, and with it came a degree

of muscular inco-ordination, amounting to an ataxia of the upper extremities.

In the first days of May she became bedridden. The urine, which had been several times examined between the date of admission and this time, now showed diminution of the chlorides and phosphates, the presence of an excess of urea, uric acid, indican, a trace of albumen, and numerous granular, hyaline, and epithelial casts.

Bed-sores formed within a few days over the sacral region and progressed rapidly as the circulation decreased in force. On the 17th of May she had an epileptiform seizure with spasmodic twitchings of the arm, leg, and lower facial muscles of the right side. She never afterwards recovered full consciousness. These muscular spasms were repeated at intervals, and in a few days became universal. Death occurred on May 30, 1898. Never was there any amblyopia, katatonic symptoms, or the evidences of heart-lesion or œdema.

AUTOPSY.—The autopsy was made 15 hours after decease. Rigor mortis was present in the inferior but not in the superior extremities. Besides the bed-sores there was nothing to note upon the exterior of the body.

The cranial bones showed no disease. The dura peeled off readily from the bones, and was non-vascular. The subdural space contained a little fluid. The pia was very slightly gelatinous over the mid-regions of the brain, but showed no undue adherence to the cortex, neither were its meshes filled with distended and engorged vessels. The encephalon with the soft membranes weighed 1070 grams. Except for a few atheromatous patches the basal vessels showed no signs of disease; they were not diffusely thickened and collapsed on cross-section. The only anomaly in the formation of the fissures was that the right occipito-parietal sulcus penetrated into the external surface of the hemisphere to an unusual extent. On section the gray matter showed distinctly from the white, and was of moderate depth. The substance of the centrum ovale and ganglia was rather anæmic than hyperæmic. The ventricles were not dilated, contained little fluid, and their ependyma was not thickened. The choroid plexuses were moderately granular. The cerebellum, pons, medulla, and cord showed no focal or general lesion. So negative was the autopsy, so far as the brain was concerned, that bits of the ascending frontal convolution in its upper third only were preserved for after-examination in 96 per cent. alcohol.

The heart weighed 215 grams. The thickness of the left ventricle wall was 10 mm. The aorta near the heart and coronary arteries showed

no arterio-sclerosis, though at the arch a small patch of atheroma was noted. The valves, aortic and mitral, were perfect.

Both lungs showed emphysematous patches, and in the lower lobe on the left side there was some hypostatic congestion.

The spleen weighed 95 grams. The capsule was very adherent to the parenchyma. This substance was very resistant to the knife.

Each kidney weighed 120 grams. The capsules were firmly adherent to the cortical portion which was reduced to 2 mm. in thickness. The liver weighed 1010 grams, and was normal in appearance.

The staining of the brain tissue was made with methylene-blue according to Nissl, iron-hematoxylin, Van Gieson's picric-fuchsin, hematoxylin-eosin, and safranin.

Pia Mater.—The changes in the pial membrane are slight. There is a minor degree of proliferation of round nuclei, and the vessels show hyaline degeneration of the media of the arteries, which, however, is not universal, but only in individual arteries here and there. The intima in these diseased vessels is slightly thickened, the change being principally in the subendothelial tissue. Lesions in the adventitia are not marked. At only one point was an adhesion between the pia and brain surface noticed, and that near a large vein. The lymph spaces of the pia are comparatively free from debris, but do contain some hematoidin crystals.

The Cortex.—Vascular lesions. These are well marked everywhere in the sections, though more intense in some places than in others. The perivascular spaces are immensely widened, but contain nothing beyond a few hematoidin crystals. The intravascular space is also distended focally by accumulations of crystals and hematoidin debris.

The arteries and veins present quite a variety of lesions, periarterial changes predominating. This inflammation of the external coat in itself is very variable. In some of the vessels it is just beginning, and has a well-marked nodular appearance; in others, while recent, it has extended around the whole circumference of the vessel, nearly filling the dilated perivascular space with round-cell proliferation; but, though florid, it has left sufficient space for the lymph flow. The media of these moderately diseased vessels is sometimes almost normal, the muscular cells with their nuclei being distinct; while in others there is a beginning break-down of the muscular lamina, the cell protoplasm appearing hyaline, the nuclei shrivelled and distorted. Other vessels show a more pronounced proliferation of the round elements with thickening of the fibrous substance of the adventitia and complete filling up of the extravascular space. The intima in none of these several forms is decidedly thickened or otherwise disturbed, and the nuclei are well stained and apparently healthy.

There is still another and peculiar form of periarteritis noticeable in a considerable number of the smaller arterioles. The endothelial and subendothelial elements are not markedly increased, and are well stained, but outwardly there is not the slightest trace of a muscular layer to be found, while in its place lies a trabeculated tissue, with slight proliferation

of nucleated elements lying in a pale, faintly striated, or homogeneous matrix. The adventitial layer now either partially or completely fills the perivascular space, and, now and then, within it are found one or more large lymph-splits, this especially being the case when the canal is completely filled by the new growth. The lymph passages in the neoplasm are nearly always lined by a membrane of appreciable thickness, containing a few nuclei. The nucleated and fibrillary tissues of the adventitia show no evidences of necrosis of the cells, but on the contrary are well stained, and the nuclei show chromatin granules. The lumen of the arteriole is invariably pushed to one side of the perivascular space, and is sometimes closely applied to its margin.

The veins show everywhere a moderate degree of periarteritis, but their inner lamina is not disturbed. The capillaries are much widened and irregular in outline, their nuclei are few in numbers, but show no evidences of a degenerative process occurring in them.

In some of the larger arteries the changes in the media were more pronounced than those above described. The nuclei of the muscular fibres had entirely disappeared, and the layer is converted into a slightly fibrillated substance staining brown-yellow with picric acid. In these vessels there is more decided implication of the innermost lamina, with some narrowing of the lumen from fibrillary thickening of the subendothelial tissue. Only two arteries were found stopped by blood thrombi.

The arteries and veins on the immediate surface of the brain show nowhere the same intensity of disease as those lower situated. The height of the vascular morbid process is in the third and fourth cellular layers. A number of irregular bulgings from one side of an artery were also noticed.

Nerve-cell lesions are wide-spread and entirely of an atrophic order. The protoplasm of more than one-half of all the larger cells is shrunken, the apical process has dwindled to a stump, often having its apex bent upon itself in hook form, while the other dendrites are almost equally affected. The cell space, after allowing for alcohol-shrinkage, is enormously widened, but contains no lymphocytes, and often the reduced protoplasm occupies but one small corner of the space. Here and there cells are seen that have entirely lost their prolongations, and are lying almost free in the space. The cells show finely granular with hematoxylin and safranin, while scattered among the fine molecular granules are slightly larger ones of comma form. The normal pigment is not increased but rather diminished. The nuclei also show decided changes of an atrophic order. The nucleus is indistinct, irregular in outline, or, though regular, shows uniform shrinkage with departures from the normal in the character of its caroplasmic contents. The chromatin threads are never seen, but the nuclear substance is filled with rather coarse, deeply-stained particles of angular character, which may be numerous or scant in the several cells. The department of the nucleolus is varied. It may be enlarged and irregular, or its place occupied by a vacuole, or it may have entirely disappeared, in which event the entire nucleus is greatly atrophied. The

shrinkage of the cell protoplasm is in nearly all the bodies greater in proportion than that of the nucleus, and the amount of atrophy in the latter does not become immediately apparent. The nucleus is sometimes centrally situated, more frequently driven to one side of the protoplasmic margin.

With the Nissl methylene-blue, the cellular degeneration is as distinct and profound as by the other dyes. Very few cells show the normal granula, but are stained an uniform blue, and that of a very deep shade. Within the protoplasm a few very small angular particles are seen irregularly scattered through the substance, which is greatly shrunken. Occasionally this shrinkage is very great, but the reduced nucleus remains always visible. The nucleus in less degenerated cells is often covered by the dense blue stained protoplasm so as to be indistinct, unless very carefully looked for when it becomes apparent. The nuclear changes are of the same order as those already described, though less distinct from the imperfections peculiar to the dye.

Neuroglia Elements.—Everywhere, but particularly in the stratum zonale, are numerous stellate cells, with prominent bodies and tentacles. The body is stained yellowish by safranin, differing from anything in the adjacent tissue; also their extensions, while deeper stained, are equally prominent, running in fine, thread-like lines long distances from the cellular body. On the whole, the neuroglia elements do not seem to have undergone proliferation, but are simply swollen and unduly prominent. They are visible by reason of their peculiar staining throughout all the deeper cellular layers, and in the white masses at the foot of the convolutions. The neuroglia nuclei are distinct, well stained both in membrane and chromatin contents. Nothing definite could be determined about the vascular elements.

There was no reason to doubt the very brief history of the case given by the sister of the patient in respect to the short duration of the mental symptoms and their immediate cause, the loss of the child. The patient was very anæmic when admitted to the hospital, and this, together with the mental shock, was thought at the time to be sufficient to induce the departure from mental health. The somatic symptoms also were misleading. True, the reflexes were slightly above normal, but increase of the knee-jerk is found in a considerable number of instances of anæmic insanity, and pupillary symptoms were absent. Articulation, while drawling, showed none of the drunken defect of the paralytic, but rather the inhibition so often noticed in cases of mental confusion. This last symptom was the prominent feature of the case, and resembled so greatly that of the intoxication psychoses that a careful search was made in the urine for the ethereal sulphates or other poison.

Perhaps had the patient been a man the progressive character of the disease would have excited the suspicion of an atypical form of paresis, but in a woman the functional psychoses are so much more frequent than the organic that it was at first unhesitatingly diagnosed as a functional trouble, and only when the patient tended downward under an increased supply of food and tonics did suspicion become aroused.

Only toward the end of life did the patient manifest indications of grave renal trouble, which eventually ended in her death after a series of convulsions simulating in many respects the ordinary epileptiform crises of the paralytic, and only differentiated from them by the long-continued coma, with continuance of the convulsive movements. A typical uræmic respiration was not observed.

While there are no pathological lesions pathognomonic of paretic dementia, the lesions of the cerebral arteries, chiefly in the form of periarteritis, with secondary implication of the media and intima, and dilatation of the intra- and extravascular spaces, are among the most characteristic. Next to these are the atrophic lesions of the nerve cells, which may assume a number of forms according to the slight or severe degree of stoppage of the nutrient supply and difficulty in the return to the thorax of the effete plasma. The neuroglia lesions found count for little, but they are quite as well marked as in the majority of the demented types of paresis, where there have been few previous indications of an acute cortical trouble. The same may be said of the alterations in the soft membranes of the brain, which certainly were as well marked as are found in the milder varieties of paresis.

From a pathological standpoint there is but one diagnosis to make as to the nature of the cerebral disease present in this patient, but unfortunately it offers a choice between several poisons. There were no clinical indications from first to last of the presence of syphilis, but in the face of the rather characteristic lesions of the brain vessels this toxin cannot be definitely excluded. Furthermore, we had to deal with a form of mental alienation which is certainly uncommon in paresis, but which may be readily induced by the presence of other poisons than the syphilitic circulating through the blood-channels. Whether

the renal lesions, which, from the appearance of the kidneys must have been of long standing, were sufficient to store up in the tissues and blood uric acid and its derivatives in sufficient quantity to completely overwhelm the functions of the cerebrum, may be doubted. There was until a few days before death a fair amount of urine secreted, and this contained at all times rather an excess than diminution of urea and uric acid.

Despite these facts, I am inclined to attribute the mental symptoms to an overpowering of the brain functions by an excessive amount of waste tissue products circulating with the blood, and disturbing the general nutrition of the arteries and nerve elements; perhaps, also, there was a storage of irritating poisons (ammonium carbamate) that reacted upon the cortical vascular tissues in the same way as a luetic poison would.

The case, while not clear, opens up the very grave question, whether we have not been overlooking in our examinations of paretics and other organic dementias, the fact that lesions of the renal organs may be a frequent etiological factor in the causation of a portion of the symptoms that we recognize as the clinical picture of progressive dementias, and the kidney lesion may be primary, and not secondary, to the brain disease. Nephritis, as we all know, is comparatively frequent in progressive paresis, but usually begins long after the first appearance of the mental alteration, and cannot play any other part than that of an intensifier of the final symptoms. In the present instance there was only the most trifling disease of the great vessels either of the chest or cranium and no hypertrophy of the heart, or anything else indicative of other than primary disease of the renal organs.

While mental confusion is not the uncommon sequence of uræmic poisoning, it ordinarily is seen toward the end-stage of the disease, but in this instance we apparently have the disorder beginning several months before any indication of renal disease could be ascertained. Psychoses are not infrequently met with when there is contracted kidney, but not of the present type. (Vide Honigman, *Zeitschrift für prakt. Aerzte*, Oct., 1896; and Bischoff, *Wiener Klin. Wochenschrift*, 1898.)