ARACHNOIDAL PROLIFERATION AND CYSTIC FORMATION IN THE SPINAL NERVE-ROOT POUCHES OF MAN

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(Received for publication October 10, 1957)

In preliminary communications in 1947 and 1949 Rexed\textsuperscript{12,13} described certain pathological changes in human nerve-root pouches. The lesion consists of pathological thickening and proliferation of the arachnoidea, in extreme cases deforming and compressing the nerve roots, and often associated with cystic formations in and about the root bundles. The lesion is common, and is not associated with syphilis, tuberculosis, or other specific infections involving the central nervous system. By means of roentgenological studies on cadavers, Lindblom\textsuperscript{7} in 1948 confirmed Rexed's observations, and demonstrated the cysts as round filling defects in the contrast medium in the root pouch. In these cases there was no communication between the cystic cavity and the subarachnoid space. Arnell\textsuperscript{2} described certain roentgenological changes noted during clinical myelography, which he related to the findings of Rexed. He did not examine the preparations histologically.

A variety of changes of the root pouches have been described in the literature. Pathological proliferations of the membranes associated with cystic formations have been noted in and about the nerve roots in acute and chronic meningeal infections such as tabes dorsalis\textsuperscript{11} and tuberculous meningitis.\textsuperscript{20} In his work on the pathology of the spinal ganglion, Marburg\textsuperscript{9} described cystic changes in the spinal ganglion, which he interpreted as sequelae of haemorrhage. He noted, however, that the arachnoidea in the distal part of the root pouch was sometimes thickened and hypertrophied, "dass es den Anschein einer tumorartigen Wucherung gewinnt." He did not relate this arachnoidal proliferation to the cystic formation, possibly because he did not make serial sections of the nerve roots from the spinal ganglion and proximal to it. Hinrichs\textsuperscript{6} described a case of multiple cysts in the spinal nerve roots, in which there was also proliferation of the enveloping membranes. Tarlov described during the period 1938–1952\textsuperscript{17–19} macroscopical cysts in the region of the sacral root pouches, which he called "perineurial cysts." He observed no concomitant proliferation of the arachnoidea. It has been shown by Tarlov\textsuperscript{18,19} and others\textsuperscript{1,4,10,12} that such cystic formations are capable of producing clinical signs of compression. In some cases cysts have been demonstrated by myelography.\textsuperscript{1,4,10,15}

The present work is devoted to a comprehensive study of the incidence and distribution of arachnoidal proliferations and cystic formations in the
spinal root pouches. The changes are examined in relation to the age of the patient, and it is established whether they are confined to isolated pouches or whether they involve the whole spine. The investigation is so far restricted to the lumbar and sacral regions, but it is intended to examine and compare all regions of the spine, and to correlate the roentgenological findings with the histological changes.

MATERIAL

The material consists of 26 lumbar spines from D12 to S2, with nerve roots, ganglia, and part of the spinal nerve removed in one piece with the dura mater. The preparations were obtained shortly after death, and were fixed in 10 per cent formaldehyde. The spinal root, ganglion, and part of the spinal nerve were sectioned serially, and stained by the Alzheimer-Mann-Häggquist technique (AMH). In some cases Bodian's silver technique was employed, occasionally in conjunction with azan or haematoxylin-Weigert-Hansen staining. In some cases only a few roots were examined, but where pathological changes were present most of the roots round the inferior part of the cord were sectioned serially. A total of 176 spinal nerve roots from 26 cases were examined. The subjects were aged 27–82 years, and had been selected at random from the necropsy material available. Death had been caused by a variety of diseases, only a very few involving the central nervous system. In one case the cause of death was acute tuberculous meningitis, but in none other was there any sign of infection of the brain, spinal cord, or meninges.

RESULTS

Normally the spinal nerve roots, as they enter the foramen intervertebrale, are enveloped by a sheath of dura mater which distally approaches the roots and then becomes continuous with the perineurial tissue of the root bundles immediately proximal to the ganglion. In this way the dural root pouches are formed. The spinal roots lie in this pouch and are surrounded by arachnoidea, which ordinarily forms a thin covering, and which also is connected distally with the perineurial tissue (Fig. 1). Between the root and the arachnoidea is an empty space, narrowing distally, which communicates with the subarachnoid space.

In many cases this normal picture is changed. The arachnoidal tissue is thickened, in some cases only slightly, without producing compression of the root bundles, but in others with great proliferation and marked compression of the roots (Figs. 2B and 5). The arachnoidea is sometimes seen invading the roots, or penetrating parts of the dura mater (Fig. 7). Occasionally the entire dural pouch may be dilated by the proliferative process. Cyst-like cavities may appear in the proliferated arachnoidea. In other cases the proliferation may appear proximally, gradually lessening distally, to be replaced finally by cystic formations (Fig. 2A and D). In a fair number of cases cysts appear even in slight degrees of arachnoidal proliferation. The relatively thin arachnoidea is sometimes split into several layers, between
which cavities may develop (Fig. 6). It is difficult, in these sections, to establish whether the cysts communicate with the rest of the subarachnoid space, but in most of them this would not appear to be the case.

The cysts vary in size, the largest having a diameter of 3 mm. and being visible to the naked eye. When the cysts are very small, several often can be detected in the same section, and they are not seen to communicate with each other. The cysts may appear as a widening of the subarachnoid space, with the normal root bundles at the centre; the spinal nerve roots may be greatly compressed and constitute only a thin lining; or the cysts may develop intrafascicularly, and separate the nerve fibres; finally cysts may de-

**Fig. 1.** (Above) Diagram of a nerve root as it penetrates the surrounding normal meninges. (Below) Transverse section at distal end of root pouch, which here is very narrow and covered with thin arachnoid and dura mater. The meninges about the upper ventral root have partially changed to perineurium. (AMH stain. S3/42, L4 left, X19)
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Fig. 3. Large intraganglionic cyst. The nerve tissue forms a thin covering about the cyst, and the whole is enclosed by the tense perineurium. (AMH stain. S63/42, L1 left, ×16)

velop within the dura mater. The cystic formations sometimes extend distally, and continue as far as the beginning of the ganglion. Some penetrate into the ganglion, and they may even extend right through it. The cavities are, in the microscopical sections, empty, but sometimes may be filled, wholly or partially, with loose arachnoidal tissue. The wall is made up of thin endothelium-like tissue, surrounded by the dura mater, the spinal root tissue or the ganglion tissue. In the case of large cysts the dura mater is very thin and stretched (Fig. 3). Vessels from the spinal root or the dural wall often are seen lying along the wall of the cyst and sometimes even ramifying on it. Occasionally the dura mater is found to be thickened, in association with the arachnoidal proliferation, and to show hyaline degeneration, and these changes may dominate the picture (Fig. 8).

The changes are limited entirely to the region in which the meninges of the root pouch approach the spinal nerves, and eventually form their perineurium. In pronounced cases the cysts may penetrate the ganglion, partially or completely (Figs. 4, 5 and 6). The spinal nerve roots proximal to the wall of the great dural pouch and the spinal nerves peripheral to the ganglion appear quite normal. In only a few cases, where there is extreme compression,

Fig. 3. (A) Diagram of a nerve root as it penetrates meninges in which there is arachnoidal proliferation. B, C and D indicate positions of following sections. (B) Transverse section at proximal end of the root pouch. The arachnoid is markedly proliferated. (C) Transverse section more distally, The ventral root is dilated. (D) Transverse section through the ganglion, at the site of a large subarachnoid cyst, which is compressing the nerve severely. (AMH stain. S63/42, L2 right; B × 19, C × 19, D × 13)
can degeneration of the nerve fibres be detected. There is no correlation with lateral disk compressions. No collections of granulocytes or lymphocytes, as a sign of active infection, can be noted.

The changes involve both dorsal and ventral roots. They are less marked in the ventral roots, however, where they commence and end more proximally than similar changes in the dorsal roots.
Several nerve roots were sectioned serially in a considerable number of cases, in order to get some idea of the distribution of the lesions. The findings are shown in the following summary of the cases examined.

No. S06/42. Woman of 27. Pulmonary tuberculosis. No meningeal changes or changes in the neural root tissue were seen.


No. K346/41. Man of 31. Subarachnoid haemorrhage. Slight arachnoidal proliferation in all roots, particularly the more caudal roots. Recent haemorrhage into the root pouches was also seen, and most strikingly in the more caudal ones. In S1, right, the haemorrhage infiltrated both dura mater and nerve bundles, and continued some distance into the ganglion.


No. S69/42. Man of 44. Cardiac insufficiency. No changes in spinal root pouches.


No. K71/42. Man of 45. Pneumonia. Slight arachnoidal proliferation in isolated nerve roots. No cyst formation was seen.

Fig. 7. Arachnoidal proliferation penetrating part of the dura mater.
(AMH stain, S846/41, S1 left, ×74)

Fig. 8. Transverse section of a diseased nerve root in which the thickening and hyalinization of the dura mater predominate over the arachnoidal proliferation. (AMH stain, S63/42, S2 left, ×19)
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No. S51/42. Man of 54. Endocarditis. Slight arachnoidal proliferation in isolated nerve roots. No cyst formation was seen.

No. S38/42. Man of 55. Pulmonary tuberculosis. No changes were seen in most roots. In S1, left, there was slight arachnoidal proliferation with formation of small cysts which compressed the nerve root bundles slightly.


No. S325/41. Woman of 61. Cerebral haemorrhage. Recent haemorrhage into the root pouches increasing distally and infiltrating the meninges, nerve roots and part of the ganglion (where the haemorrhage formed a sharp contrast with the normal nerve tissue). Marked degeneration of the infiltrated nerve fibres. No arachnoidal proliferation was seen.

No. K79/42. Man of 62. Pneumonia. Abundant inflammatory cells (chiefly polymorphonuclear) beneath the arachnoid, lying in a fibrous network and infiltrating dura mater and nerve roots. Slight arachnoidal proliferation was seen in only a single root pouch.

No. S63/42. Woman of 63. Arteriosclerosis. Very marked arachnoidal proliferation, cystic formation and compression of nerve fibres in all roots but most striking in the upper lumbar nerve roots.


No. S73/42. Man of 66. Arteriosclerosis. Slight arachnoidal proliferation in all roots with small cysts in some.

No. K81/42. Man of 66. Arteriosclerosis. Slight arachnoidal proliferation in almost all roots. No cystic formation was seen.

No. K83/42. Man of 67. Arteriosclerosis. Slight arachnoidal proliferation in all roots with formation of small cysts. In some roots the cysts were larger and compressed nerve root bundles.

No. K86/42. Man of 67. Sarcoma. In some roots no changes were seen; others showed slight arachnoidal proliferation, cystic formation and compression of nerve fibres.

No. K224/43. Woman of 67. Marked arachnoidal proliferation in all roots, and in some roots formation of small cysts with compression of nerve root bundles.


No. K58/42. Man of 72. Carcinoma of penis. Slight arachnoidal proliferation in all roots with formation of small cysts. In some roots these cysts were very large and compressed the nerve root bundles markedly.

No. S80/42. Woman of 72. Pulmonary tuberculosis and acute tuberculous meningitis. In all roots very marked arachnoidal proliferation, cystic formation and compression of nerve fibres. No signs of acute inflammation.

No. S54/42. Woman of 75. Cerebral glioma. Slight arachnoidal proliferation in some roots. No cystic formations were seen.

No. K75/42. Man of 82. Carcinoma of oesophagus. Marked arachnoidal proliferation in all roots and also small cystic formations.

Of the series of 26 cases, in 10 there were changes in the form of arachnoidal proliferation and cystic formation (cases in which there were only slight changes are not included amongst these). Arachnoidal proliferation was commoner than cystic formation, and cysts were never present without
concomitant involvement of the arachnoidea, even though the two types of change were not always of the same degree of severity. In isolated cases the arachnoidea surrounding a single nerve root was thickened and proliferated, whereas the meninges enveloping the other nerve roots from the same spinal cord were normal. In most cases, however, the changes were closely similar in all spinal roots on both sides of the cord; but, with a few exceptions, an increase was noted in the segment L5-S2 compared with D12-L3. No difference in sex incidence was noted.

Positive findings were commoner among the older subjects, but were also found among the younger ones. The youngest subject in the present series showing marked changes was 31 years old; the oldest showing no changes was 68 years old; and slight changes only were noted in a woman aged 75 years. Increased fibrosis within the nerve roots and a tendency to subdivision of them into several smaller fasciculi was a constant finding among the older subjects. The perineurial tissue, both arachnoidea and dura mater, was commonly very thin, however, in these subjects and showed atrophic changes, in contrast to the marked hypertrophy of the arachnoidea described earlier. The older subjects commonly showed degenerative vascular lesions, but no difference between the vascular changes in subjects with and without proliferation of the arachnoidea could be seen.

DISCUSSION

The proliferation of the arachnoidea always precedes the development of cystic formations in root pouches and ganglia. In the series now presented, arachnoidal changes were commoner than cysts, and cysts were never present in the absence of the arachnoidal lesion. The cysts may be said to form as a result of proliferation of the arachnoidea with subsequent shutting off of part of the normal subarachnoid space, or to be caused by adhesions of two or more laminae of the arachnoidea with the formation of a cavity between them. The cyst would then increase in size as a result of transudation from the small vessels in its "wall."

The changes in the meninges are not confined to the arachnoidea, however. The dura mater is often involved because of penetration by the arachnoidea, by which it is disjoined; secondary cystic formation may then take place. This condition is reminiscent of the extradural cysts communicating with the subarachnoid space, described in the literature and ascribed to congenital herniation of the arachnoidea through the dura mater. These small intradural arachnoidal processes have sometimes been interpreted as spinal arachnoid villi or pacchionian bodies. Such formations have not been encountered regularly in the present investigation in cases in which the arachnoidea was otherwise normal. Hassin suggested that the intradural processes of the arachnoidea might be a feature of aging.

Proliferation of the arachnoidea about the spinal nerve roots is clearly very common. Aetio logically it may be, (1) a change caused by aging or by degenerative processes, or (2) a reaction to irritation, especially inflammation, of the meninges.
(1) Arachnoidal proliferation is commoner in older subjects, but the changes cannot be caused exclusively by aging since they have been encountered in young subjects, and are not always present in the elderly. Furthermore, there is a great difference between the almost atrophic picture seen in certain older subjects and the hypertrophic form of arachnoidal proliferation that occurs in others. Nor can the incidence of degenerative vascular changes among the elderly explain the meningeal changes.

(2) Tuberculosis, syphilis and other infections involving the central nervous system can be excluded as sole causes of the meningeal lesions described. No signs of acute inflammation and no accumulations of cells were noted. However, the general resemblance to lesions of tuberculosis and syphilis occurring in this region, and the involvement of all the spinal nerve roots, at any rate in the lumbar region, would indicate that the basic stimulus in the cases described in this paper also is inflammatory, although it is milder and perhaps also more chronic. Mild infections, even if subclinical, might well provide the stimulus. The region where the meninges turn into perineurium may be a "locus minoris resistentiae" to such stimuli. There was no previous history of meningeal infection in any of the cases now examined. Veith also has shown that inflammatory changes in the distal part of the spinal nerve roots are not unusual.

There may be other causes of meningeal irritation, such as sedimentation of blood cells after a subarachnoid haemorrhage.* Extrameningeal irritation, such as disk herniation, might be capable of causing local changes in a single nerve root, but would not explain the widespread distribution of such changes.8

In none of the cases reported was there a previous history of "back-ache," but in some of these, it would seem improbable, judging from the extent of the lesions, that clinical symptoms can have been absent entirely. The cystic formations described by Tarlov and others gave rise to marked clinical signs of nerve compression. The fact that the lesions are as common as the material of this investigation shows, justifies a discussion as to whether such changes may not in many cases constitute a feature of the lumbago-sciatica syndrome.

The lesions described are fundamentally similar to the changes occurring in tuberculous meningitis and syphilis, but are less pronounced. Marburg's "ganglion cysts" would seem to be identical with the cystic formations encountered in this work; but, since Marburg did not section the nerve roots serially, he was unable to establish the relationship between the arachnoidal proliferation and the root-pouch cysts. Tarlov's "perineurial cysts" are very probably macroscopical variants of the cystic formations described here. The fact that Tarlov did not observe any arachnoidal changes may be because those lesions were less striking in relation to the macroscopical cysts.

* Tarlov has attributed cystic formations to subarachnoid haemorrhage. Two of the cases of this series show a similar picture, with recent haemorrhage infiltrating the dura mater, arachnoidea and nerve roots as well as ganglia of the inferior spinal nerves.
In a study of human lumbar and sacral nerve-root pouches, meningeal changes were encountered in the form of arachnoidal proliferation often combined with cystic formations in and about the nerve roots and spinal ganglia. These lesions are common, and are present in 10 of a series of 26 cases selected at random. They are usually widespread, and in any one case are of the same degree of severity in all roots involved, on either side of the spinal cord. They are commoner among the elderly, but are also encountered in younger subjects, and are not to be regarded as changes caused by aging or as expressions of degenerative processes. They are fundamentally similar to the lesions of tuberculosis and syphilis, and are probably caused by some irritative, chiefly inflammatory, process in the meninges.

REFERENCES


