Stenosis of central canal of spinal cord in man: incidence and pathological findings in 232 autopsy cases

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The central canal of the spinal cord is generally regarded as a vestigial structure that is obliterated after birth in 70% to 80% of the general population. This report describes the first detailed histological study of the human central canal in 232 subjects ranging in age from 6 weeks' gestation to 92 years. Whole spinal cords were harvested at autopsy and sectioned serially from the conus medullaris to the upper medulla. Histological findings and morphometric analysis of the cross-sectional luminal area were used to grade stenosis at seven levels of the canal. Varying grades of stenosis were present at one or more levels in none (0%) of 60 fetuses, one (3%) of 34 infants, three (18%) of 17 children, 21 (88%) of 24 adolescents and young adults, 67 (96%) of 70 middle-aged adults, and all 27 adults aged 65 years or older (100%). The stenotic process was most pronounced in the thoracic segments of the canal and involved more levels with higher grades of stenosis in older individuals. Histological findings consisted of disorganization of the ependymal epithelium, formation of ependymal rosettes or microcanals, proliferation of subependymal gliovascular buds, and intracanalicular gliosis. These features are consistent with a pathological lesion involving ependymal injury and scarring and are less compatible with an involutional or degenerative process. Stenosis of the central canal probably influences the anatomical features of syringomyelia and may account for variations in cavity formation such as the prevalence of holocord syrinxes in children, the formation of focal and paracentral syrinxes in adults, and the rare incidence of syrinx formation in many older individuals with acquired lesions known to produce syringomyelia.

Key Words • spinal cord • ependymitis • central canal stenosis • aqueductal gliosis • syringomyelia

To examine the incidence and pathological features of central canal stenosis in man, 232 whole spinal cords were harvested at autopsy from 60 fetuses, 34 infants, 17 children, 24 adolescents and young adults, 70 middle-aged adults, and 27 adults older than 65 years. The spinal cords were sectioned serially from the conus medullaris to the upper medulla, and histological findings were correlated with clinical data and general autopsy findings. Evidence is presented that stenosis of the central canal is an occult pathological lesion that is likely to influence the anatomical features of syringomyelia.

Materials and Methods

Study Protocol

Protocols for the use of human autopsy material were approved by the Institutional Review Board for Human Experimentation at Kings County Hospital Center, University Hospital of Brooklyn, and The Long Island College Hospital.
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Autopsy Material

Whole-brain and spinal cord specimens were harvested at autopsy from 60 fetuses aborted by saline injection between 6 and 23 weeks' gestational age, 16 premature infants (24 to 36 weeks' gestational age), and 156 individuals who had died from various causes between 1 day and 92 years of age. Autopsies were performed within 24 to 36 hours of death except in the case of fetuses, which were fixed in 10% buffered formalin for 2 to 6 weeks prior to postmortem examination. Following a standard complete autopsy, the brain was removed from the cranial cavity and the upper end of the spinal cord was sectioned transversely at the cervicomedullary junction. The remainder of the spinal cord was removed through the abdominal and thoracic cavities. Osteotomies were made with the aid of a Stryker circular saw through the junction of the pedicles and the vertebral bodies from L-5 to C-3 bilaterally. The anterior half of the vertebral column was elevated and the spinal cord was removed with the dura intact by sectioning the nerve roots. To mobilize the upper end of the spinal cord, the head was extended maximally and the nerve roots were divided with a long-handled knife. Specimens were fixed for a minimum of 10 days in 10% buffered formalin prior to sectioning.

Clinical Data and General Autopsy Findings

For each individual, autopsy and medical records were used to establish a database that included details of the present illness, the medical history, and a review of systems. If the individual had died after admission to a hospital, data were extracted from the medical record concerning physical findings, radiographic findings, pertinent laboratory results, and serology for syphilis, human immunodeficiency virus, and hepatitis B. General autopsy data consisted of causes of death, age groups: fetuses, premature infants, term infants, children (1 to 12 years), adolescents and young adults (13 to 29 years), middle-aged adults (30 to 64 years), and older adults (65 to 92 years). The I/O ratio of completely patent canals was always less than 100% owing to the area occupied by the lining ependyma. Stenosis of the central canal was graded as a percentage reduction of the normal age-related I/O ratio as follows: Grade 0 = no stenosis; Grade 1 = 1% to 25% reduction; Grade 2 = 25% to 50% reduction; Grade 3 = 50% to 75% reduction; Grade 4 = 75% to 99% reduction; and Grade 5 = 100% reduction.

Results

Morphometric Studies

The normal I/O ratio of the central canal was calculated at seven different levels in seven age groups from more than 1600 histological sections. Although the diameter of the canal relative to the total diameter of the spinal cord decreased dramatically during growth and development, the average I/O ratio was found to vary less than 10% at each level of the canal through nine decades of life (Fig. 1). Once a normal I/O value was established for each level and age group, it was possible to grade stenosis on a scale of 0 to 5 based on the percentage of I/O ratio reduction. Representative grades of stenosis as determined by morphometric analysis of the cross-sectional luminal area are shown in Fig. 2.

Incidence and Extent of Central Canal Stenosis

Table 1 shows the age-related incidence and average grade of stenosis at seven levels of the central canal in 228 of the 232 spinal cords studied. In four patients, the spinal cords were found to have occult syrinxes; these cases are summarized in Table 2.

As shown in Table 1, stenosis of the central canal was not encountered in fetuses or premature infants. Grade 1 to 3 stenosis was present at one to four levels in one (6%) of 18 term infants and three (18%) of 17 children under the age of 10 years. Varying degrees of stenosis (Grades 1 to 5) involving one to seven levels, were present in 20 (87%) of 23 adolescents and young adults, 65 (96%) of 68 middle-aged adults, and all 26 adults aged 65 years or older (100%). In general, the stenotic process involved more levels and was more complete in older individuals, and the highest grades of stenosis were found between T-2 and T-8, with relative sparing of the rostral and caudal ends of the canal.
FIG. 1. Morphometric analysis of normal cross-sectional area of the central canal in different age groups. Upper Left: Central canal of medulla in a 260-gm fetus (inner/outer area (I/O) ratio 0.75). Upper Right: Central canal of medulla in a 43-year-old man (I/O ratio 0.79). Lower Left: Central canal at T-2 level in a 18-month-old child (I/O ratio 0.69). Lower Right: Central canal at T-2 level in a 45-year-old man (I/O ratio 0.71).

Occlusion (Grade 5) of the entire central canal (seven levels) was present in only four individuals (aged 43, 59, 60, and 73 years). By way of contrast, five adults older than 20 years had completely patent canals and 18 others had patent canals except for partial stenosis (Grades 1 to 3) at one or two levels.

Histological Findings

The histological features of central canal stenosis were characterized by subependymal gliosis, disorganization of the ependymal epithelium, and intracanalicular gliosis. The most constant finding was a proliferation of fibrillary astrocytes and capillaries in the subependymal tissues with compression of the canal by gliovascular buds (Fig. 3 upper left). In the lower grades of stenosis, the canal was narrowed but patent. Ependymal cells adjacent to gliovascular buds were typically clumped and flattened. In the higher grades of stenosis, the ependymal epithelium was increasingly disorganized and gliovascular buds were found to extend through areas of ependymal disruption and to obliterate the lumen by intracanalicular adhesions and astrocytosis (Fig. 3 upper right). Holzer staining confirmed the presence of glial fibers within the lumen of the canal and in the subependyma surrounding the perimeter of the canal.

Astrocytosis produced several patterns of ependymal disorganization. As a consequence of gliosis in the subependymal tissue, the epithelium was frequently compressed into a tight cluster of jumbled cells (Fig. 3 lower left). Formations of densely clumped cells gave the impression of ependymal proliferation, but staining with proliferating cell nuclear antigen proved negative. A second pattern of ependymal disorganization was intracanalicular gliosis, which tended to bury the epithelium between layers of astrocytes. In some cases, the tend through areas of ependymal disruption and to obliterate the lumen by intracanalicular adhesions and astrocytosis (Fig. 3 upper right). Holzer staining confirmed the presence of glial fibers within the lumen of the canal and in the subependyma surrounding the perimeter of the canal.

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TABLE 1
Incidence and extent of central canal stenosis in 228 autopsy cases

<table>
<thead>
<tr>
<th>Age Group</th>
<th>No. of Cases</th>
<th>Stenosis</th>
<th>Average Grade of Stenosis at Each Level*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No.</td>
<td>Percent</td>
</tr>
<tr>
<td>fetuses (6-23 wks)</td>
<td>60</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>premature infants</td>
<td>16</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>infants (0-12 mos)</td>
<td>18</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>1-9 yrs</td>
<td>17</td>
<td>3</td>
<td>18</td>
</tr>
<tr>
<td>10-19 yrs</td>
<td>3</td>
<td>2</td>
<td>67</td>
</tr>
<tr>
<td>20-29 yrs</td>
<td>20</td>
<td>18</td>
<td>90</td>
</tr>
<tr>
<td>30-39 yrs</td>
<td>27</td>
<td>26</td>
<td>96</td>
</tr>
<tr>
<td>40-49 yrs</td>
<td>16</td>
<td>15</td>
<td>94</td>
</tr>
<tr>
<td>50-59 yrs</td>
<td>16</td>
<td>16</td>
<td>100</td>
</tr>
<tr>
<td>60-69 yrs</td>
<td>19</td>
<td>18</td>
<td>95</td>
</tr>
<tr>
<td>70-79 yrs</td>
<td>14</td>
<td>14</td>
<td>100</td>
</tr>
<tr>
<td>80-92 yrs</td>
<td>2</td>
<td>2</td>
<td>100</td>
</tr>
</tbody>
</table>

* For explanation of grading system, see Materials and Methods section.

TABLE 2
Extent of central canal stenosis in four (of 232) autopsy cases with occult syringes in the spinal cord

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Description of Syrinx</th>
<th>Etiology of Syrinx</th>
<th>Central Canal Stenosis</th>
<th>Grade of Central Canal Stenosis*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>56, M</td>
<td>central cavitation of cord at T6-9, lined by ependyma</td>
<td>idiopathic</td>
<td>yes</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>49, M</td>
<td>central cavitation of cord at C2-T1, lined by ependyma</td>
<td>Chiari I malformation</td>
<td>yes</td>
<td>3</td>
</tr>
<tr>
<td>3</td>
<td>79, M</td>
<td>central cavitation of cord at C5-7, lined by ependyma</td>
<td>huge cervical discs at C4-5 &amp; 5-6</td>
<td>yes</td>
<td>syrinx</td>
</tr>
<tr>
<td>4</td>
<td>25, F</td>
<td>C2-T7 syrinx with paracentral dissection below T-2; central segment (C2-T1) lined by ependyma; para-central segment (T2-7) lined by gliosis</td>
<td>Chiari I malformation</td>
<td>yes</td>
<td>3</td>
</tr>
</tbody>
</table>

* For explanation of grading system, see Materials and Methods section.
† At T-2 and T-5, the central canal was stenosed and the syrinx cavity was situated dorsal and lateral to the stenotic segment.

ependyma was widely disrupted and the cells were separated into small islands within a broad field of gliosis (Fig. 3 lower right). There appeared to be some attempt at ependymal regeneration as evidenced by the formation of microcanals and true rosettes (Fig. 3 upper right). However, staining with proliferating cell nuclear antigen failed to confirm any recent proliferation of ependymal cells.

Histological evidence of ependymitis such as exudates, inclusion bodies, or necrosis of ependyma was not encountered in this study. In two of the 232 spinal cords, hemosiderin deposits were found in association with subependymal gliosis at several levels. Histological review of four occult syringes (Table 2) revealed that each cavity was defined rostrally and caudally by varying degrees of central canal stenosis. Three syringes were lined wholly or partially by ependyma and appeared to represent dilated segments of the central canal. In Case 4, the upper end of the cavity (C2-T1) was lined by a discontinuous layer of ependyma, but below T-2 the central canal was obliterated and the syrinx had dissected paracentrally to the level of T-7 (Fig. 4). The lower end of the cavity (T2-7) was lined by glial fibers and spongy white matter.

Clinical Data and General Autopsy Findings

There was no correlation between the incidence of central canal stenosis and any condition other than age. The lesion appeared to develop in an occult manner and was present in apparently normal adults dying acutely of accidental trauma. Chronic diseases and causes of death including pneumonia, acquired immune deficiency syndrome, sepsis, bacterial meningitis, cardiovascular disease, cerebrovascular disease, subarachnoid hemorrhage, diabetes, hypertension, cancer, and intracranial tumors did not play a statistically significant role.
FIG. 3. Histological features of central canal stenosis. H & E, X 200. Upper Left: Axial section at the T-5 level in a 37-year-old man demonstrating a glial bud with central capillary (gliovascular bud) compressing the lumen of the central canal. The ependyma is clumped and disorganized. Upper Right: Central canal at the T-5 level in a 33-year-old woman with Grade 4 stenosis. Note intracanalicular gliosis (asterisk) and formation of rosette or microcanal (arrow). Lower Left: Dense clump of ependymal cells at the C-5 level in a 60-year-old man with Grade 5 stenosis. Staining with proliferating cell nuclear antigen was negative. It is likely that ependymal clusters are formed by adhesions and constrictive gliosis rather than cellular proliferation. Lower Right: Islands of ependymal cells are buried within a dense field of gliosis at the C-2 level in a 55-year-old woman. The central canal is not recognizable.

Discussion

Although it is generally accepted that the central canal of the human spinal cord is obliterated after birth as part of an involutional or degenerative process, the scientific basis for this conclusion is not impressive. In 1933, Cornill and Mosinger examined 27 adult spinal cords and reported that the central canal was occluded in 47 (71%) of 66 randomly selected sections. On the basis of the histological findings, the authors suggested that the condition was caused by a proliferation of ependymal cells and gliovascular scarring. Netsky, in a more widely cited reference, estimated that approximately 80% of adult spinal cords had occluded canals. It is doubtful that the author intended this as a precise estimate, because his evidence was based on histological material from the files of Montefiore Hospital and no other findings were reported. Kasantikul, et al., reported that the central canal was usually patent during the first two decades of life and was occluded in most individuals older than 20 years. Histological descriptions of the condition have been largely anecdotal in nature.

The current report represents the first detailed study of central canal stenosis in man and describes the histological findings at seven levels of the spinal cord in 232 individuals ranging in age from 6 weeks' gestation to 92 years. As summarized in Table 1, the condition was not encountered in fetuses and premature infants, occurred with increasing incidence after the 1st year of life, and was present to some extent in almost every individual examined by the early years of adult life. The stenotic process was most pronounced in the
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narrowest segments of the canal (T2–8) and involved more levels with higher grades of stenosis in older individuals.

Under normal conditions, the diameter of the central canal relative to the total diameter of the spinal cord decreases significantly during the first few years of life.4,25 This occurs as a consequence of myelination and the development of white-matter tracts,26 and continues through early adolescence when the canal assumes its adult size and configuration. There was no evidence in the current study that the central canal undergoes involutinal narrowing. Although the size of the tubule relative to the spinal cord decreased significantly during growth and development, measurements of I/O luminal area were found to be relatively constant at each level of the canal through nine decades of life. Even in older individuals with severe stenosis at multiple levels, the patent segments of the canal were found to have normal I/O luminal areas.

The histological features of central canal stenosis were characterized by disorganization of the ependymal epithelium, formation of ependymal rosettes and microcanals, proliferation of subependymal gliovascular buds, and intracanalicular gliosis. The predominant pathological finding appeared to be astrogliosis, and this was confirmed by Holzer staining. Staining with proliferating cell nuclear antigen failed to demonstrate a recent proliferation of ependymal cells, although some attempt at regeneration can probably be inferred by the formation of microcanals and rosette patterns. The histological features of central canal stenosis were found to be indistinguishable from those occurring in acquired stenosis (gliosis) of the aqueduct of Sylvius13,23 and resemble those in aqueductal gliosis resulting from experimentally induced necrotizing ependymitis.5,10 These similarities are consistent with a common mechanism of causation involving ependymal injury and scarring, and suggest that central canal stenosis in man is an acquired pathological lesion rather than a degenerative process related to aging.

From a clinical standpoint, the most common causes of ependymal injury and scarring are infection, hemorrhage, and neoplastic seeding.15 While it is possible that catastrophic illnesses such as bacterial meningitis or traumatic myelopathy could contribute to central canal stenosis in a small percentage of cases, hemosiderin deposits were present in only two cases in the current series and there was no evidence that bacterial infections or neoplastic diseases played a significant role. In considering the pathogenesis of this condition, it is necessary to explain the occurrence of a lesion that develops in an occult manner, exhibits an increasing incidence after the 1st year of life, and affects the vast majority of apparently normal individuals. Among the few diseases that could account for this epidemiological pattern are infections with viruses that selectively attack the ependymal epithelium. Mims19 has shown that influenza A and pox viruses replicate selectively in ependymal cells, and there is experimental evidence that a number of endemic viruses including parainfluenza 2, measles, mumps, and Reovirus type I are able to infect and destroy ependymal cells in the absence of clinically apparent disease.1,7,10 In view of the epidemiological pattern of central canal stenosis, it is interesting to consider whether repeated episodes of ependymitis occurring over succeeding decades of life as a consequence of common virus infections could play a causal role.

The incidence and extent of central canal stenosis in man almost certainly affect the clinical features of syringomyelia. In patients with hindbrain deformities, for example, uniform enlargement of the central canal (holocord syrinx) is usually encountered only in pediatric patients, whereas comparable deformities in adult patients tend to produce focal syrinxes, paracentral syrinxes, or no syrinxes at all.2,15,16 These variations cannot be explained on the basis of conventional hydrodynamic theories, and may be due to the availability of patent segments of the canal to participate in the dilatatory process or to a secondary reduction of cavity length by age-related stenosis. A histological review of four occult syrinxes (Table 2) revealed that three were confined between stenotic segments of the canal and the fourth had dissected paracentrally around a stenotic segment. The patency of the lumen above and below syrinxes may be an important factor in determining which cavities are likely to elongate and whether they do so by dilating the lumen or by dissecting paracentrally into the spinal cord parenchyma.

Finally, although there is nothing to suggest that age-related stenosis is associated with clinical consequences, little is known about the normal function of the central canal. In vertebrates, the central canal appears to function like a “sink” and is capable of clearing substances as varied as vital dyes, horseradish peroxidase, and cellular elements from the parenchymal tissue of the spinal cord.13,14,18 Histocytochemical studies have demonstrated that the central canal is surrounded by numerous pericanalicular and CSF-contacting neurons which are rich in biologically active substances including vasoactive intestinal peptide, cholecystokinin, muscinol, oxytocin, substance P, met-enkephalin, somatostatin, serotonin, dopamine, neurotensin, adrenocorticotropic, and acetylcholine.5,6,9,11,12,21,22,24,27 Some of these substances are involved with complex autonomic functions. The possibility that stenosis of the central canal interferes with neurochemical activities of the spinal cord and contributes to age-related problems such as constipation, orthostatic hypotension, and reduced sexual potency in males has not been previously considered.

Acknowledgments

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References

2. Barnett HJM, Fostier JB, Hudgson P: Syringomyelia. Lon-


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