A CASE OF CHRONIC INTERNAL HYDROCEPHALUS DUE TO EPENDYMITIS GRANULARIS.

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It is well recognised that chronic internal hydrocephalus can simulate many conditions. The following case serves as an illustration of the difficulty which is encountered in its clinical diagnosis. Clinically, intracranial tumour of undetermined localisation was considered the most probable cause of the symptoms, whereas at post-mortem examination the pathological condition was found to be chronic internal hydrocephalus, caused by a lesion situated in the ependyma and generally known as ependymitis granularis. The clinical study was rendered more interesting, as a case with a similar clinical picture was admitted to the wards later. In this latter case a diagnosis of cerebral softening was made and at autopsy pachymeningitis hæmorrhagica interna was found.

CLINICAL HISTORY.

J.M., female, age 50, was admitted to the Royal Infirmary, Glasgow, on August 8, 1921, complaining of "weakness" of seven days' duration. She consulted her doctor on account of inability to use her limbs, in which there was a feeling of stiffness. For a month prior to admission she had suffered from diarrhœa, passing fluid stools which contained mucus but no blood. She had had no headache or sickness and there was no history of lethargy or of disturbance of vision.

In 1916 she had experienced a similar illness which had been diagnosed as influenza. She was then confined to bed for two weeks and did no work for eleven weeks. On that occasion the paresis was more marked on the left than on the right side and that disparity has been maintained. Otherwise, her general health had been good.

Physical examination on admission: Temperature 98.2° F., pulse 102, respirations 32. The patient was well developed and well nourished; her complexion was fresh and she did not look ill. She lay comfortably in bed. The skin over both shins was pigmented and an ulcer, possibly varicose in nature, was present on the left leg. There was a bedsore over the left buttock.

She was very apathetic and spoke only when a question was addressed to her, answering in a slow, deliberate, but intelligible fashion. There was some impairment of mental processes, for she professed that she was able to sit up in bed and to turn herself, although when asked to do so she made no attempt to comply. All her movements were feeble but there was no evidence of actual paralysis. The face was almost devoid of expression or emotional play. In speech the right angle of the mouth moved only slightly, the left even less, due apparently to rigidity.

The pupils were circular, regular in outline and equal in size, and reacted sluggishly to light. Convergence on looking at near objects was defective. There was no nystagmus

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orstrabismus, and no evidence of actual facial paralysis. The tongue was slightly tremulous but could be protruded without deviation. There was no cervical rigidity.

The arm and the knee jerks were present and there was a degree of ankle clonus on the right side. The plantar reflexes were flexor in type. The abdominal reflexes were not obtained. There was no disturbance of sensation. Both arms and both legs showed rigidity. The patient could raise the right arm slowly above the head and the left to the level of the shoulder only. The right hand grip was feeble; the left was powerless. There was involuntary evacuation of the bladder and bowels.

During her five weeks' residence in hospital, the patient continued to be apathetic and became very helpless. She was unable to feed herself or to move in bed, except that at times she could draw the knees up. Knee clonus was noted on the right side. She continued to have involuntary evacuation of the bladder and rectum. The temperature, which had been subnormal, rose on the sixteenth day and became swinging in character. The left knee joint became swollen, but she did not complain of pain. She developed cystitis, due to a *B. coli* infection, and the number of bed sores increased. She was very feeble and had some difficulty in swallowing. The rigidity became less marked. She became semi-unconscious on October 26, and died on October 30, 1921.

Pathological Report.

Nothing abnormal was found in the thoracic and abdominal organs except in the kidneys, which were the seat of chronic nephritis. There were no indications of syphilis or of chronic alcoholism.

Head: A small amount of ante-mortem clot was present in the superior longitudinal sinus. The vessels of the dura mater appeared congested. The convolutions were flattened.

When after hardening in formalin a horizontal section of the brain was made, marked hydrocephalus associated with diminution in thickness of the brain substance was observed (see Fig. 1). The walls of the anterior and posterior horns of the lateral ventricles were deeply furrowed and the ridges between the furrows were each surmounted by a dilated vein. The floor of the ventricles presented a reticulated appearance.

The brainstem was separated from the hemispheres by a coronal section and various sections were made at different levels through the mesencephalon, pons and medulla. The hydrocephalus affected the whole ventricular system. The aqueduct of Sylvius was distended to about four times its normal diameter. Serial sections were made from paraffin blocks of the medulla and pons and stained with (a) hæmalum and eosin; (b) Heidenhain's hæmatoxylin and v. Gieson, and (c) toluidin blue.

Microscopically the fourth ventricle was the seat of granular ependymitis (see Fig. 2). This pathological ependymal condition consists in the formation of 'granulations' on the walls of the cavities lined by ependyma. In the present case there was marked proliferation of the subependymal glia, which could easily be distinguished from the normal tissue in that it was differently disposed. The fibres were for the most part closely packed together, arranged in layers, concentrically, or in whorls. In the centre of the whorl the neuroglia was rich in cells. At the junction of normal and abnormal tissue rarefaction was observed, the structure being much looser in character. In various situations there was marked vacuolation of the glia in the neighbourhood of blood vessels. The tissue also appeared to be œdematous. Another feature of the less dense glia was the aggregation in some places of small homogeneous bodies which appeared to be either of a fibrinous or hyaline nature and might have been thrombosed capillaries. The new formed tissue was very vascular and the vessels showed marked hyaline changes.

The 'granulations' which surmounted the subependymal gliosis appeared as 'hillocks' or polypoid outgrowths of various shapes and sizes projecting into the fourth ventricle. These projections consisted of neuroglial fibres, and were very rich in cells, the nuclei of

Fig. 1. View of lateral ventricles showing marked distentions.

Fig. 2. Section showing bridge of glial overgrowth spanning the foramen of Luschka.
 A. 'Granulation' showing neuroglial fibres. Note the numerous cells.
 B. Proliferated ependymal cells. C. Acinus lined by ependymal cells.

which were oval or elongated in the direction of the fibres. The ependyma at the summits of some of the 'granulations' had disappeared. In other places it had proliferated, forming three or four layers of cells. Many crypts were present, due apparently to the invagination of the ependymal lining. In addition, acini lined by ependymal cells were observed. These acini seemed to be formed either by the fusion of two projections or by invagination of the ependyma. In either case, it is possible that the epithelial lining might have been incomplete in the first instance but the gaps have been filled by proliferation of the ependymal cells. In certain of the acini fragments of choroid plexus were seen. The ependyma at some levels appeared to form the base line of the proliferated glia. The choroid plexus seemed to be enlarged and hyperplastic. Some of the cranial nerves seen in the sections showed interstitial overgrowth. In none of the pathological areas were lymphocytes, plasma cells or any inflammatory cells observed. A few corpora amylacea were present but not always in association with a blood vessel.

Fig. 3. Section of Upper Medulla.

- a. Ependymitis granularis. (Shaded part).
- b. Choroid plexus.
- c. Foramen of Luschka. (Blocked).
- d. Acinus lined by ependymal cells.

There must have been some dislocation of the brain substance in the floor of the fourth ventricle, as ganglion cells were seen in some of the ependymal projections. In this ventricle the ependymitis affected the floor, roof and walls. The excrescences had spread downwards between the restiform bodies and cerebellum, pushing the choroid plexus before them and completely blocking the foramina of Luschka (see Fig. 3).

Paraffin sections were made of the cortex and of the wall of the lateral ventricle and stained by the three methods mentioned above. The meninges and the cortex showed no perivascular infiltration such as is seen in general paralysis of the insane. Some slight chromatolysis of the cortical cells was observed. The walls of the lateral ventricles were studded with granulations in some situations, but for the most part the sections showed the *état reticulé* which is described later.

DISCUSSION.

The present case revives an interest in the etiology of chronic internal hydrocephalus and in the etiology and characteristics of lesions of the ependyma.

Clinically, hydrocephalus may be attended by symptoms suggesting intracranial tumour. Spiller¹ has described a case of internal hydrocephalus in which the differential diagnosis from cerebral tumour was very difficult. The third and lateral ventricles were much distended, while the fourth was of normal size. The aqueduct of Sylvius was occluded by overgrowth of neuroglial tissue and ependymal cells (ependymitis). Marinesco and Goldstein² have recorded a case of pseudo-tumour, the condition being in reality one of serous meningitis (ependymitis), resulting in acquired hydrocephalus.

The etiology of hydrocephalus.—According to Dandy³ every case of hydrocephalus has its specific cause. The old conception of an idiopathic variety is now practically abandoned; the essential causation of all its forms is believed to be obstructive. When the obstruction affects the foramina of Luschka and Majendie there are two types, one intrauterine with hydrocephalus present at birth and due probably to non-development of foramina, the other occurring at any age and always due to meningitis, which includes ependymitis. Stengler states that ependymitis granularis is the commonest cause of chronic internal hydrocephalus in adults.

Normally the cerebrospinal fluid is formed by the choroid plexuses of the lateral and third ventricles, and passes by the iter of Sylvius to the fourth ventricle, mixing with the fluid formed by the small plexus quarti ventriculi. Thence it escapes through the ependymal roof of the fourth ventricle by the central foramen of Majendie and the two lateral foramina of Luschka (these latter are situated at the lateral recesses between the flocculi of the cerebellum and the restiform bodies). It passes directly into the cisterna magna and thence diffuses itself upwards by the pontine and basal cisterns and the cisterns of the Sylvian fissure, and downwards in the subarachnoid space surrounding the cord.

It has been pointed out that the causal factor in the present case was ependymitis granularis obliterating the foramina of Luschka. Regarding the etiology of granular ependymitis, Delamere and Merle⁴, in their article on chronic lesions of the cerebral ependyma, have compiled an exhaustive bibliography of cases of pathological affections of the ependyma recorded between 1694 and 1909. They remark on the indifference which has been shown to lesions of that tissue. In their opinion most authors treat the affections as anatomical curiosities without any clinical interest. Ependymitis granularis may be found, according to these authors, in a large number of conditions, such as senility, chronic alcoholism, and syphilis. Some authors, whom they quote, hold that syphilis is the only causal factor. Many do not emphasise the causal relationship, but mention ependymitis granularis as an invariable accompaniment of general paralysis of the insane.

Delamere and Merle classify changes in the ependyma as follows :—

(a) Granular ependymitis, the most common form.

- (b) *État réticulé*, a further stage of (a), where the granulations have coalesced to form a network.
- (c) *État aréolaire*, a still further stage where the gliosis is in the form of a covering of equal thickness.
- (d) *État varioliforme* of Pierre Marie, seen in the brains of normal adults, where the changes macroscopically resemble the surface lesions of smallpox.
- (e) *État cryptique*, seen in the brains of adults. The crypts in this form are due to sinking of the ependymal surface and are determined by rarefaction of the subjacent tissue.

The causes of the conditions, according to their own investigations, may be tuberculosis, syphilis, tænia echinococcus, senility, alcoholism and other chronic diseases. Tubercular lesions may be identified by the presence of tubercular follicles, and syphilitic granulations by the presence of plasma cells, lymphocytes and, conclusively, by the presence of the *spirochæta pallida*. They discuss the question whether hydrocephalus is a sequel to ependymitis granularis or *vice versa*, or whether they are independent sequelæ of the same toxin. They cite the analogies of a pleurisy with or without hydrothorax and of a hydrothorax without pleurisy, and suggest that, in the same way an ependymitis may or may not be accompanied by hydrocephalus and that a hydrocephalus may occur independently of an ependymitis.

Bolton⁵, in discussing lesions in the brain in cases of mania, states that granularity of the ependyma is probably due to a loss of function of the epithelium, due to its being bathed with abnormal cerebrospinal fluid, which contains products of neuronc degeneration. The condition occurs chiefly in the regions most subject to stagnation of the cerebrospinal fluid and probably corresponds to the normal proliferative condition of the epithelium of the central canal of the cord seen in adults. There the canal is decreased in size, owing to the development of the white matter, with a consequent absence of flow of the fluid.

Kaufmann⁶ considers that inflammations, "serous meningitis of the ventricles," occasioned by alcoholism, injury, and acute infections, are etiologi-cal factors. He quotes Margulis, who holds that chronic hydrocephalus internus is due to a chronic periependymal gliosis which for its occurrence depends on a disturbance of development of the glia following on intra-uterine pathological conditions. Through trauma, alcoholism, etc., the latent and innate power of proliferation on the part of the glia is set free. The condition, he adds, is frequently accompanied by syringomyelia, which repre-sents merely a different localisation of the process.

The cord in the present case was not examined but no sign of syringo-myelia was present in the medulla.

Schrottenbach⁷ states that acquired internal hydrocephalus may occur in early life in cases of rickets, but the etiology is obscure. Aschoff⁸ mentions the occurrence of ependymitis granularis in general paralysis of the insane, but states that the ependymal condition is not confined to that disease nor is it pathognomonic of it. Granular ependymitis has also been described in disseminated sclerosis by Dawson⁹.

It would appear, then, that the etiology of granular ependymitis is still undecided; according to one view it is of inflammatory origin, according to another it is of non-inflammatory origin and of the nature of a sclerosis.

The brain in this case was examined for the presence of the *spirochæta pallida* by Dr. J. A. W. McCluskie, Western Infirmary, Glasgow, with negative results.

The ventricles of the following brains were examined for comparison.

(1) Case of chronic encephalitis lethargica. Macroscopically, the ventricular walls had an appearance of vesication; microscopically, ependymitis of the *aréolaire* type was found.

(2) Case of internal hydrocephalus. Unfortunately the brain had been cut up for other purposes, and the cause of the hydrocephalus could not be determined. The Wassermann reaction (blood) was negative. Ependymitis granularis was present in a slight degree in the fourth ventricle and in the aqueduct of Sylvius.

(3) Case of pachymeningitis hæmorrhagica interna of non-syphilitic origin. No definite pathological change was found in the ventricular walls.

(4) Case of general paralysis of the insane. Granular ependymitis was present. Plasma cells and lymphocytes were observed in the new-formed tissue, but not in abundance.

SUMMARY.

(1) In the present case it would seem that the internal hydrocephalus has been the result of occlusion of the foramina of Luschka, due to an overgrowth of the subependymal glia commonly designated granular ependymitis. Since the roof of the fourth ventricle was also the seat of the ependymal change it seems possible that the foramen of Majendie may have been occluded in the same fashion.

(2) No stigmata of syphilis (unfortunately the Wassermann reaction had not been performed, nor had the cerebrospinal fluid been examined cytologically), of tuberculosis, or of any other chronic inflammatory lesion have been observed; and, similarly, there is inadequate evidence to justify the view that the condition is of the nature of a gliosis.

(3) The very marked proliferation of glial tissue projecting through the foramen of Luschka seems to warrant the opinion that internal hydrocephalus has been a secondary phenomenon, although it cannot be denied that progressive stagnation of the cerebrospinal fluid may have exaggerated the glial overgrowth.

(4) Chronic nephritis was present, but its relationship to ependymitis granularis cannot be defined.

(5) It would appear from the examination of the present case and the other cases considered that granular ependymitis may occur in non-syphilitic conditions.

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