Clinical Notes and Cases.

A Case of General Paralysis of the Insane, with Syphilitic Meningomyelitis.

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THE case about to be described is that of a male patient who was admitted to the Belfast District Lunatic Asylum on October 31st, 1899, from the Union Infirmary, Belfast.

R. A—, æt. 33, ex-policeman, married, no family.

Family history.—Good, as far as could be ascertained.

Personal history.—Had always been healthy. Intemperate as regards the use of alcohol. Patient stated that twelve years ago he had syphilis and was under treatment for varying periods in different hospitals. Abscesses broke out on his legs; no other complications. A short time after his recovery and return to duty he became incapable of attending to his occupation owing to weakness in his legs. Stated he "staggered on the street like a drunk man," and that his "talk became loose," and "nothing would lie on my stomach."

On June 11th, 1898, patient was nearly drowned while walking on the sands at Ballycastle, where he had been sent to recruit himself. He lay unconscious on the sand for several hours. This he explained as due to a fall caused by "the shifting of the sand." Patient remained in bed five days and then found his hands began to shake and his legs became weaker, so that he fell frequently on attempting to walk.

Admitted to the Royal Hospital on August 6th, 1898. On examination his knee-jerks were found to be exaggerated. Pupils reacted slowly. Sensation unimpaired. Speech slurring and indistinct. Distinct tremor of hands and of tongue. No nystagmus, no sphincter trouble, no wasting. Remained in hospital about one month. Case diagnosed provisionally as disseminated sclerosis.

Present illness.—Duration three weeks. First attack. Medical certificate states that he has degraded habits, tears his clothes, and beats the other patients (in the infirmary).

On admission.—Patient appeared rather delicate, but not wasted. Complained of weakness in his legs and trembling in his hands.

Cranial nerves.—Vision and hearing good. Pupils dilated and somewhat irregular in contour, with partial adhesion of left iris. No inequality, no iridoplegia, no nystagmus or diplopia. Discs normal. Fine tremor in tongue, which is protruded and withdrawn abruptly. Speech hesitating, jerky, with pauses between the words and syllables.

Muscular system.—Fairly well developed and no wasting.

Head and neck.—Distinct rotatory tremor.

https://doi.org/10.1192/bjp.51.215.718 Published online by Cambridge University Press

Upper extremity.—Marked tremor in both arms, especially the right, which is increased by an effort to do anything. Cannot raise a cup of tea to his mouth without spilling the greater portion, and is quite unable to feed himself. Considerable weakness of both arms and inco-ordination of movement.

Lower extremity.—Marked weakness of both legs, so that he is unable to walk without assistance. Marked tremor in muscles of left thigh on attempting to move, and tremor is present in right leg while at rest. Right knee and ankle-joints somewhat rigid on passive movement; left less markedly so. On endeavouring to walk a few steps the stiffness becomes so pronounced that he is quite powerless to move the right leg. His gait is reeling, and he is inclined to fall to the right side.

Reflexes.—Knee-jerks greatly exaggerated, especially the right, and both limbs are in a distinctly spastic condition. Ankle clonus present in right leg. Plantar and abdominal reflexes marked.

Sphincters.—Slightly constipated.

General.—Numerous cicatrices of ulcers on both legs, and scar of a chancre on penis.

Mental condition. — (Abstract). Complains of being unable to remember things as formerly. Is rather quiet and dull, but answers questions intelligently, and can give a good account of himself. No evidence of delusions or hallucinations. Clean and tidy in person.

After a fortnight—Is brightening up considerably, laughing and talking when spoken to. A little elated and self-satisfied. Is sleeping and eating well. Temperature subnormal, about 97·4° F. About a week later seems to have an exaggerated idea of some little money his wife had. Is inclined to bolt his food. At end of a month is restless during early part of the night. Is becoming more elated. States he is well enough now to join the Royal Irish Constabulary again, although quite unable to raise himself out of his chair. Has been assaulting the other patients at night without any apparent reason. Pupils have become irresponsive to light and unequal. On January 5th weakness became more marked, and he required to be fed with fluid nourishment owing to great difficulty in swallowing. His speech became much weaker, but he still is able, he asserts, to take two men to the police barracks at once, etc. Very restless at night. Constantly making and remaking his bed. Towards end of month began to lose flesh, and the spasticity in his legs diminished as well as the knee-jerks. Became drowsy and apathetic, with a pleased expression on face. Swallowing very much affected, and almost speechless. Took cellulitis in left thigh with diarrhœa, and died four days afterwards, January 10th, 1900.

In asylum 3 months 10 days. Certified cause of death, general paralysis of the insane.

Autopsy.—General bodily condition fair. Cicatrix of chancre on penis. Lungs normal. Heart slightly hypertrophied. About two drachms of fluid in the pericardial cavity. Commencing atheroma of aorta, and some soft nodules on the mitral valves. Venous congestion of the liver, and a more marked congestion with slight interstitial overgrowth in spleen and kidney. A few small patches of congestion on the small intestine.

Brain.—The membranes are greatly thickened, and so closely adherent to the fronto-parietal regions on both sides that they could not be separated without tearing the brain tissue. About two ounces of cerebro-spinal fluid was obtained. The brain is congested. The convolutions are atrophic and considerably narrowed. The vessels at base of the brain, especially the basilar artery, are thickened and opaque. The brain on section appears normal except for a slight general congestion. In the left hemisphere, lying beneath the island of Reil and involving the upper portion of the claustrum and putamen, is a small circular cavity about the size of a large pea occupied by a clear fluid. Its wall is smooth, well-defined, and unstained.

Spinal cord.—Dura mater is thick and opaque, but not to the same extent as the cerebral, and is practically non-adherent. The arachnoid is also thickened, rough, opaque, and quite adherent to the pia mater except where it is distended in places with small collections of fluid. The whole cord is slightly larger in circumference than normal, especially in the cervical and upper dorsal regions.

Microscopical examination.—Brain shows the typical condition found in general paralysis of the insane in a fairly advanced stage, *i.e.*, chromatolysis and atrophy of the neurons in the cortex with overgrowth of neuroglia cells and fibrils, extensive deposit on surface of brain and around the blood-vessels of lymphocytes, plasma-cells, and some mast-cells, with collections of pigmented granular material. These changes are most marked in the parietal and frontal regions.

Spinal cord.—The appearances of the cervical and dorsal regions of the cord are very similar. The pia arachnoid is much thickened, coarsely fibrous, and very vascular. This increased vascularity extends also into the roots. Around these vessels and in the meshwork of the hypertrophied meninges is a diffuse infiltration of lymphocytes. The vessels are all congested, and the majority of the veins are thrombosed. Their walls are slightly thickened, especially the adventitia; and in some cases, as the anterior spinal artery and its branches, extending into the basilar artery, there is a distinct endarteritis. Around the cord is a marginal zone which does not stain with Weigert-Pal hæmatoxylin, but readily takes up carmine (Figs. 1–3). In the lateral columns this band is very extensive, involving practically the whole of the columns including the crossed pyramidal and direct cerebellar tracts. Anteriorly it is narrower and extends into the anterior median fissure. The posterior columns are immediately noticeable owing to the limited area of this border. Radiating from the marginal zone inwards are noticed a large number of wedge-shaped areas (Geschwulstzapfen of Siemerling and Oppenheim) which extend practically to the grey matter. Between the apices of these processes and the grey matter and even in the grey matter itself are numerous oval, elliptical, and circular areas, similar in structure to the former, but isolated from them and each other. These are most marked in the posterior columns. In all these sclerotic areas is observed a hyperplasia of the neuroglia cells and fibrils. In some places these cells have undergone hypertrophy, and, degenerating later, have left their thickened and elongated processes to form a dense network. The vessels in the cord are thickened, and some have collections of lymphocytes and a few plasma cells (?) in their perivascular lymph

sheaths, but not nearly so extensively as in the brain. The nerve-cells show swelling and chromatolysis, chiefly central. A few excentric nuclei and swollen and vacuolated nucleoli are visible. On the whole, the cells are comparatively healthy and have undergone very little alteration. The anterior roots show some congestion and sclerosis with a diminished number of healthy fibres in several segments. The posterior roots are apparently normal.

The lumbar and sacral regions (Figs. 4–6) differ from the foregoing in that the amount of sclerosis is much less extensive. The marginal zone is narrower and almost entirely confined to the lateral columns, and the wedge-shaped and other areas are much fewer in number. In the posterior roots of the sacral region several bundles of nerve-fibres are quite swollen and atrophic, taking up only a trace of the stain, while other neighbouring bundles are quite normal. The vessels of this region are noticeable by their hyperplasia and congestion. Very few, however, are thrombosed. A peculiar feature of the lateral columns of the lumbar region is the presence of great numbers of hypertrophied neuroglia cells, with coarse, branching processes, "spinnenzellen" or "astrocytes." These are found scattered in the marginal zone with their processes radiating towards the periphery of the cord, or are collected in the form of tubes round the blood-vessels.

In vertical sections of any region of the cord a very evident hyperplasia of the smaller neuroglia cells is evident, noticeably so in the areas around the blood-vessels and in the sclerosed patches. Some of these cells have elongated and swollen nuclei and contain granules in their interior; possibly these are the "neuronophage" cells which Marinesco considers to owe their increase in number to the chemiotaxic action of the toxin, and to be attracted to the areas of degeneration, thereby taking on a phagocytic function. He also considers these cells to have a destructive action on the unhealthy fibres, hastening their degeneration and absorption. In the sclerotic areas (Fig. 7) there are practically no medullary sheaths or axons visible, a rather marked variation from the persistence of the latter in typical cases of disseminated sclerosis. On the internal border of these areas, however, one finds a considerable number of fibres which are swollen, irregular, and take the hæmatoxylin stain feebly. On staining by Marchi's method there is evident a slight diffuse degeneration of the white fibres, perhaps a little more marked in the pyramidal tracts than elsewhere. There is no trace of myelin to be found in the sclerosed areas, it having probably been removed by the granular glia cells. These sclerotic patches appear, therefore, to be composed of blood-vessels and small neuroglia cells, and especially of their fibres, which show hyperplasia.

There are no true system degenerations in the cord, neither are there any gummatous nodules or collections of cells in any part of the brain, cord, or membranes, nor are any areas of ischæmic softening or hæmorrhage visible, except the small cavity in the left hemisphere. The small nodules of sclerosis, whether connected or isolated, are nearly always associated with blood-vessels, and in some of them one can trace the vessel in a longitudinal section as if forming the axis of the elongated nodule (Fig. 8).

The area affected in the cord is much more extensive in the cervical

and dorsal regions, and here no large glia cells are visible, their coarse fibrous processes alone remaining, while the cell bodies have already vanished. Apparently in the lumbar region the disease is more recent, as evidenced by the smaller extent of sclerosis, the more marked congestion, and the abundance of hypertrophied neuroglia cells and processes.

The membranes covering the pons and medulla are also thickened, and immediately beneath them there is a hyperplasia and hypertrophy of glia cells and fibrils. In the subependymal tissue in the floor of the fourth ventricle this alteration is very marked, giving rise to coarse and irregular nodules. The whole system of veins on the surface of pons and medulla is thrombosed.

The pathological interpretation of this case is interesting. The affection of the spinal cord is evidently the primary one, the disease extending later to the brain, and here giving rise to the degeneration of the higher neurons typical of general paralysis of the insane.

Owing to its extensive blood and lymph supply the spinal cord apparently furnishes an excellent situation for the influence of the syphilitic toxin. The course of the morbid process appears to be along the connective-tissue septa, the hypertrophic processes of pia mater and vessels forming the wedge-shaped growths being considered by many authorities distinctively characteristic of spinal syphilis. The morbid process extends imperceptibly from the vessels themselves (Bechterew ([1])), and gradually leads to the degeneration and absorption of the contiguous nerve fibres and cells and their replacement by neuroglia fibrils. In this case the venous lesions predominate, especially in the cervical and dorsal regions, as has been specially emphasized by Lamy ([2]), Goldflam, and Sottas ([3]).

In individual cases, under special conditions which are as yet unknown, the nervous system seems to have an extraordinary tendency to the formation of syphilitic nodules, with the consequence that the specific affection of the nervous tissue takes on a disseminated character, but is distinguished from disseminated sclerosis by the preference that the nodules have for the neighbourhood of blood-vessels, and also by their small size. This opinion, enunciated by Bechterew, ([1]) is fully borne out by the present case.

The commencement of the nervous symptoms so long after the primary affection is of interest, as according to Gilbert and

Fig. 1. Photograph. Seventh Cervical.

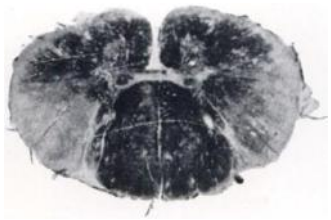

Fig. 2. Photograph. Fourth Dorsal.

Fig. 3. Photograph. Eighth Dorsal.

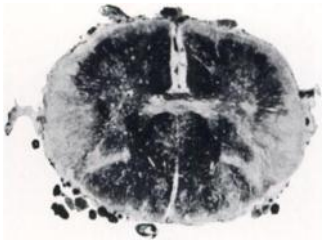

Fig. 4. Photograph. Second Lumbar.

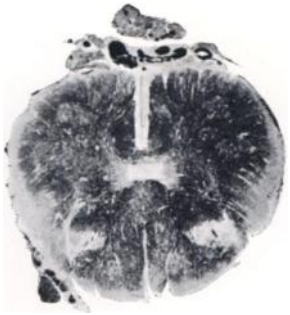

Fig. 5. Photograph. Fifth Lumbar.

Fig. 6. Photograph. Third Sacral.

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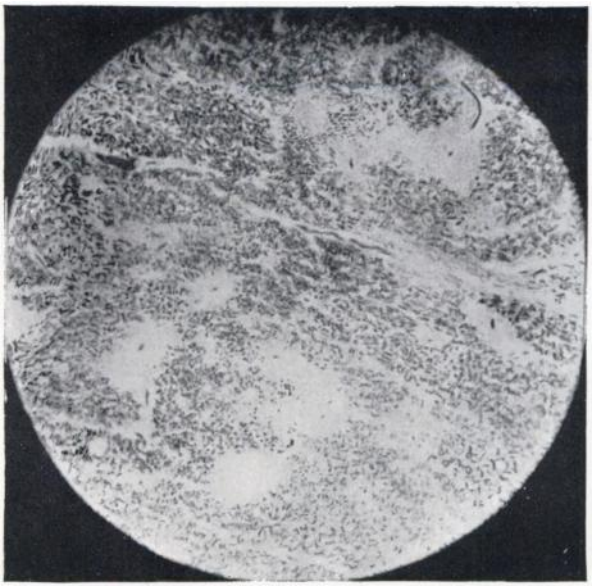

Fig. 7. Photomicrograph. Low Power. Third Cervical.

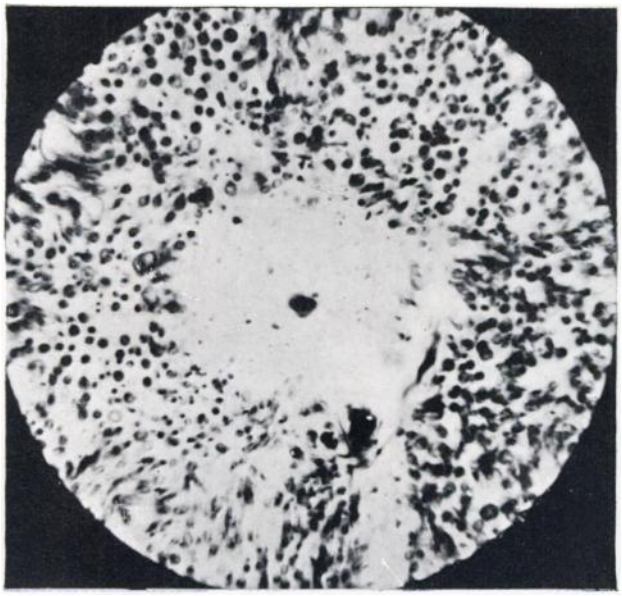

Fig. 8. Photomicrograph. High Power. Third Cervical,

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Fig. 9. Photograph. Longitudinal section through posterior half of cord in the cervical region, showing the sclerosis (pale areas) in the lateral columns on both sides, with small nodules in the posterior columns.

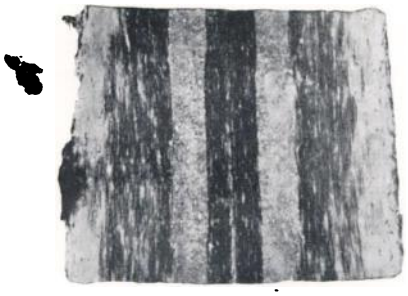

Fig. 10. Photograph. Similar section through anterior half of cord at the same level, including the anterior cornua. There is less extensive marginal sclerosis. The grey matter of the cornua has a mottled appearance, due to small nodules of sclerosis.

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Lion (4) the meningeal symptoms usually arise in the first three years after luetic infection, and are a very rare complication after eight years. Nonne (5) has met a case occurring within three months of the primary infection. If the lesion appears after an interval of several years, as in this instance, its course becomes chronic and it is usually of the sclerotic type. Gilbert and Lion (4) divide the infection into a primary group appearing early, without any distinct macroscopic lesion, and characterised by an "infiltration embryonnaire diffuse" around the blood-vessels, "méningo myélite embryonnaire diffuse," succeeded in the second group, "diffuse sclereuse," by the involution of this infiltration into the sclerotic type. In this case the prevailing spinal lesion conforms more to the latter, while the brain lesion follows the former type.

It is also noteworthy in this case that, while the sclerotic lesion is maximal in amount, the vascular is minimal in comparison, the toxin apparently not being in sufficient concentration to cause an active inflammation of the vessels, but being by its slow diffusion capable of injuring the more highly organised and vulnerable nervous tissue.

The interest attached to this case clinically consists in the fact that one year previous to the patient's admission to the asylum his case was diagnosed as one of disseminated sclerosis. For some time afterwards there was considerable doubt as to the nature of the disease. It was probable that the mental development could be explained as a form of psychical enfeeblement which frequently accompanies the later stages of disseminated sclerosis, but in the course of a few weeks the symptoms began to point towards paretic dementia with grandiose ideas, Argyll Robertson pupil, inequality of pupils, etc. The rather puzzling point, however, is to account for the spinal symptoms. Here is a case of chronic meningomyelitis with isolated nodules in the cord, giving rise to symptoms exactly similar to those in the early stages of disseminated sclerosis, but (what is remarkable) with no symptoms whatever referable to the meningeal lesion, such as marked pain, tenderness or spinal rigidity, muscular atrophy or disturbances of sensation, and no evidence of the special diagnostic symptoms observed by Oppenham, *e.g.*, interrupted course of affection, oscillation of individual symptoms, and the difficulty of their localisation. In all the literature available to me the only two cases which at all approach clinically

and pathologically to the present are described by Greiff (7), and here the similarity is most marked except that the involvement of the posterior columns was more extensive in both instances.

Zacher (8) describes a case similar in many respects to those of Greiff, except that clinically there were symptoms of hemiplegia, facial paralysis, and epileptiform convulsions, in addition to those described above; while the pathological findings tended more in the direction of a multiple sclerosis without the same extent of meningeal involvement.

Numerous other cases are described in pathological literature where there are distinct specific meningomyelitic lesions with arteritis and a termination in general paralysis of insane, but at the same time show nodules of sclerosis, impossible to distinguish from those of disseminated sclerosis, distributed irregularly throughout the cord and brain (Bechterew (1), Schultz (9), Claus (10), Siemens (11), Otto (12), Petroff (13), Schüle (14), Hunt (15), Crouzon (16)).

How far the three cases quoted and the one described bridge over the separation area between typical disseminated sclerosis and spinal syphilis, or how far they demonstrate a line of demarcation between these two complex groups of diseases, I do not feel competent to decide. To me the whole case serves to illustrate the complexity of most of the diseases involving the nervous system, and the peculiar tendency of quite different types of lesions when affecting certain regions of the spinal cord to give rise to almost identical symptoms, thus rendering an accurate clinical diagnosis almost an impossibility.

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Discussion

At the Meeting of the Irish Division held at the Stewart Institution on May 9th, 1905.

Dr. Rainsford said the paper raised the question of the diagnosis of general paralysis, which he considered a very indefinite entity. The only symptom of the disease in Dr. Graham's case appeared to be slight elation. He thought that there was too great readiness to call any general disease in an asylum general paralysis.

Dr. Norman thought the Division was to be congratulated on Dr. Graham's paper, and hoped it would be published with the micro-photographs.

Dr. Leeper expressed interest in Dr. Graham's study of the descending degenerations, and alluded to the selective action shown by the syphilitic poison. He thought that the slight degree of the mental involvement was to be explained by the small extent to which the cells were affected.

Dr. Dawson said that the spinal disease seemed to him to have preceded and been quite distinct from the cerebral disease, which was a separate lesion altogether.

Dr. Eustace asked a question as to the duration of the illness.

Dr. Graham, in reply, said that the diagnosis between disseminated sclerosis and general paralysis had long been in doubt, but that the autopsy had decided in favour of the latter. He fully agreed with Dr. Dawson as to the order in which the diseases had attacked the patient.

Occasional Notes.

The Annual Meeting.

The Annual Meeting of this year was of more than ordinary duration owing to its being preceded by the adjourned Annual Meeting, at which the new statistical tables were finally adopted. The attendance of members was larger than in