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A Case of Progressive Muscular Atrophy with Sclerosis of the Lateral Columns.

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THE following case is of interest in its relation to the pathology of progressive muscular atrophy, and also in view of the recent division made by Prof. Charcot of this disease into two groups. I have to thank my friend Dr. B. A. Segur for the opportunity of seeing this patient. The first part of the case was observed by him, the latter part by me.

Male, aged 44, with apparently no neurotic family history; at 20 years of age he had gonorrhœa, followed by stricture, gleet and its accompanying pain in back, hips, &c., but otherwise he enjoyed good health. In 1870, his first impairment of health began; in February of this year, after an exposure to wet and cold, he became quite sick, the exact nature of which sickness is not known; it was of such a nature, however, as to confine him to his room for two and a half months, and he was unable to engage in any occupation for one year after; he thinks he never entirely recovered his former vigor; following this he had some pulmonary hemorrhage and expectoration, which was slight. In October, 1875, the first symptoms of his present difficulty appeared; he began to notice fibrillary twitchings in the small muscles of hands, especially those of the thumb, and simultaneously there was a wasting of these muscles, their function was also impaired, as shown by inability to tear up pieces of paper, &c., which is done by the index and thumb; the condition was alike in both hands. The atrophy went on so rapidly in the muscles of the hands that in January, 1876, he was unable to write; the atrophy and fibrillary twitchings then began in the muscles of the arm and forearm. He began to have bulbar symptoms about May of this year, and by October the glosso-laryngeal paraly-

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sis was quite marked, and his speech was almost unintelligible; at this time he was also unable to walk with his accustomed firmness, tiring easily.

I first observed him in May, 1877, when his condition was as follows: Unable to utter a word, could make simply a grunt, tongue immovable in floor of buccal cavity, a mass of furrows and wrinkles, and the seat of continuous fibrillary contractions; he has the remains of a harelip, a good deal of difficulty in swallowing, upper extremities and chest a skeleton, the muscular atrophy has become so great arms hang by his side quite flaccid and limp, no contracture present, fibrillary contractions wherever there is any muscular tissue left, lower extremities in good condition to inspection, patient can stand and walk but is easily fatigued, no anæsthesia, no rectal or vesical difficulty, the atrophied muscles are the seat of soreness, and when the muscles are pressed or stretched it causes discomfort and pain; what muscular tissue is left reacts normally to faradism; this condition advanced, and the lower extremities began to atrophy rapidly, and in the middle of August, 1877, he was unable to stand, and had to keep his bed; he existed in the most deplorable and helpless condition until September 27, 1877, when he died, evidently from exhaustion and the bulbar disease.

Post-mortem twelve hours after death. Unfortunately I had to make the examination in a great hurry. The spinal cord and the brain were the only parts examined by me. I regret not having been able to examine the peripheral nerves and the muscles. The pectoral muscle was the only one examined; to the naked eye it had a pale appearance, what was left of it; the cerebrum to the naked eye presented nothing abnormal; the spinal cord also showed nothing unusual when intact, but when transverse sections were made in it at various points previous to hardening, the grey matter was seen to be much more vascular than normal; the anterior nerves were apparently not diminished in size, but presented an unusual translucent appearance.

Histology. Specimens hardened in solution bichromate potassa; the cord was divided into fifteen segments of about equal length, and transverse sections made from each of these

segments; stained in carmine and extractum hæmatoxyli and mounted in Canada balsam after Lockhart Clark's method.

The cervical region was the point at which the disease began, and was examined first; here the morbid changes were of a very marked character; examination of the sections made from other regions (of the cord) soon showed that the changes which had taken place were identical throughout the cord, but differing in degree and in some minor respects, but differing in such a manner as to render important aid in the interpretation of some of the points in the pathological physiology of the case, and in the sequence of the pathological changes which are seen to be present. Two very decided pathologic changes are seen in the cord:

1st. Atrophy of the ganglion cells in the anterior horn.

2d. Sclerosis of the lateral columns.

The atrophy of the ganglion cells of the anterior horn in the cervical enlargement is very nearly complete. In almost every section nothing is to be seen but a very small mass of yellowish brown pigment, here and there, occupying the place of the cell. In only one section from this region did I find a cell in fair preservation; but without any processes, and containing a considerable amount of pigment, but having a nucleus and a fair amount of protoplasm around it sharply stained by the carmine.

In the dorsal region the cells are almost as much atrophied, but as you pass down to the lower dorsal region you find more and more cells in a fair degree of preservation; none, however, in a normal condition. In the lumbar region, the largest amount of cells are to be seen, and in some places the number is almost normal, but there is not one cell which has not been affected; the pigmentation, atrophy and the absence of processes are the characteristic changes in these cells; the pigmentation takes place in the body of the cell, usually at one edge, and encroaches upon the nucleus; the pigment is of a yellowish brown color; the atrophy of the processes appears to come about in an entirely different way, they become more and more translucent and attenuated, and at last melt away, from the distal end first, without any more positive change, and they refuse to take up the carmine; this method of disap-

pearance of the processes gives a peculiar appearance to the stump; it looks as if the process was cut off somewhat abruptly, not sufficiently so, however, but as to leave behind a vestige of the process, showing this peculiar translucent appearance, which, in some cells, contrasts very decidedly with the thick, sharply stained body of the cell; it would appear that all the processes do not undergo this mode of change, for occasionally there is to be seen in the grey matter of the anterior horn a few processes in fair condition, which evidently have been cut loose by the section knife; these, however, are very few.

The sclerosis of the lateral columns is most intense in the cervical enlargement, and becomes less so as we go down to the end of the cord; the accompanying wood-cuts show the distribution of the sclerosed area; it differs greatly in the different regions; the sclerosis is of a very light character throughout the cord; it is a very limited region in which the nerve tubes are much altered; the nerve tubes in the sclerosed region have simply become a little smaller, have a cloudy appearance and a tendency to run together, and a light granular material around them; the septa running between the nerve bundles are a trifle thicker, and, therefore, appear more numerous in this region, and take up the carmine staining very sharply, so that to the naked eye the sclerosed region appears more diseased than microscopic examination shows it to be in those sections; from the cervical enlargement quite a number of spider cells are to be seen, similar to those described by several authors in various pathological conditions of the nervous system, also by Dr. E. C. Seguin and myself in disseminated cerebro-spinal sclerosis;* but they are quite small; in the other regions there appears to be very little change in the neuroglia cells; there is an increase of blood-vessels in the diseased regions, grey as well as white matter; everywhere the blood-vessels appear normal. In the cervical region the central arteries are surrounded by, and their perivascular spaces distended with an opaque material which is

*"A Contribution to the Pathological Anatomy of Disseminated Cerebro-Spinal Sclerosis," Drs. E. C. Seguin, J. C. Shaw, and A. Van Derveer, JOURNAL OF NERVOUS AND MENTAL DISEASE, April, 1878.

lightly stained by hæmatoxylin, and which I take to be an exudated fluid of some kind, albuminous probably, and which has become coagulated; moreover, there is a cloudy appearance in the entire diseased area in this region, grey as well as white matter, and which is evidently due to an infiltration of the same kind of material; the question of its being a defect in the method of preparation was soon settled by making many sections in different ways, and the additional facts that in the same section those parts of the cord remaining normal were not in the least cloudy, and that the dorsal and lumbar regions prepared in the same way, did not present the same appearance. Sections made very near together, through the decussation and into the medulla, showed that the sclerosis extended into the anterior pyramids of the medulla; but the sclerosis became more and more light until, in sections made through the middle of the olivary bodies, it was a very difficult mat ter to tell if there was any sclerosis present; but after making a great number of sections through the decussation so as to find where the sclerosis ceased, and, after a most careful examination of all the specimens in their order, I was able to satisfy myself that there is a very slight sclerosis here, and that it has been growing less and less intense up to this region; but I was also able to determine that there is a slight sclerosis in this region (sections through middle of olivary bodies) in that part of the medulla which Meynert considers as belonging to the lateral columns of the cord (see Fig. 4, B), and that a very light fine strip extended from this down almost to the pyramids (see Fig. 4). Almost all the nerve cells in the nuclei of origin of nerves have suffered atrophy, the cells in the pneumogastric nucleus are wasted and indistinct, but the nucleus of the hypoglossus is where the disease is greatest, the cells have undergone extensive pigmentation and atrophy, not one nerve cell is to be seen with a process; the cells in the nucleus of the sixth and seventh nerves are in good condition.

Sections through the middle of pons and crura (left) shows nothing abnormal.

The pectoral muscle shows simple diminution in the size of the muscular fibrils, and nothing more.

The question immediately arises, what is the connection be-

tween the symptoms in this case and the pathologic changes found? Numerous cases have now been reported in support of the spinal origin of progressive muscular atrophy, and this case is an addition; this view we can now consider almost definitely settled; the myelitis of the anterior horn and disappearance of the ganglion cells explains the muscular atrophy; but as to the connection which the lateral sclerosis bears to the myelitis of the anterior horns and to the symptomatology we are still in doubt.

In recent years Prof. Charcot* has announced and taught that what has heretofore been called progressive muscular atrophy really comprehends two distinct diseases, having a special symptomatology and distinct pathological anatomy; a first form he calls progressive muscular atrophy protopathic (type Duchenne-Aran), a second form progressive muscular atrophy, deuteropathic or lateral amyotrophic sclerosis.

In the first form muscular atrophy is the first and predominant symptom, the disease lasts many years, and bulbar symptoms do not occur; myelitis of the anterior horns is the pathological condition; in the second form, first paralysis or paresis, then muscular atrophy and contracture, finally bulbar paralysis; the disease lasting about three years, with fatal termination; pathology, lateral sclerosis and secondary myelitis of the anterior horns.

Now what is my case, one of lateral amyotrophic sclerosis with bulbar paralysis?

Clinically, the contracture which Charcot appears to consider as constant is wanting, there is not even the least contracture in the hands, and the muscular atrophy here was certainly the first symptom; the rapidity of the case and the bulbar paralysis corresponds to the clinical picture given by Charcot of lateral amyotrophic sclerosis. Now, when we come to examine the cord there are what appear to be at first sight changes which place the case as one of lateral amyotrophic sclerosis, but a most careful study of the sections lead me to consder it otherwise.

These are my conclusions: the myelitis of the anterior horns (commencing in the cervical enlargement) was the primary lesion; the extent and severity of the lesion and the time of

**Archives de Physiologie*, 1875, and *Maladies du Systeme Nerveux*, Tome II.

appearance of the muscular atrophy lead me to this opinion; the lesion in the lower part of the cord and in the analogues of the anterior horns in the medulla was simply a matter of extension; the sclerosis of the lateral columns I look upon as entirely secondary, and rather as a form of secondary degeneration than a true sclerosis; I cannot conceive how a sclerosis of the lateral columns can exist for such a length of time (if it had been the primary lesion) and yet produce so slight an effect on the nerve tubes as was found to be the case here.

I have spoken of this condition of the lateral columns as sclerosis, because it has been so called by most observers, but to me this appears incorrect, for there certainly is a difference between this change and that which takes place in disseminated cerebro-spinal sclerosis, and to this latter condition would I restrict the word sclerosis as indicating peculiar, active, and primary changes in the neuroglia cells; the condition spoken of in this case is, as far as the neuroglia cells are concerned, comparatively a passive one, and resembles more the condition seen in so-called secondary degeneration due to primary brain lesion, where the nerve tubes appear to be the primary seat of trouble; the same appearance of the neuroglia cells is seen in the sclerosis of the posterior columns in locomotor ataxia, and is a different process from that in disseminated sclerosis.

The presence of contracture in these cases, as a symptom, which is always present and due to the sclerosis of the lateral columns, and which is one of the distinguishing points of this variety, as Charcot supposes, is certainly not correct. I have had the opportunity of seeing another case similar to this one which I describe (but in which I obtained no post-mortem). Here there was no contracture, and Prof. Leyden has recently recorded several cases* in which post-mortem showed, like my case, very light sclerosis of the lateral columns; contracture was absent in several of his cases. Leyden's cases, although beginning with bulbar symptoms, are evidently the same disease, having its origin in a different point of the cerebro-spinal axis.

* "Ueber progressive, amyotrophische Bulbarparalyse, etc." *Archiv fuer Psychiatrie und Nervenkrankheiten*, Band 8, heft 3.

The connection between the lesion in the grey matter and that in the lateral columns is one which has created much interest and some discussion. Charcot is the father of the view that in those cases which present the clinical history and symptomatology, as previously given, and in which microscopic examination has shown myelitis of the anterior horns and symmetrical lateral sclerosis, that the sclerosis is primary and the lesion of the anterior horn secondary. Upon this he has founded the disease, lateral amyotrophic sclerosis. This view of Charcot's has been pretty widely accepted, and recently Gombault* has published a monograph on the subject; it has, however, met with sharp criticism from many quarters, especially German neuropathologists. At this time it appears impossible to come to any very definite conclusion on the subject. Many more observations will have to be recorded before it is settled; this, however, is certain, that there are lesions of the grey anterior horns which will produce secondary lesions of the lateral columns. The idea that the lesion of the lateral columns is due to a bilateral lesion in the cerebrum is not confirmed, and appears, to say the least, rather doubtful. It is true, as Flechsig says, that the lesion is most intense in what he calls "Pyramidenbahnen" (at least it is so in my case), but it certainly is not equally intense throughout this bundle, but rather occupies the inner part of it; and the idea that the lesion shades off from this is to me incomprehensible, as the shading off, if it were so, goes almost entirely to the anterior white matter. The sclerosis being most intense in the cervical region, shows that it is not dependent upon lesion above the cord, and the fact that the sclerosis disappears in the medulla, supports this, and argues that it is dependent upon the myelitis of the anterior horn. I do not deny that there is a primary lateral sclerosis with secondary lesion of the anterior horns; but there are certainly cases running the course (about three years) having the symptomatology, bulbar paralysis, etc., of what Charcot calls lateral amyotrophic sclerosis, in which the symmetrical lateral sclerosis is not the primary lesion (my own and Leyden's cases).

Secondary changes are seen in the lateral white matter in

* *Etude sur le Sclerose laterale amyotrophique.* 1877.

Fig. 1

Fig. 2.

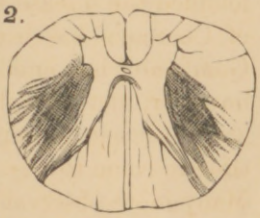


Fig. 3.

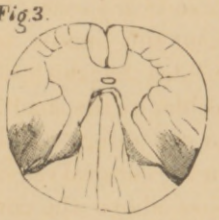
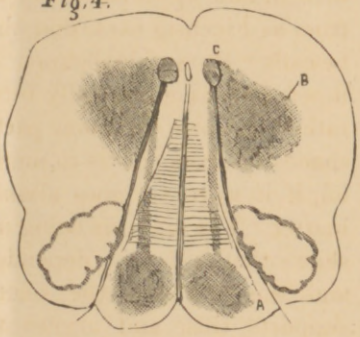


Fig. 4.



cases of infantile spinal paralysis in which the lesion is an acute myelitis of the anterior horns. No special attention appears to have been paid to this condition, nor has the question arisen why it is there. It must be said that Charcot states that he has never seen a case in which the myelitis of the anterior horns caused secondary degeneration of the lateral columns, but he does not appear to think that it is impossible.

One point appears to me of great importance in the microscopic examination of these cases, and that is a careful observation and record of the degree of change in the different regions (anterior horns and lateral columns). The conclusion from all this is evident, that the symptomatology and the interpretation of the pathological changes seen in the so-called lateral amyotrophic sclerosis of Charcot will have to undergo modifications, and cannot be considered so absolute as Charcot has laid it down.

Explanation of Wood-cuts.

The shaded regions indicate the sclerosis.

Fig. 1.—From cervical enlargement, showing distribution of sclerosis in lateral white matter.

Fig. 2.—From dorsal region ; it will be observed that the sclerosis does not occupy exactly the same region as in Fig. 1, but keeps very near to the posterior horn. In some sections from this region the sclerosis extended pretty well forward, and as far as the anterior border of the anterior horn, and keeping close to the grey matter.

Fig. 3.—From lumbar region. Here the sclerosis is very limited in extent and is well indicated by wood-cut.

Fig. 4.—From section through middle of olivary bodies; here the sclerosis is of an exceeding slight character. Fig. *a.*—Sclerosed anterior pyramid. Fig. *c.*—Nucleus of hypoglossus. Fig. *b.*—Sclerosed region in district which Meynert considers as belonging to the lateral regions of the spinal cord; also a light band of sclerosis extending from this down almost to the sclerosed anterior pyramid.