Charcot-Marie-Tooth Disease

The credit for discovering a "new disease" is often given not to the one who describes it first but to the one who describes it when the time is ripe. Thus, Virchow, Schultze, and others had reported cases of peripheral atrophy previously, but in 1869 medical knowledge had advanced sufficiently to accept this entity as a nosologic addition. The simultaneous publications by Charcot and Marie in France and by Tooth in England do not attest to coincidence but to the fact that the medical world was ready to appreciate this rare clinical distinction existing within the large group of progressive muscular atrophies.

Jean Martin Charcot and his pupil Pierre Marie studied the multitude of infirm and paralytic inmates at the Salpêtrière, as asylum in Paris, and left a scientific discipline where there had been a muddle. Their description of peripheral atrophy is only one of the many contributions of Charcot's school to our basic conceptions of the nervous diseases.

Howard H. Tooth, whose paper was a thesis for the MD degree at Cambridge University, was aware of the work by Charcot and Marie, which had been published earlier the same year. In a footnote he justified his own paper as follows: "Since this thesis has been commenced, and some months after the line, in which it was intended to work, had been laid down, there has appeared in the Revue de Médecine for Feb. 1869, a paper by MM. Charcot and Marie on the same subject, illustrated by five cases."

To Tooth belongs the credit for emphasizing the early atrophy of the peroneal muscles and introducing the term "peroneal type of progressive muscular atrophy." Tooth's description is otherwise similar to Charcot and Marie's, but the former author, referring to the postmortem examinations of others, including Virchow, proposed that the condition is a peripheral neuropathy, whereas Charcot and Marie favored the possibility of a myopathy. Subsequent autopsy studies have shown degenerative changes in peripheral nerves, thus confirming Tooth's idea. Degeneration seen in the dorsal columns may be secondary to involvement of the spinal nerve roots, but the possibility of a primary myopathy of the spinal cord cannot be completely excluded in certain cases (see the discussion by England and Denny Brown). The finding of decreased nerve conduction velocities in patients with Charcot-Marie-Tooth disease is further evidence of a peripheral neuropathy, and conduction studies may even be used to detect genetic carriers of the disease. The report of a primary myopathic change in this condition must be reconsidered in view of the demonstration that such changes in muscle biopsy specimens may occur in chronic degeneration.

Although Charcot-Marie-Tooth disease was described and families were described in which some members show the features of Friedrich's ataxia and some the features of peroneal atrophy,9 nevertheless, peroneal muscular atrophy is usually encountered as the pure character and specific form described by Charcot, Marie, and Tooth.

References

variations, we would have to admit that the extensors are generally reached after the hand muscles proper, and this especially for the extensor muscles of the long abductor of the thumb. As for the other muscles of the forearm, the pronators and supinators are affected much later. In all of our patients (especially Henri X \ldots&), we noticed a marked laxity of the adventitious articulations, allowing the foot to move freely in various directions. This laxity did not seem to be pronounced as in some cases of infantile atrophic paralysis. In a word, it is not completely "des vieilles ligaments."

Vasomotor disturbances are usually very intense in the affected parts, especially in the lower limbs. In all our patients the antero-posterior and medial portions presented a bluish or reddish coloration with widespread mottling. The general shape of the foot is slightly altered, not that it is improperly speaking, an edema or a volume augmentation, but the contours are less distinct, less well drawn. It looks somewhat like a foot that has remained some time in an immovable apparatus. We should also note that a few of our patients, especially the women, had considerable subcutaneous adiposity of the affected parts, completely analogous to that observed specifically by J. L. L. Landouzy in various cases of atrophic paralysis.

Finally, the temperature is much reduced in the affected limbs. A hand applied to the feet and legs presents a feeling of coldness. In all our patients, and especially in the women, this lowering of temperature is very clearly localized to the parts immediately above the knee, the shin, and the sole of the foot. In ordinary cases, these limbs are the least warm. This lowering of temperature is, as we said, considerable. In one of the women, the difference between the temperature of the mid-foot and the mid-leg was not less than 6° C. The vasomotor and trophic disturbances which described also exist in the hands, but incomparably less marked than in the lower limbs.

There is another phenomenon that is more or less painful but is evident in another type and manifests itself in a completely different way. We refer to cramps. They occurred in almost all of our patients with a characteristic frequency and intensity such that they never failed to attract our attention. These cramps appear preferentially in the thigh muscles, especially on brisk voluntary movement and on electrical stimulation and the movement of the thigh.
the thigh muscles as hypertrophied, although in our opinion this view is not exactly right. Foot-drop is present. There is little or no deviation of the foot when the patient is on the floor, but they place themselves in varus or valgus when they support the weight of the body. The calf-less legs are almost cylindrical, at the most slightly conical. The interosseus of the toes are prominent. When the legs are placed together in the correct position at the ankle, there is only slight atrophy of the muscles. Above and below, large empty spaces can be seen. The upper part comes from the flattening of the internal part of the thigh due to atrophy of the vastus internus. The lower part of the thigh above the patella is not in proportion with the upper part as a consequence of the greater atrophy at this level. Concerning the hands, it will suffice to recall, without wishing to repeat ourselves, that at a certain period they have the distinct appearance of the interosseous claw.

Moreover, the functional disturbances are not less characteristic. One finds a marked step-gait owing to the paralysis of the toe extensors. The step-gait is such that a similarity to the walk of a horse is very striking. Furthermore, even while resting in the standing position, the patient cannot stand in place and is constantly obliged to sit in order to maintain his balance. All these functional disorders are by far the most striking due to the atrophy of the leg muscles. Eventually the hip and knee articulations are no longer fixed, and the malposition is in a state of pronounced instability with respect to the foot. Balance is compromised and cannot be maintained only by moving the whole leg into a more suitable position. Thus, one sees that the comparison with stilted walks naturally comes to mind and which Eulenburg has already made. It is not exact since it is not the poor function of the knee but the hip and knee articulations that are the main cause of these functional disturbances. It is for the same reason that the case becomes more difficult for those patients who have no visible hip and knee articulations that prevent them from leaning forward.

So far we have dealt with the symptomatology of this affection. We have still to discuss its onset and progression.

The onset is usually in childhood or adolescence. This has been true in the five cases we observed. Among the 19 cases that we could gather from other authors, the disease appeared before age 22. During childhood, it is especially likely to appear at the age of 4 years; during adolescence at 15 or 16. In one of Eichhorn's cases (Ernest) it was perhaps congenital. It seems, though, that it can appear later. One of Eichhorn's patients was 36, and two members of the Wetterbee family were stricken at the age of 39.

Another important fact concerning etiology is the influence of heredity. It is found in all the cases of the various authors. The patients of Eulenburg are twin brothers; ten members of the family studied by Eichhorn had the affection, seven of them being distant ancestors; in the Wetterbee family the great-grandfather, his two sons, his two daughters, his second son's children, and his first son's children were equally affected.

From the preceding, it is evident that hereditary influence is indispensable and that, in some cases, the disease has the distinct appearance of a familial malady.

Is it always so? From the facts we have observed, we can confidently answer: no. In our cases I, IV, V, none of the members of the family was affected, and we could verify this in others in the same way. Of course, it cannot be asserted that it will not begin later in some of them, but, in the ancestors at least, it is certain that nothing similar occurred. On the other hand, it is true that a distinct familial factor was found in our cases II and III, which were both brothers. Henri and Gonzalo X. We may add that their 5-year-old sister is still completely normal, as we ascertained by a thorough examination.

We conclude that a familial factor, although very evident in a large number of cases, is missing in others and that even in families where several members are stricken, others are completely spared. This is a fact already noted in the cases of Eichhorn and Eulenburg. Can we say that the girls are affected less often than the boys? The facts do not seem to be numerous enough to allow a definite statement.

Concerning the cause of this distress, we know nothing for certain. Neuropathic heredity in its largest sense seems to deserve some attention here. For example, the father of our patients Henri and Gonzalo X... while not present any muscular atrophy, was so affected mentally that he was placed in a mental hospital.

There is still the matter left of the nature of this affection. In the absence of an autopsy it is impossible to ascertain anything on this subject. However, we have reviewed all the cases available in the literature, arrived at hypotheses, some of which are at least at least probable. In the presence of muscular atrophy having the appearance of a familial disease, occurring during childhood or adolescence, and having a slowly progressive course one can and must ask if it is not a myopathy.

We do not think this is the case here, for the following reasons. All that we know about the localization of the affected muscles is simple progressive atrophy: it is completely contrary to what exists in the disease we are studying. In the former it always starts either in the trunk muscles or in the proximal muscles of the limbs. In the latter, on the contrary, it always starts in the muscles of the distal extremities (feet, legs, later the lower part of the thigh muscles, the intrinsic hand muscles), and the trunk muscles are not affected. This is a clinical fact of great importance. The two diseases are therefore completely different in localization, and it could almost be said that one attacks those muscles which the other spares. The Leyer-Mobilis form seems to be the first to come close to our cases because of the predominance of atrophy in the lower limbs. However, after careful examination, this form is seen to be much further from our cases than from the different forms of simple progressive myopathy. Moreover, our patients show some signs that are in contradiction to the way in which we meet in myopathy. Definite fibrillary contractions occur, which are never found in the latter. Also, there is a reaction of regeneration, whereas in the latter there is only a diminution of elasticity without alteration of the formula.

It seems to us that these are serious arguments against the idiocy or at least the similarity of these two diseases. As the hereditary character of the disease is well to remember that this is not peculiar to myopathies and that it can be present in diseases of an established myopathological nature. This occurs:


2. Eichhorn's method and Osgood's cases, considered them myopathic and classified them in the first line of myopathic atrophies at Eichhorn's familial type. This point of view still seems to be the best interpretation of symptomatology and of evolution reported by Eichhorn as well as by the hereditary character of the affection. We explained above why the examination of cases at the Salpetriere does not allow us to accept the nongenic interpretation proposed by Menet and Lamy. Apparently, and in the opinion of the present editor, the word "myopathic" is a term inadequate to characterize the clinical aspects of this affection in which the alteration of the muscular musculature is at once, quite secondary, while the second of the two factors, muscular atrophy, is the more primary one. We also think that the name of Eichhorn should not be retained, since Eichhorn's observation preceded Eichhorn's by 17 years and is not definite in the study of the atrophied cases. Moreover, the idea of heredity is also mentioned by Eulenburg for example, in the hereditary ataxia of Friedrich, which we know, is a familial disease associated with very gross lesions of the cord.

Are we therefore, in the presence of a myopathy? Is it a peripheral polyneuritis? Here, we must confess, the question becomes much more difficult. Especially in the presence of the cases where there is no pain or various sensory disturbances. Up to a certain point the hypothesis of a myopathy appears preferable to us, but it seems difficult to make an absolute statement.

From the thought it would be of some interest to gather similar cases from the medical literature. It will be seen that all these are similar to ours and in reality concern the same disease. It is quite strange that none of the authors who observed these patients has described them objectively and completely. Most of them noted only one aspect of the matter, especially heredity. Considering the rarity of publication, it is readily understandable that Eichhorn considered his patients simply an example of hereditary progressive muscular atrophy, as did Eulenburg and Hammond. It has, therefore, been necessary to affirm the existence of this clinical entity and to give a complete description of the disease, since no author had yet done so. This has been our aim.

To maintain all the documentation of this work, the present characterization of a form of muscular atrophy that we have attempted to isolate and describe themselves the following:

Progressive muscular atrophy, first invading the trunk and then the extremities in the upper limbs (hands first, then forearms) several years later; thus, slow evolution.

Relative integrity of the proximal muscles of the limbs, and at least much longer preservation than the distal muscles. Integrity of the muscles of the trunk, shoulders, and face.

Existence of fibrillary contractions in the muscles undergoing atrophy.

Vacuum disturbances in the affected segments of limbs.

No notable tendon contractions on the side of articulations where the muscles are atrophied. Scoliosis is present, but at least in altered in various ways.

Frequency of cramps.

Reaction of degeneration in the muscles undergoing atrophy.

Beginning of the disease usually during childhood, often among several brothers and sisters; sometimes it exists not only in collateral relatives but also in the forebears.