ARGYROPHILE BODIES IN THE HUMAN SPINAL CORD

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Certain argyrophile bodies have been found in the adult human spinal cord which do not seem to have been described before. These bodies occur mainly in the anterior horns of the lumbosacral region, and they have been found in every case of a large series of patients dying from a variety of conditions.

The purpose of this paper is to describe and illustrate these argyrophile bodies, to discuss their significance, and, especially, to consider whether they are artefacts or whether they are pathological or anatomical structures.

Material and Method

Over 80 spinal cords were examined. In 40, the patients had undergone the operation of antero-lateral chordotomy to relieve the pain of cancer not involving the central nervous system. The other cases had been collected at random from necropsy material in a general hospital to form a control group. In this group there had been no operation on the spinal cord; these patients had the following conditions at the time of death: myasthenia gravis, peritonitis, Parkinson's disease, uraemia, alcoholism, pulmonary tuberculosis, and malignant disease; one young man died as the result of an accident.

The argyrophile bodies which are to be described were found in all 80 cords examined; that is to say they were present in all the control group as well as all the cords from patients who had had chordotomy.

All descriptions in this paper refer to every cord examined. The ages of the patients varied from 20 to 84 years, with the majority in the 50 to 70 year group. The length of the illness varied from a few hours to several years; in one case (accident) there was no illness before death. The interval between death and necropsy varied from one hour to three days.

Sections were examined from all segments of each cord in the chordotomy series and from representative segments in the control series. In all cases celloidin sections, and in some cases paraffin sections also, were prepared. The staining methods used were haematoxylin and eosin, haematoxylin and van Gieson's method, thionin, Anderson's Victoria blue, Holzer's method, Mallory's phosphotungstic acid haematoxylin, Gros-Bielschowsky's silver impregnation, Loyez's myelin

stain; in adjacent blocks in most cases Weigert-Pal and Marchi preparations were also made.

Results

In every case, in the silver preparations of the lumbar and sacral segments numerous rounded argyrophile bodies are present (Figs. 1 and 2). The great majority of them are in a definite group lying in the anterior part of the anterior horn; a very few are also scattered about the anterior and posterior horns in some cords. The anterior group in the lumbosacral cord lies close to the white matter, medial to the antero-lateral column of motor cells, in a region where there are few large neurons but many axons of motor cells. This site is shown in Figs. 1 and 2. The number of silver bodies in a transverse section varies from segment to segment and from case to case. They are present from the first lumbar to the third sacral segment; the largest number of bodies usually occurs in the third or fourth lumbar and the second sacral segments, where there are from eight to 60 in a section, while there may be only four or five of them at the other levels. A very few are also present in a similar site in the lower cervical segments.

The bodies are rounded or pear-shaped, and in many a "stalk" can be seen at one pole. They lie among the axons. Whether they are attached to the axons or not could not be determined in longitudinal or transverse sections, for the dimensions of the bodies are such that it is difficult to obtain all parts of the body in one plane of section. It looks as though some are attached to the axons, but the majority appear to be free (see Figs. 3 to 5). The stalk itself is usually of lesser diameter than the large axons, but in some instances a thicker stalk is present. The bodies have the same appearance in transverse and longitudinal sections.

The greatest diameter of the bodies varies between 5 and 30 μ ; in the majority it measures 14 to 20 μ .

Allowing for the difference in sections after celloidin and paraffin embedding, the bodies have the same appearance in both preparations, and are

FIG. 1

similar after impregnation by the Gros-Bielschowsky or the Holmes method. No abnormality in any section stained by the other methods could be detected, other than those clearly associated with the chordotomy.

Discussion

Are Argyrophile Bodies Artefacts?—It is now necessary to consider whether these argyrophile bodies are artefacts, and, if so, what are the possible factors involved.

FIG. 2

Delay before Fixation.—The bodies were found in all the spinal cords examined. The interval between death and fixation of the cords varied from one hour to three days. This range would appear to eliminate the possibility of this interval being a factor in the production of the bodies. No correlation between the number of argyrophile bodies in a case and the duration between death and fixation could be established.

Trauma at Necropsy.—The bodies have the same staining reactions as axons. In view of this it would seem likely that, if they are the result of trauma, they represent damage to axons.

All the material, including the control group, is part of a planned investigation on the central nervous

system, entailing the examination of the entire cord and brain for histological changes associated with the operation of chordotomy. For this reason care was taken at necropsy to avoid any trauma to the cord or nerve roots which might complicate interpretation of the histological appearances.

In some cases the cord was removed unfixed, and then fixed in 20% formol-saline. In others it was fixed *in situ* by the injection of 20% formol-saline into the cisterna magna, while cerebrospinal fluid was drained by lumbar puncture. The cord was removed 24 hours later. No more tension was exerted on the lumbosacral anterior nerve roots than on those of any other part of the cord, or on the cranial nerves. A very few argyrophile bodies were found in the cervical cord, but none in the cranial nerves or brain, even in association with nerves subjected

FIG. 1.—Low-power view ($\times 40$) of anterior horn of L.3 in transverse section, showing concentration of argyrophile bodies in antero-medial region.

FIG. 2.—Low-power view ($\times 40$) of sagittal section of L.3 showing distribution of argyrophile bodies between white matter and longitudinal column of motor neurons.

FIG. 3.—Argyrophile bodies in transverse section of S.1 ($\times 110$).

FIG. 4.—Higher power view of Fig. 2 ($\times 110$).

FIG. 5.—Argyrophile bodies in transverse section of L.3 lying among axons ($\times 325$). In some a "stalk" appears to be present.

All photographs are from Gros-Bielschowsky preparations. Figs. 1, 2, and 4 are counterstained with thionin.

to a fair degree of inevitable tension at necropsy.

Further evidence regarding the absence of trauma to the lumbosacral nerve roots comes from the Marchi preparations from the same region of the cord. In nerve fibres subjected to post-mortem trauma a pseudo-Marchi reaction is constantly found. No such staining was ever observed in the area occupied by the argyrophile bodies, although there might be a marked degree of it in other parts of the central nervous system in the same case. If the myelin sheaths should show a reaction to pulling and other trauma it would seem probable that if any axons were damaged it would be those associated with the damaged myelin.

It would then appear to be unlikely that the bodies resulted from any post-mortem trauma of an avoidable nature.

Silver Impregnation Artefacts.—Artefacts may occur in sections prepared by silver impregnation methods, but not in all cases in a constant distribution, nor do they have the same appearance as the argyrophile bodies.

Silver impregnation artefacts occur in the form of a scattered dust of small angulated particles throughout the section, giving a dirty appearance to the whole preparation, and obscuring the picture of the axons; or they may be larger and concentrated intensely in one area, forming a dense black

FIG. 4

spot. Both forms are completely unlike the bodies described here.

Corpora Amylacea.—Corpora amylacea, in silver preparations, might be confused with the bodies, but their concentration in the white matter, their constant spherical appearance and free state, and their affinity for other stains render them clearly distinct.

FIG. 3

FIG. 5

Peculiarity in Impregnation Technique.—The possibility that the bodies represent a peculiarity of the impregnation technique is unlikely in view of the similar appearance they have in Gros-Bielschowsky and Holmes preparations. It may be noted also in this context that the appearance of these bodies was identical in sections prepared by different technicians.

No evidence in favour of regarding the argyrophile bodies as being artefacts has been obtained. Nevertheless, their affinity for the same stains as axons does suggest a relationship between them, and it is still considered possible that the bodies do represent some post-mortem alteration in certain axons, the cause of which has not been found.

Are these Bodies Pathological?—The cause of death in the cases examined was varied. In about three-quarters of the cases cancer was a contributory final factor, but in the remaining cases death was due to other causes. The length of the final illness varied from no time at all (accident) to many months; the general health of the patient at the time of death, and the degree of cachexia, if any, were also widely varied.

In the light of these facts it is difficult to see how structures of such a constant appearance and distribution could be caused by widely varied pathological conditions, in particular as they were found in every single case of a series, of which half were collected at random from the necropsy material in a general hospital.

When a nerve fibre is cut, or its continuity is otherwise interrupted, the central end of the axis cylinder forms a retraction ball. The argyrophile bodies described here undoubtedly resemble to some extent these retraction balls. But the absence of any other appearance suggesting a degeneration of axons, of myelin sheaths, or of neurons, at this site, would make it very unlikely that these

argyrophile bodies do in fact indicate a lesion of axons.

It would appear then that the bodies are not pathological in nature, or, at least, are not consequent on a specific pathological condition.

Are they Anatomical?—The argyrophile bodies have been found in every single cord of the large series examined; they have also been seen in sections picked out at random from the silver preparations in three other laboratories. In all the cases they are localized to a limited region of grey matter of certain lumbosacral segments. This constant occurrence and restricted localization appear to support the view that the bodies are anatomical structures. The possibility that they are associated with the processes of ageing in the cord has been considered, but as they have been found in the cord of a healthy young man of 20 years this seems unlikely.

Conclusions

A discrete column of argyrophile bodies is present in the lumbosacral region in every cord examined from a series of 80 patients dying from a variety of pathological conditions.

These argyrophile bodies do not appear to be associated with any pathological process. The bodies stain in the same way as axons and lie among axons, and are therefore thought to be in some way related to them. Their constant occurrence may indicate that they are anatomical structures. There is no evidence that they are artefacts, nevertheless the possibility that they represent some post-mortem alteration in axons, probably of an unavoidable nature, has not been wholly excluded.

Unless it is recognized that these argyrophile bodies are a constant feature of adult human cords, their resemblance to the retraction balls seen after section of axons might lead to the misinterpretation that they indicate a lesion of axons.