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Journal

Neurosurgery, 32(2)

ISSN

0148-396X

Authors

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[et al.](#)

Publication Date

1993-02-01

DOI

10.1227/00006123-199302000-00021

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Peer reviewed

Neurosurgery

Issue: Volume 32(2), February 1993, p 298-302

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Publication Type: [Case Report]

ISSN: 0148-396X

Accession: 00006123-199302000-00021

Keywords: Brain neoplasm, Genetics, Meningioma, Multiple meningiomas, Neurofibromatosis

[Case Report]

Multiple Spinal Meningiomas: A Case of 47 Distinct Lesions in the Absence of Neurofibromatosis or Identified Chromosomal Abnormality

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Received, December 18, 1991. Accepted, August 28, 1992.

▼ ABSTRACT

THE AUTHORS PRESENT a unique case of multiple spinal meningiomas with the late development of intracranial lesions. The patient had 47 distinctly separate, yet histologically identical, lesions excised, with many others noted at the time of surgery and by radiographic studies. He was evaluated for neurofibromatosis and was found to have neither Type I nor Type II. Genetic analysis, including restriction fragment length polymorphism analysis, was performed and detected no abnormalities.

Multiple spinal cord meningiomas are rare. Reported cases have been either malignant meningiomas [7](#), in association with von Recklinghausen neurofibromatosis (NF1) [9](#) or have reported only two intraspinal lesions [8-10,12,15,16,21](#). We describe a patient in whom 47 histologically confirmed spinal meningiomas were removed and in whom many others were identified by scanning techniques. The patient also developed meningiomas of the cervicomedullary junction and the cerebellar hemisphere late in his course.

CASE REPORT

A 32-year-old right-handed white man initially developed lancinating right posterior thigh pain after mild trauma. Onset was gradual, and the pain slowly increased in frequency and intensity. He sought chiropractic treatment but had no significant improvement. Ten months later, he noted decreased sensation along the lateral aspect of his left thigh and calf, as well as the lateral aspect of the sole of his left foot. Over the next 14 months, the region of hypesthesia spread to the right buttock, perianal region, and right scrotum. The region of numbness slowly spread anteriorly to the right hip and trunk and ascended to the level of the nipple. Within 4 months, he had difficulty ambulating because of right leg pain. At this point, the patient sought neurosurgical evaluation. He had no complaints of bowel or bladder dysfunction, and he had normal sexual function. He was seen at an outside institution, where a myelogram was obtained. He was then referred to the University of California, Irvine.

His examination demonstrated increased tone in both lower extremities. No motor deficits were present. Hypalgesia and hypesthesia were detected on the right below T6 and were more pronounced below L4. Proprioception was normal. Tendon reflexes in the upper extremities were normal. The patellar reflexes were hyperactive bilaterally. The Achilles tendon reflex was normal on the left and absent on the right. Plantar reflexes were flexor bilaterally. Abdominal reflexes were normal, and cremasteric reflexes were present. Rectal tone was normal. A review of the myelogram revealed multiple intradural lesions of the cauda equina at the L4-L5 level, a left lateral intradural lesion at T9, and a small lesion posteriorly at T3 ([Figure 1](#)).

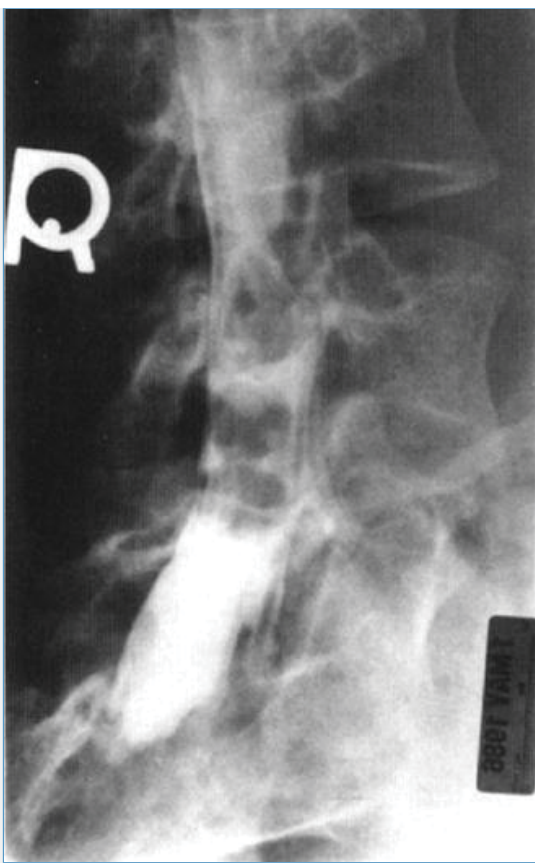


Figure 1. Initial myelogram demonstrating multiple lesions at the L4-L5 level.

Because the patient's chief complaint was lower-extremity pain, he was taken to the operating room the following day for resection of the cauda equina lesions. An L3-L4 laminectomy was performed. At the time of surgery, a total of eight lesions were identified. Five of these were dissected free from the nerve roots. Multiple small (1-2 mm) nodularities were also noted on many different nerve roots. The lesions were intimately intertwined in individual fascicles of the roots and could not be removed without sacrificing the roots. Pathological examination of the resected lesions demonstrated benign meningiomas (Figure 2). Postoperatively, his sensory deficits persisted, but his right lower-extremity pain resolved. He had mild weakness in the right gastrocnemius, but his motor examination was otherwise normal. Rectal tone remained intact. The abdominal reflex was now absent on the right. His tendon reflexes were unchanged.

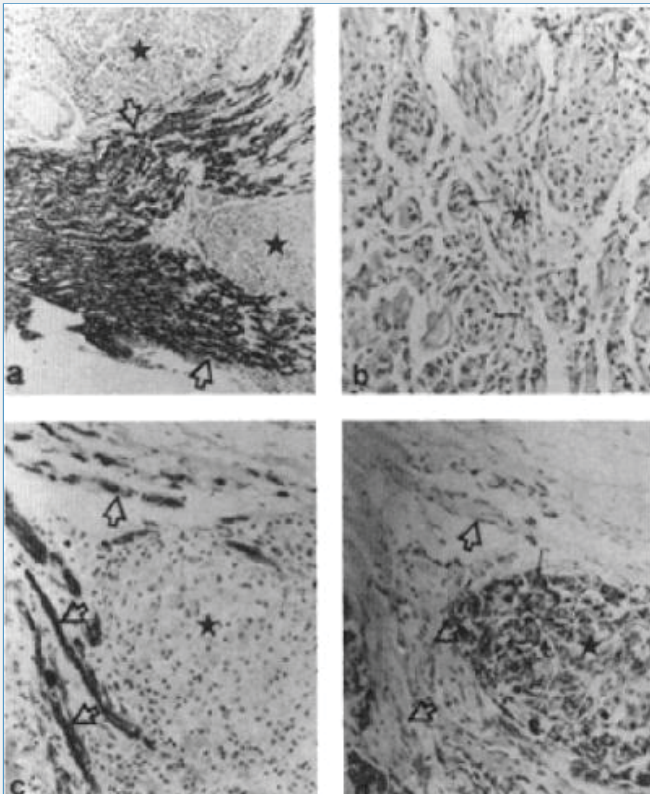


Figure 2. *a*, Photomicrograph showing a segment of peripheral nerve (*open arrows*) branching into the tumor mass (*stars*). Immunoperoxidase staining for S-100 protein is strongly positive in the myelinated nerve fiber. Magnification, $\times 60$. *b*, Photomicrograph of typical tumor tissue (*star*). Note clusters of tumor cells separated by fibrous connective tissue septi. The tumor cells are relatively uniform and form whorls (*arrows*). Hematoxylin and eosin, $\times 200$. *c*, Immunoperoxidase staining for S-100 protein showing immunoreactive nerve fibers (*open arrows*) encircling tumor cells (*star*). Magnification, $\times 200$. *d*, An adjacent section processed for vimentin immunoperoxidase staining shows strongly immunoreactive tumor cells (*arrows*) while nerve fibers remain vimentin negative (*open arrows*). Magnification, $\times 200$.

Magnetic resonance imaging (MRI) of the craniospinal axis was obtained, and intradural extramedullary lesions were noted in the following locations: a 9-mm lesion located posterolaterally on the left at T2-T3; an 11-mm lesion located posteriorly at T3-T4; a 4-mm lesion located anteriorly at T5-T6; a 3-mm lesion located posteriorly at T6-T7; a 7-mm lesion located laterally on the left at T9; a 2-mm lesion located posteriorly at T9-T10; a 4-mm lesion located anterolaterally on the left at T12; and a 5-mm lesion located posteriorly at L4 (Figure 3). No intracranial lesions were detected. Twenty-three days after his first operation, he was returned to the operating room where a T2-T4 laminectomy with removal of the T2-T3 and T3-T4 lesions was performed. Postoperatively, he had marked weakness in both lower extremities and urinary retention that required intermittent catheterization. He underwent 3 weeks of inpatient rehabilitation. At the time of discharge, his examination showed a T4 sensory level on the left and a T5 sensory level on the right, 0- to 1+/5+ motor strength on the right lower extremity and 3+/5+ motor strength in the left lower extremity, hyperactive patellar and absent Achilles deep tendon reflexes, an extensor plantar reflex on the right, decreased rectal tone, a 1+ bulbocavernosus reflex, and a neurogenic bladder. On the day of discharge, a questionable left Horner's syndrome was noted. An MRI scan of the cervical spine was obtained. No lesions were present at the cervicomedullary junction. Likewise, no lesions were seen in the cervical spine. The only postoperative changes were seen at T2.

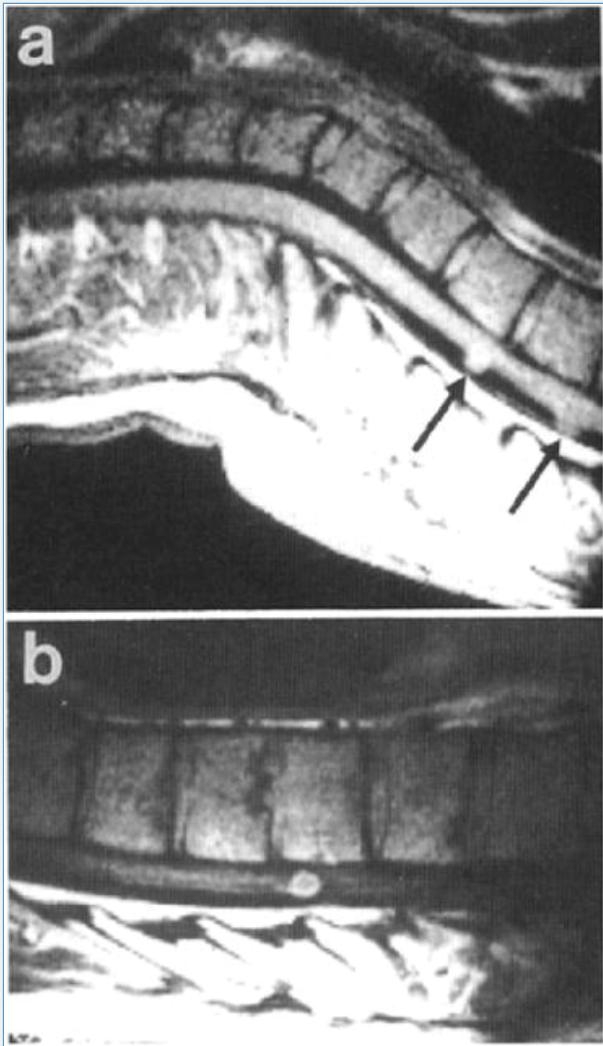


Figure 3. Second echo of a T2-weighted MRI of thoracic spine. *a*, lesions at T2-T3 and T3-T4. *b*, lesion at T9.

Over the next 21 months, the patient continued to have complaints of radicular symptoms in the cervical thoracic and lumbar regions. Serial MRIs detected many new lesions as well as increasing size of the known lesions. The patient had six more spinal procedures during this time, including a cervical laminectomy for removal of a new C2 lesion. In total, the patient had eight operations for the removal of 34 distinctly separate lesions. In each case, the histological appearance was identical-benign meningioma.

Twenty-six months after his initial admission to the University of California, Irvine, Medical Center, the patient was wheelchair bound and still experienced extreme pain in the lower extremities. He underwent a bilateral T1 chordotomy with reasonable control of his pain. The following month, the patient was hospitalized for the treatment of a urinary tract infection. During that admission, he complained of right neck pain. He also noted that his right gums and tongue were numb when he brushed his teeth, and the right side of his face felt numb. He then began to experience episodic spells of nausea, vertigo, and syncope. During one syncopal spell, his systolic blood pressure was noted to decrease from 120 to 80 mm Hg. This hypotension was not associated with a postural change. Examination revealed decreased pinprick and light touch sensation on the right in the distribution of the first and second divisions of the trigeminal nerve, with absent corneal sensation on that side. There was no nystagmus, dysphagia, or dysarthria. An MRI scan revealed a $2 \times 2 \times 1$ cm lesion on the right at the cervicomedullary junction and a small lesion near the left inferior cerebellar peduncle. One week later, both lesions were resected via a suboccipital craniectomy. Again, the histology was meningioma, identical to previous specimens. The patient had a difficult postoperative course and was left with a cranial nerve IV and VI palsy, as well as a decreased gag reflex on the right. He was discharged to the rehabilitation service and eventually home.

He returned 4 months later with recurrent neck pain and stiffness, vertigo, and labile blood pressure. He also complained of a painful pressure sensation in his lower back and legs. An MRI scan revealed recurrence of the cervicomedullary junction lesion and several new cauda equina lesions. He was returned to the operating room where the cervicomedullary junction lesion was removed. In addition, the lumbar region was reexplored and 12 tumors were removed from the cauda equina.

Subsequently, the patient refused further surgical intervention. He had undergone 11 operations, and a total of 47 distinctly separate, yet histologically identical, meningiomas had been removed. In addition, many smaller lesions, presumably also meningiomas, had been identified surgically on nearly every nerve root. The patient did not meet any of the criteria for either Type I or Type II neurofibromatosis. He died 37 months after his initial admission to the Medical Center. An autopsy revealed multiple nodules along the spinal cord and medulla, measuring 0.2 to 2.4 cm in greatest diameter. Single or clusters of tumor nodules were firmly attached to the nerve roots along the entire length of the spinal cord. In the brain stem, the tumor almost entirely encircled and compressed the medulla oblongata (Figure 4). Tumor DNA was analyzed for abnormalities of chromosome 22 by genetic and molecular methods. No abnormalities were detected.

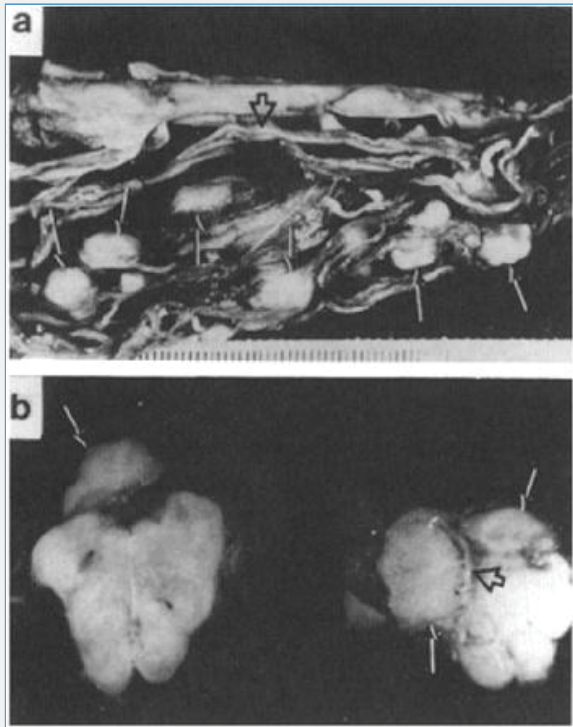


Figure 4. *a*, Gross photograph showing multiple tumor nodules (*closed arrows*) attached to the cauda equina. *Open arrow* points to nerve fibers of the cauda equina. *b*, Cross-sections of the medulla oblongata showing tumor nodules (*closed arrows*) encroaching upon the dorsolateral aspects of the medulla. *Open arrow* points to the fibrous capsule of the tumor nodules

DISCUSSION

Meningiomas comprise a relatively common group of central nervous system neoplasms, accounting for approximately 15% of all intracranial neoplasms and 25% of all intraspinal neoplasms [15,21](#). They are uncommon in children, where they comprise less than 5% of intracranial tumors [13](#). Although the intracranial and intraspinal lesions demonstrate the same histological spectrum, the two locations exhibit a marked difference in distribution on the basis of the patient's sex. Intracranial meningiomas occur more frequently in women, at a rate of 2 to 3:1 [6,12](#). Intraspinal meningiomas, however, favor women at a much higher rate, 6 to 10:1 [6,12,15](#). Receptors for estrogen and for progesterone have been identified on some meningiomas, and hormonal modulation has been suggested as an explanation for this female predilection [17](#).

Meningiomas have been associated with the genetically determined disorders NF type 1, also known as von Recklinghausen NF (NF1) [3,8](#) and NF type 2 also known as bilateral acoustic NF (NF2) [19,23](#). The genes responsible for NF1 and NF2 have recently been localized to chromosomes 17 and 22, respectively [1,11,19](#). Likewise, chromosomal analysis of a number of meningiomas has also revealed chromosome 22 abnormalities. In suggesting a genetic etiology for meningiomas, one might presume that multiple meningiomas would be a common occurrence for this common tumor. Although multiple intracranial meningiomas are well described, the incidence of multiple intraspinal meningiomas is small, estimated at only 2% of all cases of spinal meningioma [3,8](#). As previously mentioned, one rarely sees more than two concurrent intraspinal lesions.

The vast number of lesions suggests a mutation of the gene or genes responsible for tumorigenesis. This could be either a germline mutation or a somatic mutation occurring early in embryogenesis. The genetic disorders most closely associated with meningioma are NF1 and NF2. NF1 and NF2 have also been associated with an increased incidence of other central nervous system neoplasms (neurofibroma, glioma, schwannoma), and with juvenile posterior subcapsular lenticular opacity in NF2 alone [23](#). The diagnosis of NF1 is made by demonstrating two or more of the following: six or more café-au-lait macules larger than 0.5 cm in children or larger than 1.5 cm in adults, one plexiform neurofibroma or more than two neurofibromas of any type, axillary or inguinal freckling, optic glioma, two or more Lisch nodules, sphenoid dysplasia or thinning of long bone cortex without pseudarthrosis, a first-degree relative with documented NF1 [23](#). The diagnosis of NF2 is made by demonstrating bilateral cranial nerve VIII lesions or by demonstrating a unilateral cranial nerve VIII lesion with two or more of the other central nervous system lesions aforementioned in the presence of a first-degree relative with documented bilateral acoustic NF [23](#). Our patient did not meet criteria for either NF1 or NF2.

The relationship between chromosome 22 abnormalities and meningiomas has been an area of intense study by our group, as well as by several others. Chromosome 22 abnormalities have been reported in 50 to 80% of meningiomas [11](#). Frequently, the loss of one of the alleles of chromosome 22 can be appreciated on cytogenetic analysis [14,24](#). Recent studies that use restriction fragment length polymorphisms (RFLPs) have also demonstrated frequent loss of heterozygosity at chromosome 22 [4,20](#). RFLPs are variations in the length or sequence of genomic DNA, which are inherited in a stable fashion. They can change where a restriction enzyme cleaves DNA or alter the size of the restriction fragment by the addition or loss of base pair sequences. When a cell is heterozygous for RFLPs at a particular locus and the DNA is cleaved with the appropriate restriction enzyme and then probed with a fragment of labeled DNA that is complementary for a sequence within the region of the RFLP, then two bands can be identified on electrophoresis gel separation. When a portion of that chromosome is lost, one of the bands will no longer be present. When this type of analysis is applied to peripheral tissue and tumor tissue DNA from the same patient, it can identify loss of heterozygosity within the tumor at the locus of the RFLP. It has been postulated that the loss of heterozygosity at a crucial locus unmasks a recessive gene and allows expression of the tumor phenotype [19](#). Our patient was examined with multiple restriction enzymes and multiple RFLP probes for chromosome 22. Probes at the following loci were informative (peripheral tissue DNA was heterozygous): *c-sis*, *D22S1*, and *D22S9*. These probes have been previously shown to demonstrate loss of heterozygosity in meningiomas [4,20](#). There was no loss of heterozygosity in our patient. In addition, G-band karyotyping was normal.

In summary, this patient represents a unique case of multiple spinal meningiomas. Previous reports describe either malignant lesions or only two lesions in the subjects. Our patient demonstrated 47 histologically confirmed benign spinal meningiomas in the absence of NF1, NF2, or abnormalities of chromosome 22.

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COMMENTS

This report documents 47 distinct lesions in the spinal canal of one patient. Multiple meningiomas were histologically confirmed. Clinical evaluation did not demonstrate evidence of either neurofibromatosis Type I or Type II. This case is interesting for several reasons. First, it was a man; meningiomas are known to be more common in women. Second, multiple tumors have occurred in the absence of one of the phakomatoses. Meningiomas, often multiple, occur frequently in Type II neurofibromatosis, which is known to be a chromosome 22 abnormality. In this patient, neurofibromatosis Type II was excluded by clinical criteria. This case is also interesting in that the multiple tumors were examined for abnormalities on chromosome 22 with several probes. It is of interest that no abnormalities were found. It is not clear how many tumors were examined in this manner. Some tumors may have a small abnormality on chromosome 22 that cannot be detected with only a few probes. However, as larger numbers of lesions are examined, one would expect that the loss of an entire copy of chromosome 22 would most likely occur in some of them. From this case report, it is not obvious what the genetic abnormality is that caused the tumors. One cautionary point should be noted to the readers. In patients with multiple tumors, each tumor must be treated as an individual entity and it is the patient's symptoms and the patient himself or herself who must be treated, not the radiological abnormalities. Whether one chooses surgery or radiosurgery must be judged on the basis of an expanding lesion and symptoms. The mere presence of multiple tumors does not justify their removal. This must always be kept in mind when dealing with patients with multiple nervous system tumors.

Robert L. Martuza

Washington, District of Columbia

COMMENTS

Chaparro and colleagues describe a unique case of multiple spinal meningiomas without any evidence of neurofibromatosis, either clinically or on chromosomal analysis. Despite multiple surgical procedures, the patient eventually died when he developed brain stem meningiomas. This is the first such description of multiple benign spinal meningiomas that are not associated with von Recklinghausen's disease.

William A. Friedman

Gainesville, Florida

KEY WORDS: Brain neoplasm; Genetics; Meningioma; Multiple meningiomas; Neurofibromatosis

IMAGE GALLERY

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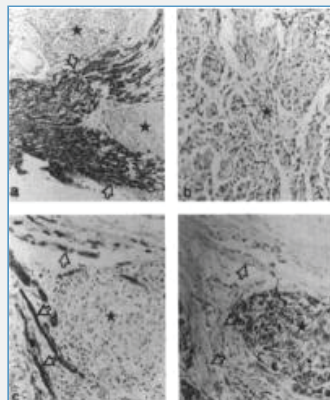


Figure 2



Figure 1

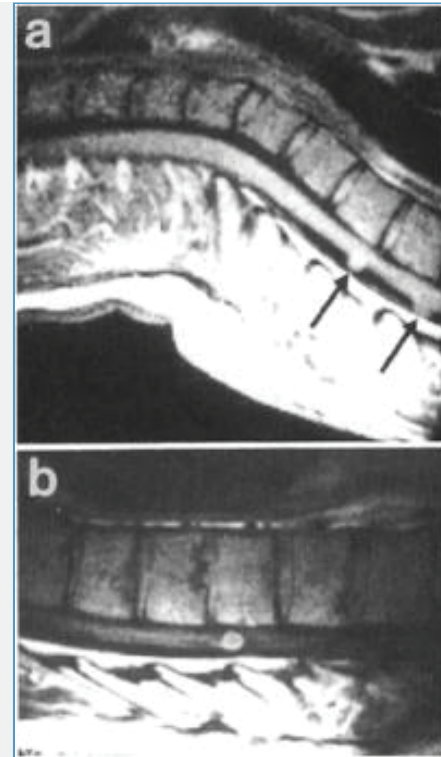


Figure 3

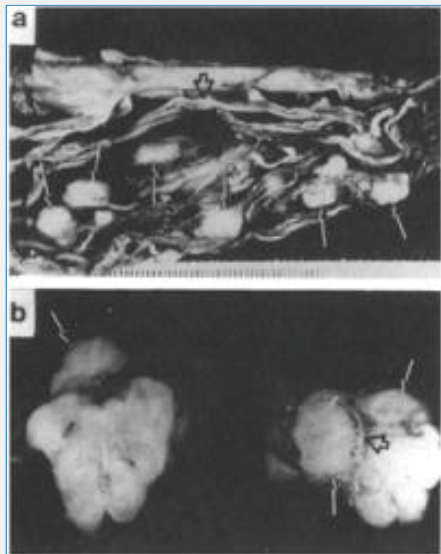


Figure 4

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