Critical Digests.

ON THE MORBID ANATOMY OF FRIEDREICH'S DISEASE.

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IN the last few years, a considerable number of cases have been recorded, illustrating the clinical history of this disease, but very few observations upon its morbid anatomy. It may be well, therefore, to give a detailed abstract of three publications, in which new pathological observations are to be found.

We will begin with two cases by Rutimeyer.¹ These have been already noticed, from their clinical side in 'BRAIN';² having been the subject of a previous communication by Rutimeyer.³

CASE I.

Heinrich Kern, æt. 20.—Onset between 6 and 7 years of age, with simple ataxia first of lower, then of upper limbs. No affection of sensibility till the sixth or eighth year of the disease. Affection of speech, curvature of spine; finally, paralysis, and wasting of the legs, dorsal contraction of the great toes; diminution of cutaneous sensibility of the legs; nystagmus. Absence of patellar reflex; no affection of pupils, no pains or girdle sensations. Death from "general weakness," after the disease had lasted about fourteen years.

Nothing special to note in the post-mortem appearances; death was ascribed to fatty degeneration of the heart, and hypostatic congestion of the lungs.

Examination of the nervous centres after hardening in Müller's fluid shewed the brain and medulla to be uniformly wasted; the pia and arachnoid of the lumbar cord thickened and adherent; the nerves of the cauda equina and posterior nerve-roots thinned.

There was degeneration of Goll's columns throughout the cord; and in the cervico-dorsal region the inner parts of the cuneate fasciculi were involved, and in the lower dorsal region nearly the whole of them. The lateral columns were also degenerated, over areas corresponding to the crossed pyramidal and direct cerebellar tracts.

¹ Virchow's 'Archiv,' Bd. 110, p. 215.

² 'BRAIN,' No. XXV. Table I., No. 7. Table II., Nos. 18 and 20.

³ Virchow's 'Archiv,' Bd. 91.

Measurements of the cord after hardening—

In mid-cervical region	14 × 8 centim.
" dorsal	" 9 × 6 "
In lower dorsal	" 9 × 6 "
In mid-lumbar	" 10 × 9 "

MICROSCOPICAL EXAMINATION OF THE CORD.

Cervical regions.—Marked degeneration of Goll's columns, which was however, a little less intense near to (within one c.m. of) the posterior commissure.

Just exterior to Goll's columns was a tract of much less intense degeneration, broadest at the posterior periphery of the cord, and narrowing further forwards. In the upper cervical region this area of degeneration did not reach the posterior commissure; but lower in the cervical region it became broader and extended further forwards, so that only a narrow tract of white substance along the edge of the posterior horn was left unaffected.

In the lateral columns was an area of degeneration corresponding accurately to the cerebellar and crossed pyramidal tracts; the degeneration was of equal intensity through all this area; less marked than in Goll's column, but increasing in intensity from above downwards.

Grey substance practically normal; anterior nerve-roots normal; degeneration of posterior nerve-roots more marked in lower than in upper cervical region.

Dorsal region.—Almost the whole area of the posterior columns were degenerated, Goll's columns intensely; the part immediately adjacent to the posterior horns of grey matter least intensely. This widespread degeneration of the posterior columns did not begin to abate till the extreme lower end of the dorsal region was reached.

In the lateral columns, degeneration of the cerebellar and crossed pyramidal tracts was present.

In the grey matter degeneration of Clarke's columns (both cells and fibres), reaching its maximum in the lower dorsal region.

Degeneration of the posterior nerve-roots.

Lumbar region.—Diminution of the degeneration in the posterior columns; especially in their antero-lateral part (angle between commissure and posterior horns). The posterior root-zones, however, particularly in the upper lumbar region, were degenerated.

In the lower lumbar region there appeared in the columns of Goll, a small oval area, mesially situated, wherein the degeneration was less intense than at other parts of Goll's columns.

In the lateral columns degeneration of the crossed pyramidal tracts.

Grey matter mostly intact.

Still considerable degeneration of the posterior nerve-roots.

Sacral region.—Degeneration (fainter but appreciable) in the median and posterior parts of Goll's columns. Lateral columns intact.

The medulla was not examined.

CASE II.

Bertha Kern (sister of Case I.).—Note of Sept. 1882. Age 14; onset of disease at age of 7. Ataxia of limbs and of trunk; slight nystagmus; speech not affected. Little if any affection of sensation, no pain. Slight dorsiflexion of great toe. In 1883 rapid appearance of a spinal curvature. Permanent dorsiflexion of both great toes. Although extremely ataxic, the patient could get about by holding on to things. In Sept. 1884 a feverish attack accompanied by great prostration and pains in the limbs, in which she died. Typhoid was suspected, but this was not a substantiated post-mortem. Fatty degeneration of the heart was found microscopically.

The dorsal cord appeared to be small. Measurements (after hardening) of

Mid-cervical region	12 × 8 centim.
Upper dorsal	" 10 × 6 "
Mid-dorsal	" 8 × 5 "
Lower dorsal	" 7 × 6 "
Mid-lumbar	" 9 × 6 "

The dura mater from the 7th dorsal vertebra downwards appeared infiltrated with blood, but there was no hæmorrhage into the dural sac. Slight adhesions of dura and pia, and some diffuse thickening of the pia mater.

After hardening in Müller's fluid, there could be seen (naked eye) degeneration of the posterior columns, limited in the upper cervical region to part of Goll's columns, but lower down spreading out towards the posterior cornua; and in the posterior part of the lateral columns a wedge-shaped area of degeneration reaching from the mid-cervical to the lower dorsal region.

The medulla oblongata was small. The brain was normal.

MICROSCOPIC EXAMINATION.

Upper cervical region.—In the posterior columns marked degeneration of Goll's columns reaching forward to the posterior commissure. Some affection of the fasciculi cuneati, chiefly in their middle third. Degeneration in the lateral columns, less marked, corresponding to the joint area of the cerebellar and crossed pyramidal tracts, and uniform in degree over all this area.

Grey substance normal; some loss of fibres in the posterior nerve roots.

Middle and lower cervical regions.—Goll's columns most affected. In the fasciculi cuneati the degeneration spread outwards so as to leave intact only their anterior parts, and the parts immediately abutting on the posterior cornua and posterior nerve roots.

Grey substance normal; posterior nerve-roots highly atrophied.

Dorsal region.—Still further degeneration in the fasciculi cuneati; their anterior and exterior parts, which were free in the cervical region, being now encroached upon. Low in the dorsal region,

though the anterior parts of the fasciculi cuneati were involved, the stripe along the posterior grey horns, and a little triangular patch at the entry of the posterior nerve-roots were more healthy than the neighbouring parts.

In the lateral columns was degeneration of the crossed pyramidal and cerebellar tracts (as in the cervical region): but it is noted that in the upper dorsal region (and here only) an additional area was involved, reaching forwards from the anterior part of the cerebellar tract, along the periphery of the cord, to the level of the forward termination of the anterior cornua.¹

Clarke's columns degenerated, especially at the lower part of the dorsal cord; the rest of the grey matter intact.

Posterior nerve-roots diseased.

Lumbar region.—Posterior columns; anterior parts of cuneati fasciculi normal again, while of their posterior parts a portion was affected, viz., the inner half of the area defined by Westphal as the zone of entry of the posterior roots; Goll's columns degenerated; the little oval zone of comparatively healthy substance which was mentioned in Case I., appeared in this case also. Lateral columns: less extensive degeneration, corresponding to the diminishing crossed pyramidal tract.

Degeneration of Clarke's columns in dorsi-lumbar region. Decrease in the degeneration of the posterior nerve-roots.

Sacral region.—Posterior columns: only the postero-median parts diseased. Lateral columns: degeneration of crossed pyramidal tracts still traceable.

The medulla oblongata could not be thoroughly examined; but degeneration could be traced in the funiculi graciles and cuneati to the upper part of the decussation.

A certain degree of degeneration was found in the nerve trunks (median and sciatic).

Histologically the spinal degeneration consisted (in both cases) of a growth of fine connective tissue replacing the nerve fibres; there was no special affection of vessels, and though the pia was thickened in places, there was no reason to think that the disease had spread inwards from the meninges.

The localisation of the disease moreover suggests that it was parenchymatous in origin: for it is obvious, as the author remarks, that it affected several distinct tracts of fibres, and was limited to these tracts: constituting therefore a "combined system disease." Thus in the lateral columns the crossed pyramidal tracts and direct cerebellar tracts were picked out with tolerable accuracy. (A slight extension beyond the areas of these tracts was noted in Case II.; for which we have suggested an explanation in the footnote.) This lateral degeneration was at its maximum in the lower dorsal region. The direct pyramidal tracts were not affected, Clarke's columns were diseased, which accords with the German view, that the cells of these columns are the trophic centres for the cerebellar tracts.

¹ This probably represents the antero-lateral ascending tract.—(Abstractor's Note.)

In the posterior columns, Goll's tracts were diseased throughout; excepting a small oval centrally placed area in the lower parts of the cord, which probably forms no part of Goll's tracts. Concerning the rest of the posterior columns it may be said that in the lumbar and lower dorsal regions the disease spread widely enough to involve the posterior root-zones, while in the upper cord it was limited to the neighbourhood of Goll's tracts. How far the changes in these parts, the fasciculi cuneati, are to be considered as "systematic" degenerations is doubtful, but they correspond broadly to those of ordinary tabes.¹

Dr. Everett Smith² gives a clinical account of six cases of Friedreich's disease, and the morbid anatomy of one. The clinical histories should be read in the original; we can here only make the following brief excerpts.

Five sisters were affected with the disease: three other sisters of the family did not suffer from it: five brothers were also unaffected.

The symptoms in the girls are summarised by the author as "a series of morbid symptoms, beginning at the age of 6 or 7, regular in order in progression. The first symptoms noticed were gastric disturbances and palpitation of the heart, followed by an unsteady gait which later became purely ataxic. The ataxia gradually extends to the hands; and here the disease seems to remain stationary for an indefinite length of time."

We may add the following symptoms from the clinical histories of the girls: club foot, spinal curvature, *wrist drop roughly resembling that seen in lead-palsy*, attacks of epileptic convulsions; of pain in the spine and limbs; of dyspnoea and collapse. Oddly enough, the only girl whose symptoms did not begin with cardiac palpitation, became the subject, later on, of organic disease of the heart from rheumatism. In another girl the tendon reflex³ persisted after the gait had become ataxic, though it disappeared subsequently.

The father of these girls suffered from an allied form of paralysis, but his case differed in the following respects.

(1) The symptoms began much later in life (æ. over 60). After an attack of rheumatism, brought on by exposure to cold, there followed a "severe gastritis." But he had had attacks of nausea and vomiting for many years. He had dilatation of the heart.

(2) Although the gait was ataxic, the tendon reflexes were present.⁴

(3) The symptoms disappeared under treatment.

This man's family was decidedly "neurotic"; his father (the girls' paternal grandfather) had some doubtful ataxic symptoms; and although the father of the five ataxic girls did not drink himself, there was a marked history of drunkenness in the two generations preceding him.

¹ For the minute localisation we must refer to the original paper.

² 'Boston Medical and Surgical Journal,' vol. cxiii. p. 361.

³ Cf. a case shewn to the Medical Society.

⁴ Cf. 'BRAIN,' No. 39-40. A woman, with spastic paraplegia had two children suffering from typical Friedreich's disease.

The patient whose case was investigated post mortem died during one of the periods of collapse (above alluded to); it was accompanied by dyspnoea and palpitation, and vomiting so intense that she had to be fed per rectum. There had been in this case considerable paresis, in addition to the ataxy; and also affection of sensation in the lower limbs.

Post mortem, in the abdominal and thoracic organs nothing was found that bore upon the nervous disease. The muscles were generally wasted. The brain was not examined.

The spinal meninges were injected and adherent to the bony walls of the canal. The cord appeared "asymmetrically atrophied, pale and in local areas softened."

The lower dorsal and lumbar regions were minutely examined, with the following results:—

The shape of the cord was altered, the posterior half being shrunken, and the left postero-lateral column looking as if it had been sliced away.

Posterior columns; their whole area intensely sclerosed, except a comparatively healthy part close to the posterior commissure. Rather more healthy nerve-fibres in lumbar than in dorsal regions.

Antero-lateral columns. Sclerosis of pyramidal tracts, crossed and direct, upon both sides, but of less intensity than that in the posterior columns.

Thickening of pia mater over the posterior and lateral columns.

Posterior nerve roots discussed; anterior healthy or nearly so.

Ganglion-cells of anterior and posterior cornua less numerous than normal, and showing degenerative changes under high powers.

Central canal blocked with round cells. In the lumbar region was a small supplementary canal just posterior to the main canal.

Dr. Pitt's case¹ is, we believe, the first reported in England in which the clinical history is supplemented by the morbid anatomy. The patient was under the care of the late Dr. Moxon on and off for seven years. He formed one of the family shewn to the Clinical Society by Dr. Gowers, and a notice of his case based on Dr. Gowers' paper appeared in a previous number of 'BRAIN.'² It should be added here that choreiform twitchings formed an early and a marked feature in his case, and that during the last years of his life failure in the organs of circulation supervened, as evidenced by dilatation of the heart, obstructive disease of some of the arteries of the limbs, bronchitis and dyspnoea. Death took place rather suddenly at the patient's own home.

Post-mortem.—The heart weighed 25 oz., both ventricles were dilated and hypertrophied, the left shewed fibroid patches, the aortic valves were diseased; the radial, on one side, could not be found, and on the other, contained an organised clot. The

¹ 'Guy's Hospital Reports,' vol. xliv., p. 369.

² No. XXV. (Table II. No. 31.)

author considers that there was obliterative end-arteritis of the small vessels.

In the brain, the only abnormal appearance was a tough and streaky grey patch "below the posterior part of the external capsule" in the left hemisphere.

Spinal cord small on section; measurements as follows:

Upper cervical region.	Normal cord.	Degenerated cord.
33 mm. lower.	13 × 10	13 × 8
39 "	15 × 9	12 × 8
51 "	16 × 9	11 × 7
57 "	12 × 8	10 × 7
67 "	10 × 8	9.5 × 7
81 "	10 × 8	8 × 7
107 "	13 × 8	8 × 8
127 "	12 × 8	8 × 7

It was of firm consistence, and there was grey degeneration of both posterior and lateral columns.

The meninges were normal.

The nerve-roots—anterior, healthy—posterior, degenerated (confirmed microscopically).

Peripheral nerves—radial, and branch of anterior crural examined and found normal.

Microscopical examination of the cord.—Weigert's method, and aniline blue black employed).

Lower lumbar region.—Posterior columns completely sclerosed, except their anterior fourth, which is healthy, and a thin strip extending therefrom backward in the middle line. Internal radicular fibres sclerosed.

Crossed pyramidal tracts shewed loss of medullary sheaths.

Upper lumbar.—Posterior columns sclerosed, except a strip along each posterior grey horn (in the anterior half of the posterior columns).

The disease of the lateral columns reaches forward along the periphery beyond the area of the cerebellar tracts.

Lower dorsal.—Similar sclerosis of posterior columns. Also of Clarke's columns. Lateral columns much as before.

Mid-dorsal.—Posterior columns as before. More extensive sclerosis of lateral columns, involving the crossed pyramidal and cerebellar tracts; and (irregularly and slightly) the periphery in front of them. Clarke's columns affected.

Upper dorsal.—Goll's columns much sclerosed. Burdach's columns become more healthy, especially their anterior third near the grey matter.

The lateral sclerosis was most marked in the dorsal region.

In both dorsal and lumbar region there was partial disease of the nerve-fibres entering the posterior grey horn.

Lower cervical.—Goll's columns completely sclerosed; slight sclerosis of posterior two-thirds of Burdach's columns.

Sclerosis of crossed pyramidal tracts less; cerebellar tracts still affected; peripheral sclerosis well marked, extending up to and slightly along the anterior fissure.

First cervical.—No degeneration in the lateral columns.

In the medulla.—Sclerosis of funiculus gracilis; slight disease of funiculus gracilis, and of funiculus rotundus.

At the level of the decussation of the pyramids two canals were visible.

The author's summary may be given thus.

1. Spinal cord extremely small.
2. Extreme sclerosis of Goll's columns, through its whole length.
3. Burdach's columns severely sclerosed, their posterior portion particularly (the disease being rather less intense high in the cord). But the strip of Burdach's columns which bounds the posterior horn and root, especially along the anterior half, is free.

In connection with (3) slight disease of funiculi cuneati and rotundi in medulla?

4. Sclerosis of crossed pyramidal tracts, most marked in dorsal region (?), not traceable above decussation of pyramids. Much less intense than sclerosis of posterior columns.

5. Sclerosis of cerebellar tracts, also not intense.

6. Slight irregular peripheral sclerosis anterior to (5); sometimes reaching along the anterior fissure.

7. Degeneration (here and there) of Clarke's columns; of posterior nerve-roots, and fibres in the posterior horns.

The localisation of the degeneration in these cases throws some light on its nature: this must be our excuse for the above lengthy abstract. All previous cases agree in this, that the posterior columns have been deeply sclerosed; and generally in this way: that the columns of Goll (postero-median) have been affected through the whole cord, the columns of Burdach (postero-external; fasciculi cuneati) extensively affected in the lower dorsal region, and less extensively higher up the cord. Here therefore the degenerative changes roughly correspond to those of ordinary tabes, and if the latter be regarded as a "systematic sclerosis," so also (quoad the posterior columns) must Friedreich's disease.

But as regards the lateral sclerosis, there has hitherto been some doubt whether this follows definite nerve-tracts, developing in them independently of the posterior sclerosis, i.e., whether it is primary and systematic; or whether it is caused by irritation spreading from the diseased posterior columns, i.e., is secondary and diffuse. Now the present cases speak strongly in favour of the former view. For in all of them the degeneration picked out known tracts of fibres, the crossed pyramidal and cerebellar in the first two, the crossed and direct pyramidal in the third, the crossed pyramidal and cerebellar in the last. In the last case also an irregular peripheral sclerosis extended round the anterior parts of the cord in its upper parts. This is reasonably ascribed to disease of the antero-lateral tract (Gowers, Hadden, Tooth); an explanation which may account for the existence, in other cases of combined sclerosis, of a peripheral degeneration not corresponding to the cerebellar tracts. And since there is no evidence that the disease spread from the posterior to the lateral columns, either by con-

tiguity or in other ways,¹ the inference is that the process has been one of independent degeneration in several nerve-tracts; the antero-lateral sclerosis probably being secondary to the posterior in point of time, but in no other sense.

Further, the mere localisation in tracts already marked out by development and function argues powerfully for the view, that the disease is *ab initio* parenchymatous and begins in the nerve-fibres. Dr. Pitt advances the view, that this nervous degeneration is itself dependent upon hereditary disposition to disease in the blood-vessels; for he finds an objection to what may be called the purely nervous view in the fact, that the most sclerosed areas (Goll's columns) are just those which develop later than the less sclerosed (crossed pyramidal tracts). But we hardly think it proven that the latest in development must necessarily degenerate first; for other factors may interfere with the working of such a law: e.g., as Dr. Pitt himself indicates, the posterior columns may break down first because they have more continuous work thrown on them. And, clinically, the vascular phenomena seem to have appeared late in Dr. Pitt's case; while some of those symptoms which he singles out in other cases as vascular, e.g., headache, vertigo, comatose attacks, may just as well have been nervous. But his remarks on the condition of the circulatory system are none the less valuable; for whatever their relation to the nervous disease, symptoms from this side must be of high prognostic importance.

A word may be added on the nomenclature of the disease. Dr. Everett Smith,² taking as text Dr. Gowers' remarks on the inconvenience of naming diseases after individuals, proposes for it the name "postero-lateral spinal sclerosis of generic origin." The term "generic" is ingeniously chosen to express a family grouping of cases, necessarily connoting transmission as "hereditary" seems to do. As a shorter name for ordinary use Dr. Smith proposes "generic ataxia." But here he would, we presume, be met by Dr. Pitt, who says that "the pathology and course of this disease and of ordinary locomotor ataxia are entirely distinct, the only common symptom being the loss of the knee-tap." We do not altogether subscribe to this latter statement, but at least it shews that till our views about a disease are thoroughly stereotyped it is difficult to find for it a rational name.

¹ It should be mentioned, however, that Dr. Everett Smith notes in his own case an inflammatory condition of the cells of the central canal like that observed by Brousse, and believed by him to represent the channel by which the disease spread from one part of the cord to the other. Dr. Smith's own opinion is that it spreads by means of meningitis. Seeing that the antero-lateral sclerosis in his case exactly corresponds to the crossed and direct pyramidal tracts, we hardly see how this can be maintained.

² 'Boston Medical and Surgical Journal,' March 1, 1888.