Paraganglioma of the cauda equina

Report of three cases

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The authors report the clinical, radiological, and pathological findings in three cases of paraganglioma of the cauda equina. In one case, magnetic resonance imaging and neurochemical study results are described. No specific identifying features were encountered either clinically or radiologically that were helpful in making a distinction between this and other more common tumors at this site such as ependymoma or neurofibroma. At surgery, these neoplasms were well-circumscribed red fleshy tumors. Histological examination of one paraganglioma showed a superficial resemblance to ependymoma, and this may be particularly true on initial assessment by frozen section or smear. The use of electron microscopy and immunohistochemical demonstration of synaptophysin in these tumors allowed a confident diagnosis to be made. Neurochemical assessment in one case showed very high levels of serotonin and a turnover of dopamine similar to that of human cerebral cortex. Paraganglioma of the cauda equina is an uncommon tumor with just over 50 cases reported in the world literature. The clinical course of these tumors is benign and they should be completely removed at surgery to prevent later recurrence.

KEY WORDS • paraganglioma • cauda equina • spinal tumor • synaptophysin

PARAGANGLIOMA is a well-recognized tumor of neuroendocrine histogenesis occurring in more than 90% of cases as carotid body or glomus jugulare tumors. Paraganglioma of the cauda equina was first described in 1972, since when over 50 cases of this tumor have been described in the world literature. With the advent of specialized neuropathological techniques, there has been an increased recognition of this tumor, previously thought of as an unusual form of ependymoma. We present a further three cases and review the neuropathology of this interesting condition. The histochemical findings of one of these tumors are presented.

Case Reports

Case 1

This 37-year-old woman was referred with a 7-year history of intermittent lumbosacral pain. On examination, straight-leg raising was limited to 60° bilaterally. Motor grade 4 weakness was detected in the right extensor hallucis longus muscle. The lower limb reflexes were symmetrically brisk, with flexor plantar responses. There were no sensory or sphincter abnormalities. Myelography revealed a globular contrast defect just below the conus medullaris. At operation, a red spherical circumscribed tumor, 1 cm in diameter, was completely excised from the cauda equina. The patient made an uncomplicated recovery and has been discharged from follow-up monitoring.

Case 2

This 36-year-old man was referred to us with a 2-year history of recurrent low-back pain radiating into the back of his right thigh. On examination, he had normal power and tone, but a reduction in sensation in the right S-1 dermatone. The reflexes were normal. A magnetic resonance image demonstrated a well-defined mass in the cauda equina (Fig. 1). At operation, a red circumscribed tumor, 2 cm in diameter, was found in the cauda equina and incompletely excised. The patient made an uneventful recovery and has been discharged from follow-up monitoring.

Case 1

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Case 3

This 53-year-old man was admitted with an 18-month history of increasing pain in the low back and anterior aspect of the thigh bilaterally. On examination, straight-leg raising was reduced to 70° bilaterally and the left knee jerk was reduced; otherwise there were no significant neurological abnormalities. Myelography with computerized tomography demonstrated a complete block at the level of the cauda equina consistent with a space-occupying lesion. At surgery, a soft red spherical circumscribed tumor was completely excised from the cauda equina. The patient made a rapid and uneventful recovery from surgery and at his 6-month follow-up examination had no residual symptoms.

Pathological Findings

Following excision, portions of tumor from all three cases were fixed at 4.5% glutaraldehyde with cacodylate buffer for transmission electron microscopy and also fixed in formalin for paraffin processing. Fresh tissue from Case 2 was frozen in isopentane cooled with liquid nitrogen for cryostat sectioning and neurochemical analysis, with the results shown in Table 1.

On paraffin-embedded sections, each tumor had the appearance typical of a paraganglioma, being composed of cords and nests of cells with epithelial characteristics. Tumor cells were arranged around small vessels reminiscent of pseudorosettes (Fig. 2). In addition, papillary epithelial structures were present with areas resembling ependymal tubules. Areas of characteristic nesting of cells to form “Zellballen” were present in all three tumors. No mitoses or necrosis were seen in any tumor.

Electron microscopy showed the presence of dense-core neuroendocrine granules at the vascular poles of the cells. Immunohistochemical examination using an antibody to synaptophysin showed positive staining in a granular pattern, with accentuation toward the perivascular poles of cells, in a distribution consistent with the electron microscopic findings (Fig. 3). No staining with antibody to glial fibrillary acidic protein was seen in any case.

Discussion

Paraganglioma of the cauda equina is being increasingly recognized, and just over 50 cases have so far been published in the world literature.1,2,7,11 The largest series was reported by Sonneland, et al.,11 who reviewed a total of 31 cases and demonstrated a mean age of 51 years with a slight male predominance. In their series,
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Fig. 3. Photomicrograph of a section stained with an antibody to synaptophysin by the immunoperoxidase method. There is diffuse staining with intense positivity adjacent to the vascular pole of cells corresponding to the localization of neuroendocrine granules, x 200.

27 patients presented with low-back pain and sciatica, but only 11 had neurological signs. All but one of the tumors were entirely intradural, with 30 being extramedullary at myelography. Evidence of bone destruction has been reported in two cases. Recurrence was unusual in the tumors that were completely excised at the original operation, but radiotherapy was recommended for those patients with incomplete excision.

The similarity between this tumor and ependymoma has led to diagnostic confusion in the past; however, this resemblance is superficial and exists at the light microscopic level only. The main confusion arises from the presence of a radial perivascular arrangement of cells which looks like the perivascular pseudorosettes of ependymoma, and occasional papillary epithelial structures which resemble ependymal tubules. The ultrastructural and immunohistochemical appearance of the paraganglioma, however, is quite distinct and easily distinguishes such lesions from ependymomas.

Synaptophysin is a recently described membrane glycoprotein specific to neurosecretory granules which can be detected by immunohistochemistry in fresh frozen or briefly fixed tissue. Synaptophysin is present in tumors with a high content of neurosecretory granules but not in other tissues, and is thus a useful marker of neuroendocrine differentiation. In these tumors, the large numbers of neuroendocrine granules detected ultrastructurally was reflected in intense granular staining for synaptophysin. We would suggest that synaptophysin is a useful marker in this respect and is more specific than neuro-specific enolase or PGP 9.5 in establishing a neuroendocrine phenotype.

There are no clues from the clinical history that differentiate paraganglioma from other potential causes of cauda equina syndrome and, at surgery, the macroscopic features of a red fleshy tumor in the cauda equina usually raises the possibility of either a peripheral nerve sheath tumor or an ependymoma. For the histopathologist, frozen section may reveal a tumor with both perivascular rosettes and epithelial cords which may initially suggest the diagnosis of an ependymoma. Subsequent paraffin-embedded sections supplemented by immunohistochemistry and electron microscopy will, however, resolve this differential diagnosis, and in particular, the immunolocalization of synaptophysin should prove extremely useful in the future.

The neurochemical studies showed that there was substantial expression of monoaminergic transmitter systems in one of these tumors. However, the high level of dopamine observed in a previous study by Llena, et al., was not confirmed, although the levels of homovanillic acid indicated that dopamine turnover was at a level similar to that seen in the human cerebral cortex. In addition, this tumor showed greater adrenaline (epinephrine) than noradrenaline (norepinephrine) synthesis, which presumably reflects greater concentrations of the enzyme phenylethanolamine N-methyl transferase than were thought to be active in the case of Llena, et al. We found for the first time that 5-hydroxytryptamine (5-HT) concentrations were present in this tumor at levels substantially higher than those for the catecholamines. Immunohistochemical studies by Sonnelland, et al., revealed that up to 75% of their tumors showed immunoreactivity to 5-HT, most noticeable in the paraganglion cells. Up to 80% of their cases demonstrated immunoreactivity for somatostatin but it was sited in both paraganglion cells and neurons. The determination of monoamine transmitters in the one case examined suggests that 5-HT is a major component of the paraganglioma transmitter system.

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References


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