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Dumb-bell Ganglioneuroma of the Spine Misinterpreted as Progressive Idiopathic Scoliosis

Case Report

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Summary. A giant ganglioneuroma generating a progressive scoliosis in a 16-year-old girl is presented. The interval between the start of the orthopaedic treatment and the diagnosis of the true nature of the disease was more than 4 years, thus allowing the development of a giant partly intracanalicularly partly retroperitonealy expanding tumormass. The report emphasizes and describes the combined neurosurgical, general surgical and orthopaedic surgical treatment and presents the results of light- and electron microsopical, immunohistochemical and quantitative neurochemical investigations of the resected tumor.

Zusammenfassung. Es wird über ein riesenhaftes Ganglioneurom als Ursache für eine progrediente Lumbalskoliose bei einem 16jährigen Mädchen berichtet. Zwischen dem Beginn der orthopädischen Skoliosebehandlung und der Diagnose der wahren Ursache der Skoliose sind mehr als 4 Jahre vergangen, so daß ein riesenhafter, teils intrakanalikulär, teils retroperitoneal wachsender Tumor sowie die Destruktion von 4 Lendenwirbelkörpern entstehen konnte. Neben der Beschreibung der kombinierten neurochirurgischen allgemeinchirurgischen und orthopädisch-chirurgischen Therapie werden die Ergebnisse der licht-, immun- und elektronenmikroskopischen Untersuchungen sowie neurochemischen Analysen des resezierten Tumors mitgeteilt.

Tumors growing in dumb-bell fashion through the intervertebral foramina and compressing the spinal cord comprise a variety of different histologic entities. Most frequently encountered are neurilemmomas including Schwannomas and neurinomas [8]. Other dumb-bell tumors are rare and include those derived from the spinal cord, roots and meninges such as meningiomas and ganglioneuromas (for a review, see [3]).

Approximately one percent of tumors located at or near the spinal cord are ganglioneuromas [14, 15]. Ganglioneuromas share with neuroblastomas a common origin from the neural crest. They secrete catecholamines, whose catabolites may be found at elevated levels in plasma and urine. Since ganglioneuromas are the mature congeners of neuroblastomas they do not give rise to metastases, are fully encapsulated and contain differentiated ganglion cells resembling mature sympathetic neurons [5, 10, 16].

Ganglioneuromas of the lower thoracic or upper lumbar spine developing in the growth period of life may rarely lead to deformation of the spine either by destruction of lateral or posterior elements of the spine or when wide excision with removal of posterior and lateral elements of two or more segments are required. Postoperative instability may be the consequence, if adequate fusion after removal of the tumor is not carried out.

False diagnosis and clinical mismanagement of dumb-bell ganglioneuromas have been reported [13, 17].

We report here on the case of a 16-year-old girl with a giant ganglioneuroma that had been erroneously treated for scoliosis over several years.

Case History and Treatment

The 16 year 3 months old girl was first admitted to the Department of Neurosurgery in 1986 with the diagnosis of a large epineural and retroperitoneal tumor of the lumbal spine, severe

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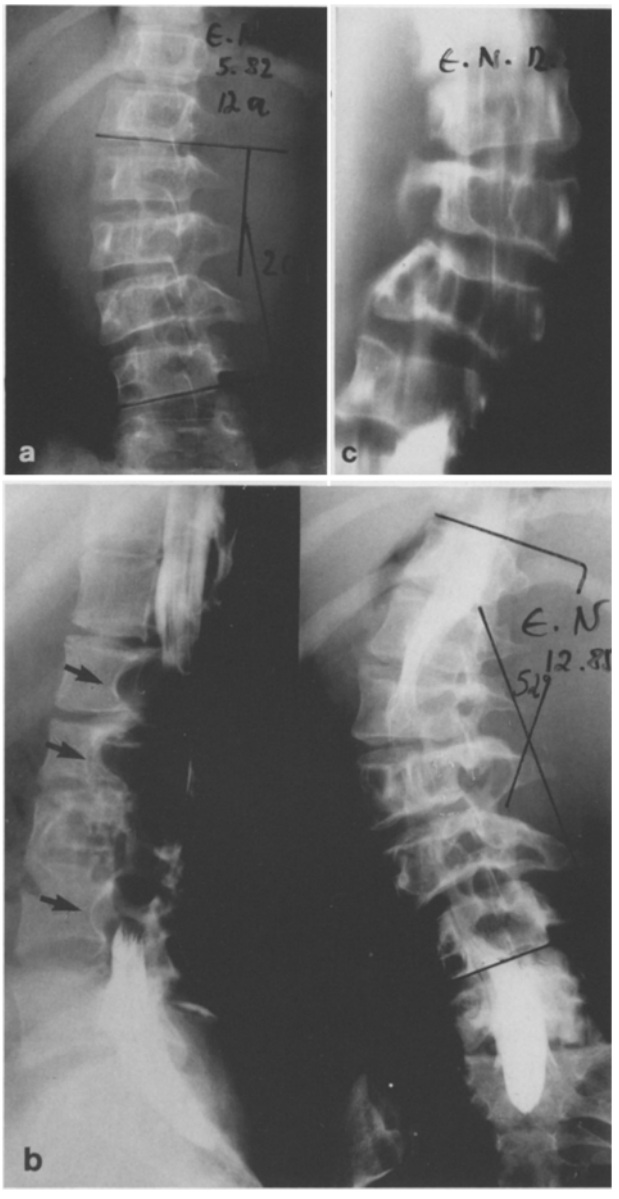

Fig. 1. **a** X-ray of the lumbar spine at the age of 12 demonstrating a 20° Cobb right convex lumbar scoliosis. A cystic expanding lesion of the base of the left transverse process of L3 was not realized. No lateral X-ray was performed of this age. **b** Lateral- and a.-p. X-ray of the lumbar spine 4 years later now presenting a scoliotic deformity of 52° Cobb and destruction of L1–L4 (arrows). The Solutrast myelogram shows the expanding intracanalicular tumor mass. **c** a.-p. tomogram of the lumbal spine taken an occasion of the Solutrast myelography (at age 16) clearly shows the cystic destructions within the lumbar vertebrae L1–L4

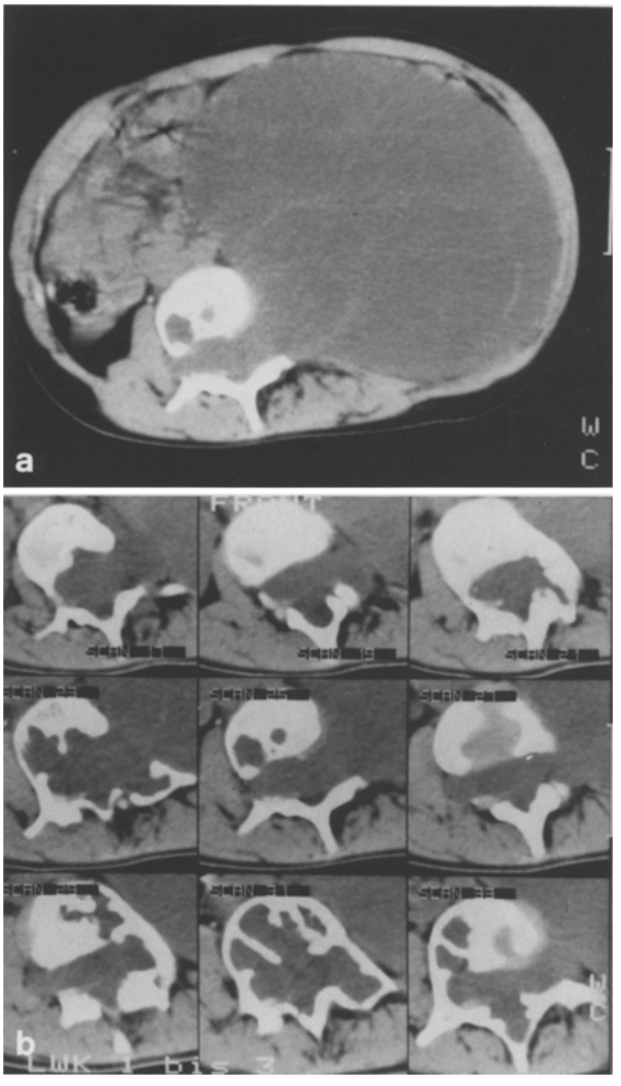

Fig. 2a, b. Preoperativ CT-scan of the lumbarspine and the abdomen of the girl aged 16. **a** Assembly of representative scans from L1 to L3 showing the intra- and extracanalicular extension of the tumor as well as the cystic destructions within the vertebral bodies. **b** Abdominal scan at L2 demonstrating a 2/3 obliteration of the abdomen by the expanding retroperitoneal tumor mass. Widening of the intervertebral hole and continuity of the intracanalicular and retroperitoneal mass are evident

progressive scoliosis and signs of incipient paraparesis. The girl had been, however, first seen four years earlier by an orthopedic surgeon complaining of backpain and a slight lumbar deformity. X-rays of the spine taken at the first contact documented a right-convex scoliosis of 12° Cobb of the lumbar spine. A program of physiotherapy was initiated and performed for one year. A control X-ray of the spine taken at the end of this period now documented a progressive right-convex lumbar scoliosis of 20° Cobb (Fig. 1a). The girl still complained of some pain and slight discomfort in her left leg. Still maintaining the diagnosis of a progressive idiopathic scoliosis a Cheneau-orthosis was applied and worn for two years. Early in 1986 the scoliosis had progressed to 52° Cobb despite brace treatment and without significant progression of neurological deficits (Fig. 1b). The girl was now-still unter the orthopedic diagnosis-referred to a scoliosis center for surgical corrective treatment (Werner Wicker-Klinik, Bad Wildungen). At this time new X-rays of the spine showed a destruction of the second, third and fourth lumbar vertebral bodies and widening of the corresponding intervertebral holes on the left side (Fig. 1c). A CT-scan of the lumbar spine verified and expand-

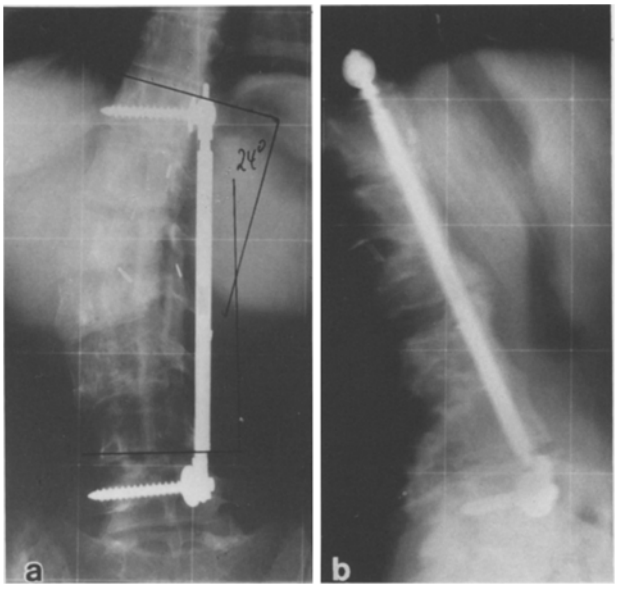

Fig. 3a, b. a.–p. and lateral X-rays of the lumbal spine 2 years after surgery showing correction and fusion of the spine by fibular strut grafting and Zielke-Askani-instrumentation

ing tumor of the epineurium from L1 to L4 with extreme compression of the contents of the vertebral canal at these levels and an expanding tumor mass in the retroperitoneum compressing and dislocating the abdominal contents to the extreme right of the abdomen (Fig. 2). MR-imaging of the tumor area confirmed the continuity of the extra- and intra-canalicular tumor mass. A paravertebral tumor biopsy was carried out at this stage confirming the suspected diagnosis of a well differentiated ganglioneuroma. With this diagnosis the girl was transferred to the Department of Neurosurgery for further treatment. A this stage routine laboratory tests were normal, an additional myelogram plus CT-scan of the affected spine segments defined the extension of the intra- and extracanalicular tumor mass to L1-L4 and visualized the vertebral excavations in L1, L2, L3 and L4 (see Fig. 1b and Fig. 2). A two stage excision of the tumor was then carried out.

1. Laminectomy L1–L4 with complete excision of the intracanalicular tumor mass, decompression of the dural sac using microsurgical techniques (Prof. Dr. B. L. Bauer, Department Neurosurgery) and grafting of the vertebral body defects with homologous bank bone. After wount healing the girl was transferred to the Department of Orthopedics.

2. Three weeks after the initial intervention the anterior retroperitoneal mass was exposed via an oblique anterior leftsided incision (Prof. Dr. D. Maroske, Department General Surgery). The tumor mass (23 × 15 cm) was well encapsulated and could be excised in one block. The orthopedic team (Prof. Dr. P. Griss) now exposed the entire lumbar spine from D11 down to L5 from the concavity of the scoliotic deformity by subperiosteal stripping. A Zielke-Askani device (see for details [6]) was introduced and fixed by two VDS-screws into D11 and L5. By expanding the device, the scoliotic curve could be corrected and stabilized. The discs of the bridged area were now resected and grafted with homologous bankbone. In addition a 20 cm long fibular strutgraft taken from the left leg of the patient was transplanted to the concavity of the fusion area, being fixed into vertebral body holes of D11 and L5 as a combined in- and onlay graft.

Postoperatively a plaster jacket including the left leg was applied and carried for 3 months. Wound healing again was uneventful. 3 months after surgery a trunk orthosis (Stagnara-type) was applied for another 6 months, routine controls one and two years after excision of the tumor did not reveal any signs of recurrence. The fusion mass was solid, an incomplete leftsided L4 paresis (after the first operation) and a weakness of the peroneus muscles of the left leg (after removal of the fibular graft) had healed completely. The scoliosis measured 24° Cobb on the latest X-ray control (Fig. 3, b).

Morphological and Biochemical Examination of the Tumor

Materials and Methods

Morphology. Immediately after removal 12 tissue specimens were sampled from various parts of the tumor and rapidly processed for light and electron microscopy as previously described [1, 2]. Routine histology of tumor specimens were performed after fixation in buffered formalin and paraffin embedding. In addition to histologic routine staining (H & E, Cresyl violet) special neurohistological methods such as Bodian-silver-stain for axons, Klüver-Barrera for neurons and Nissl substance and Gordon-Sweet-silver impregnation for reticulum fibers as well as immunohistological methods were performed. These methods comprised reactions against cytokeratin, neuron specific enolase, glial fibrillary acid protein, myelin basic protein, fibronectin, S-100 protein, neurofilament proteins and vimentin. These methods were performed in PAP modification.

Quantitative Determinations of Catecholamines

Eight randomly selected pieces of tissue were separately analyzed for their catecholamine content by HPLC and amperometric detection [2, 11, 12]. In brief, tissue was finely minced and subsequently homogenized in 900 µl Tris-HCl buffer (pH 8.6) 0.2% (w/v) Triton X-100 containing 5 m*M* EDTA-Na_2, 15 m*M* $NaSO_2$ and 100 µl of N-methyl-dopamine (100 ng/100 µl) as an internal standard in an Elviem glass potter at 4°C.

After addition of 50 µl 9 M perchloric acid the homogenate was left for 10 min in the cold and then centrifuged at 10,000 × *g* for 10 min/2°–4°C). Catecholamines were quantified in 50 µl aliquots of the supernatant after an Al_2O_3 adsorption step by HPLC and amperometric detection. Protein was quantified according to Lowry et al. [9].

Results

Light Microscopy

Toluidine-blue stained 1 µm thick sections of Araldite-embedded material revealed that the tumor tissue was composed of vast areas of connective tissue and myelinated and unmyelinated nerve fiber bundles. Large ganglion cell bodies measuring up to 100 µm in

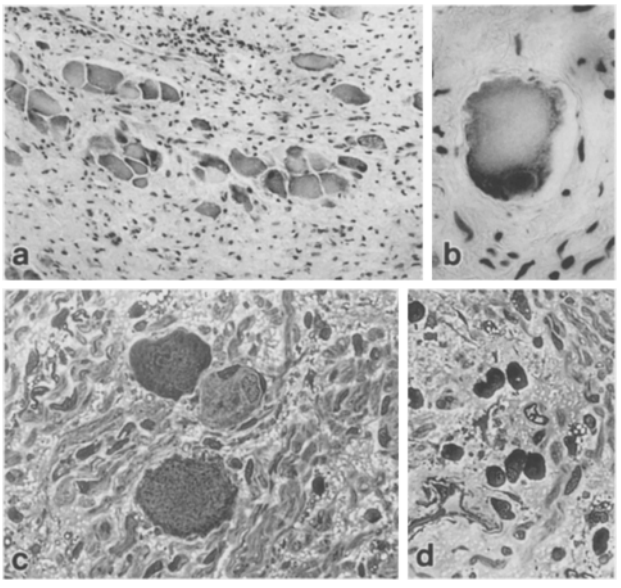

Fig. 4a–d. Light microscopical appearance of the tumor, for explanation see text

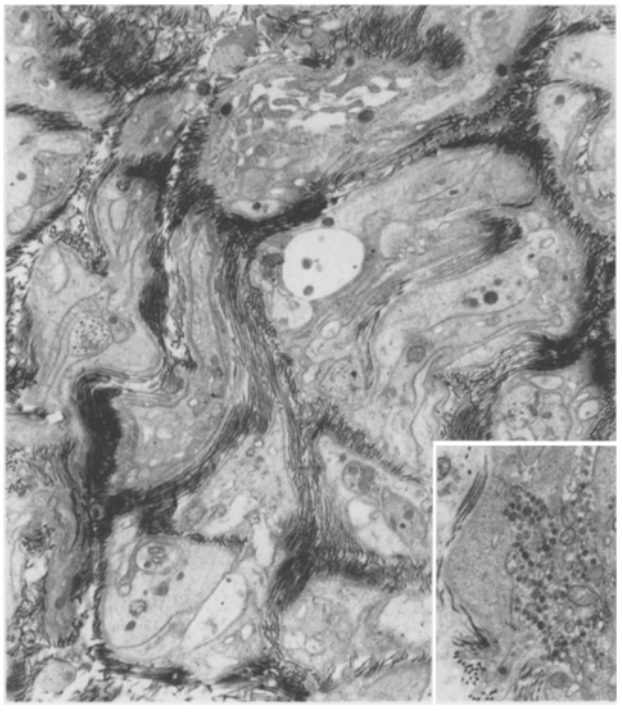

Fig. 5. Electron microscopical examination of the tumor, for explanation see text

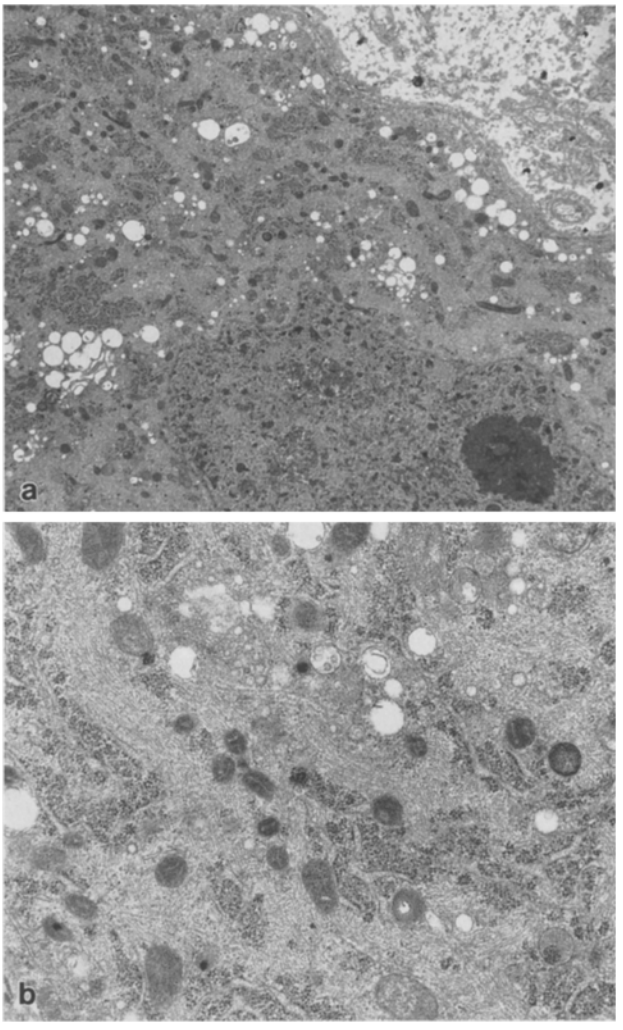

Fig. 6a, b. Electron microscopical appearance of the tumor ganglion cells, for details see text

diameter were interspersed single or in small clusters (Fig. 4a–c). Ganglion cells contained slightly irregularly contoured nuclei with large (up to 7 μm!) nucleoli. Neuronal cell bodies were consistently invested by satellite cells (Fig. 4c). Satellite cells were also seen accompanying nerve fibers (Fig. 4c). A few scattered intensely stained cells were found in addition that resembled undifferentiated neuroblastoma-like cells (Fig. 4d). Routine histological methods confirmed the impression of mature ganglion cells with a wealth of axons, both visible in Bodian impregnation and in the immunohistochemical demonstration of neurofilaments. Neurofilament proteins equally prooved strongly positive in the neuronal pericarya. The presence of myelin sheaths was demonstrated by Klüver-Barrera stain and the reaction to myelin basic protein. The participation of connective tissue within the tumor could be shown by Gordon-Sweet reticulum stain and the immunohistochemical reactions to fibronectin and vimentin. Glial fibrillary acid proteins as well as S-100 protein were not expressed neither by cells nor by the interstitial tissue.

Electron microscopy

Bundles of collagen fibrils with a few interspersed fibroblast-like cells separated small groups of unmyeli-

Table 1. Results of the quantitative neuro-chemical examination of the tumor tissue

Sample no.	Weight [mg]	Noradrenaline [ng/mg protein]	Dopamine [ng/mg protein]	Noradrenaline/dopamine ratio
1	111.9	18.5	5.8	3.2
2	101.0	32.9	10.8	3.0
3	86.0	17.3	5.6	3.1
4	186.9	20.2	7.3	2.8
5	99.0	22.4	4.0	5.6
6	97.8	16.4	3.5	4.7
7	105.0	17.6	4.5	3.9
8	136.8	30.1	6.5	4.6

nated and myelinated nerve fiber bundles (Fig. 5). Unmyelinated axons were about 0.2 to 2 μm in diameter. Most of them contained an abundance of neurofilaments together with few microtubules, mitochondria and smooth cisternae. Several axons displayed clusters of large dense core vesicles (Fig. 5 inset). Cores were mostly of medium electron density and rarely separated from the vesicle membrane by a lucent halo. Most axons were invested by cytoplasmic sheets of satellite cells, whose cell bodies contained well-developed rough endoplasmic reticulum (rER) and large lipid-like inclusions. Axon-satellite cell complexes were surrounded by a basal lamina. Myelinated axons had an approximate one percent share in the total number of axon profiles and unconspicuous ultrastructural features. Ganglion cells (Fig. 6) exhibited a number of fine structural details typical of mature peripheral autonomic neurons. Patches of rough ER and numerous free ribosomes were preferentially located in the cell periphery and separated by thick bundles of neurofilaments. Neurofilaments also formed circular bundles surrounding the nucleus. Dense bodies resembling secondary and tertiary lysosomes were frequently encountered in close proximity to Golgi areas. Although satellite cells investing the neurons contained numerous axon profiles, no synaptic nerve endings approaching the neuronal cell body were seen.

Quantitative Determinations of Catecholamines

The results concerning quantification of catecholamines in the tumor are shown in Table 1. Both noradrenaline and dopamine, but not adrenaline were detected. Total catecholamines varied from 19.9 to 43.7 ng/mg protein and noradrenaline/dopamine ratios from 2.8 to 5.6 between different samples.

Discussion

A rapidly developing spinal deformity in the growing child is always suspicions for a spine tumor, osteoid osteoma or osteoblastoma of the thoracic or lumbar spine being the most common tumors for this combination [4]. A case of ganglioneuroma and scoliosis has not been described until now in the literature accessible to the authors. It seemed therefore important to report this case in detail. Both morphological features and quantitative catecholamine data suggest a ganglioneuroma as the most likely diagnosis of this case. This notion is supported by the following observations: 1. presence of myelinated and unmyelinated axon bundles invested by satellite cells, 2. scattered ganglion cell bodies, 3. large dense-cored vesicles in some axonal profiles, and 4. large amounts of catecholamines in tumor tissue. Catecholamine levels were in the range of those found in cat and bovine sympathetic ganglia [7]. A small number of disseminated cells resembling neuroblastoma cells might point at a slightly heterogeneous differentiation pattern of this tumor. An attempt to grow this tissue in dissociated cell culture in order to further support the diagnosis [16] was unsuccessfull probably due to the low incidence and fragility of the ganglion cells.

The extreme extension of the tumor both intracanalicularly and retroperitonealy in combination with the severe destruction of 4 lumbar vertebral bodies and a scoliotic deformity afforded an interdisciplinary regimen of treatment and scientific investigation of the tumor mass. In the case presented this approach led to complete healing from the tumor and rigid stabilisation of the severed spine area. Earlier detection of the true nature of the disease would have rendered treatment less difficult, fusion of the spine most probably would have not been needed.

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