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Spinal MR Findings in Neurofibromatosis Types 1 and 2

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Purpose: To evaluate the frequency and nature of spinal pathology, the frequency of clinically silent lesions, and the potential benefit of screening spinal MR in neurofibromatosis patients. **Patients and Methods:** 28 neurofibromatosis type-1 (NF-1) patients and nine neurofibromatosis type-2 (NF-2) patients were studied with postcontrast spinal MR imaging. **Results:** NF-1: One patient had a biopsy-proven low-grade glioma; five patients, intradural, extramedullary masses (N = 23); one patient, extradural masses (N = 2) (neurofibromas); 16 patients had bony abnormalities; and three patients thecal sac abnormalities. NF-2: Five patients demonstrated intramedullary masses (five/eight ependymomas); nine patients, intradural, extramedullary masses (meningiomas, schwannomas); and four patients, bony abnormalities. Eight/10 NF-1 and four/nine NF-2 patients had asymptomatic masses. **Conclusion:** Intradural disease is common, often asymptomatic, and often presents at a young age in NF-1 and NF-2 patients. Because of the propensity to develop significant asymptomatic as well as symptomatic intradural disease, screening of the entire spine with MR is recommended in both NF-1 and NF-2 patients.

Index terms: Neurofibromatosis; Spine, magnetic resonance; Nerves, spinal; Spinal cord, magnetic resonance

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Neurofibromatosis type-1 (NF-1, von Recklinghausen disease, formerly peripheral neurofibromatosis) and neurofibromatosis type-2 (NF-2, bilateral acoustic neurofibromatosis, formerly central neurofibromatosis) have been accepted as distinct disorders with different genetic etiologies (1, 2). The cranial magnetic resonance (MR) findings of NF-1 and NF-2 have recently been described (3). Although not reported as distinct for each type, bony changes of the spine, thecal sac abnormalities, and myelographic findings of neurofibromatosis have also been well documented in the literature (4–8). The spinal MR findings of neurofibromatosis, as distinct for types 1 and 2, have not been reported.

In this study, we compared the spinal MR findings of 28 patients with NF-1 and nine patients with NF-2. The objectives of the study were: 1) determine the frequency of spinal pathology in NF-1 and NF-2, 2) better define spinal pathology in each group, 3) review the frequency of clinically silent lesions, and 4) determine if screening of the spine with MR imaging would be clinically beneficial in either group.

Patients and Methods

MR imaging of the spine was performed on nine patients with NF-2 and 28 patients with NF-1. Thirty of thirty-seven patients were imaged with a 1.5 T unit (General Electric, Milwaukee, WI). The remaining seven patients were scanned on a 0.6 T unit (General Electric). Initially, pre- and postcontrast T1-weighted images, as well as T2-weighted images, were obtained on three patients. Because of time constraints, this was later changed to enhanced T1-weighted images only. All patients had imaging of the entire spine in the sagittal plane, with axial images obtained at selected levels to better define pathology. Gadolinium-DTPA was given intravenously at a dose of 0.1 mmol/kg. A spin-echo pulse sequence was used to obtain T1-weighted images 400-1000/12-34/2-4 (TR/TE/excitations) with a matrix size of 192 × 256 with 4 excitations for sagittal and 2 excitations for axial images. Section thickness was 3–5 mm with a 1–2.5 mm intersection gap and field of view of 20–32 cm. Studies were performed between May 1988 and August 1990.

The NF-2 group consisted of nine patients (8 women, 1 man; age range of 17–41 years; mean of 23 years). The

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NF-1 group included 28 patients (20 females, 8 males, age range of 2–51 years; mean of 15 years). Diagnosis was based on clinical criteria established by the NIH Consensus Development Conference in 1988 (2). Patient selection for inclusion in this study was based on a clinically established diagnosis of neurofibromatosis with both symptomatic and asymptomatic patients included.

Each patient had a complete neurologic examination as well as review of clinical records by the Neurology Department within 1 week of the MR examination as part of this study. Clinical and pathologic information was also obtained by retrospective chart review.

Images were independently reviewed by three neuroradiologists (J.E., D.B., J.R.) without benefit of the results of the neurologic examinations. Results of MR imaging were subsequently correlated with neurologic findings to evaluate the frequency of clinically silent lesions.

TABLE 1: Results of MR findings

	NF-1		NF-2	
	No. of Patients (n = 28)	No. of Tumors/ Abnormalities	No. of Patients (n = 9)	No. of Tumors/ Abnormalities
Abnormal study	17		9	
Masses				
Intradural				
Intramedullary				
Definite	1	1	5	8
Possible	3	3	0	0
Extradmedullary	5	23	9	109
Extradural	1	2	0	0
Other masses	3	3	5	5
Bony abnormalities	16	35	4	8
Dural ectasia	3	3	0	0

Results

NF-2

Nine of nine patients in the NF-2 group had an abnormal study. Intradural disease was found in all patients. A total of eight enhancing, intramedullary masses were found in five patients, six of which were cervical in location and two thoracic.

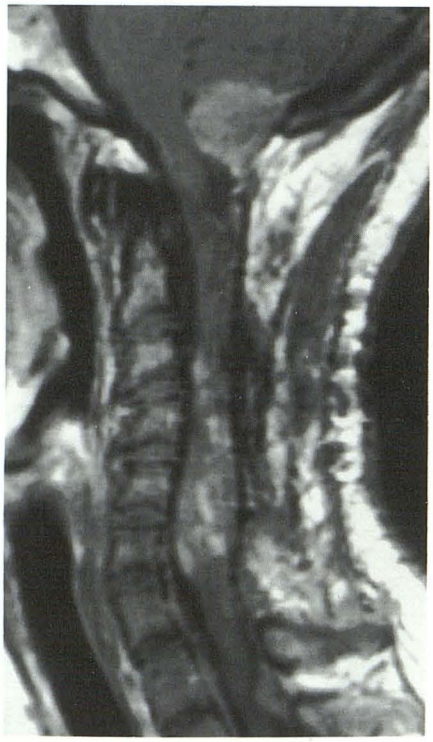
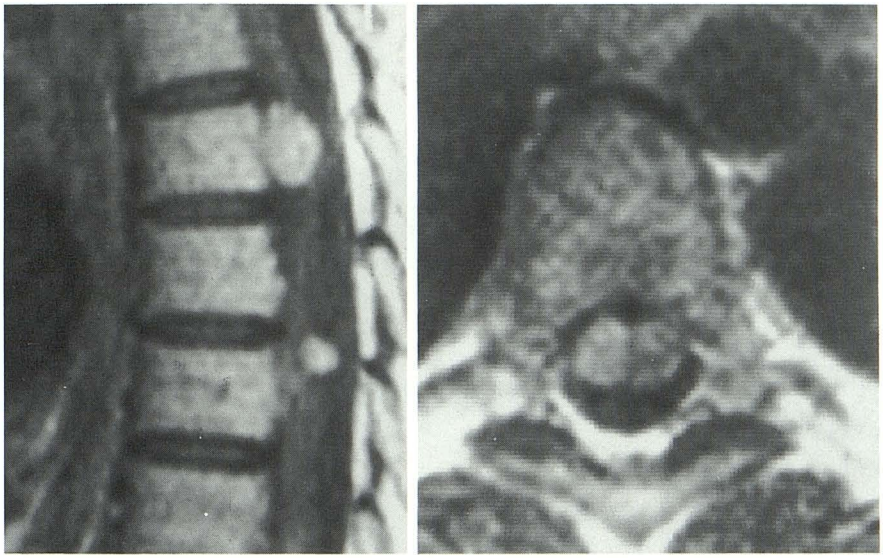


Fig. 1. An 18-year-old NF-2 patient with history of chronic right hemiparesis; no acute cervical symptoms. Sagittal T1-weighted image (500/15) of the cervical spine after contrast administration demonstrates a widened cervical cord with inhomogeneous enhancement. There is a pathologically proven ependymoma. A foramen magnum meningioma is also present.

Pathology was available on five masses, all of which were ependymomas (Fig. 1). The average patient age in this group with intramedullary masses was 25, with four of five patients less than 24 years of age (Table 1).

Nine of nine patients had enhancing, intradural, extramedullary masses consistent with schwannomas or meningiomas (Figs. 2 and 3). The number of these masses in each patient ranged from two to 34 (average of 12) with a slight predominance of masses in the thoracic and lumbar spine (C28, T38, L43). Three pathologically confirmed meningiomas and seven schwannomas were removed from one 22-year-old patient. A total of four large dumbbell-type schwannomas were found in three patients, three of which were cervical in location and one lumbar (Fig. 4). Five of nine patients had masses of more than one histology. The remaining four patients had multiple masses at different levels, however, pathologic correlation was not available. Incidental masses included a mediastinal schwannoma, two parapharyngeal schwannomas, a carotid sheath schwannoma, and a schwannoma of the neck.

Two of five patients with intramedullary masses had clinical symptomatology related to their cord lesions. The single patient with three pathologically proven meningiomas had clinical symptoms that correlated with two thoracic masses (Fig. 2). Two other patients, one with a large lumbar dumbbell-type schwannoma and one with a parapharyngeal schwannoma, had symptoms related to the location of their masses. The remaining patients in the NF-2 study group had no neurologic symptoms that correlated with findings on imaging (Figs. 1, 3, and 4).



A B

Fig. 2. A 22-year-old NF-2 patient with severe back pain.

A, Sagittal T1-weighted image (500/24) shows enhancing intradural, extramedullary masses at the T6 and T8 levels. The mass at the T6 level was pathologically proven to be a meningioma and the mass at the T8 level a schwannoma.

B, Axial T1-weighted image (500/24) demonstrates displacement of the spinal cord to the left by enhancing meningioma at T6 level.

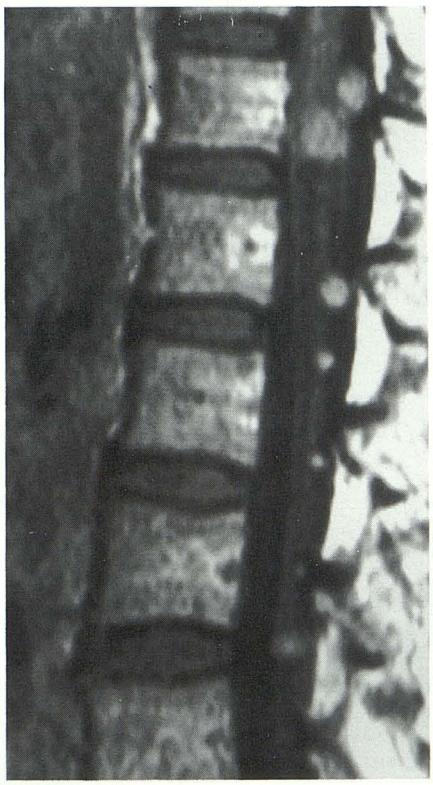


Fig. 3. A 41-year-old asymptomatic NF-2 patient. Sagittal T1-weighted image (500/24) of the thoracolumbar spine after contrast administration demonstrates typical findings of multiple enhancing intradural, extramedullary masses (schwannomas).

Secondary bony abnormalities were seen in four patients. These included enlargement of neural foramina secondary to dumbbell-type masses in three patients (Fig. 4) and posterior vertebral scalloping secondary to an intramedullary mass in one patient.

NF-1

Eleven of 28 patients had a normal study. A nonenhancing, cervical, intramedullary mass (Fig. 5) was found in a patient who presented with paresthesias of the right upper extremity. Biopsy revealed a low-grade astrocytoma. Three additional patients had findings on imaging that suggested intramedullary disease (widened cord in two, inhomogeneous signal in the cord in one).

Twenty-three enhancing, intradural, extramedullary masses, consistent with neurofibromas, were seen in five patients with a predominance in the lumbar spine (C4, T3, L15, S1). Two cervical extradural masses, consistent with neurofibromas, were seen in one patient. Incidental lesions included a parapharyngeal plexiform neurofibroma, bladder neurofibroma, and a paraspinal neurofibroma.

There were no clinical symptoms related to lesion location in the five patients with intradural, extramedullary masses; one patient with extradural masses; or three patients with possible intramedullary masses.

Bony abnormalities were found in 16 patients. Eight patients demonstrated enlarged neural foramina. In five patients, this finding was secondary to neurofibromas and, in three, secondary to dural ectasia or an arachnoid cyst. Posterior vertebral scalloping was seen in four patients. An arachnoid cyst was the etiology in one patient with the remaining three patients having no associated mass. The findings were felt to be secondary to dural ectasia in these three patients (Fig. 6). The C2 and C3 vertebral bodies were

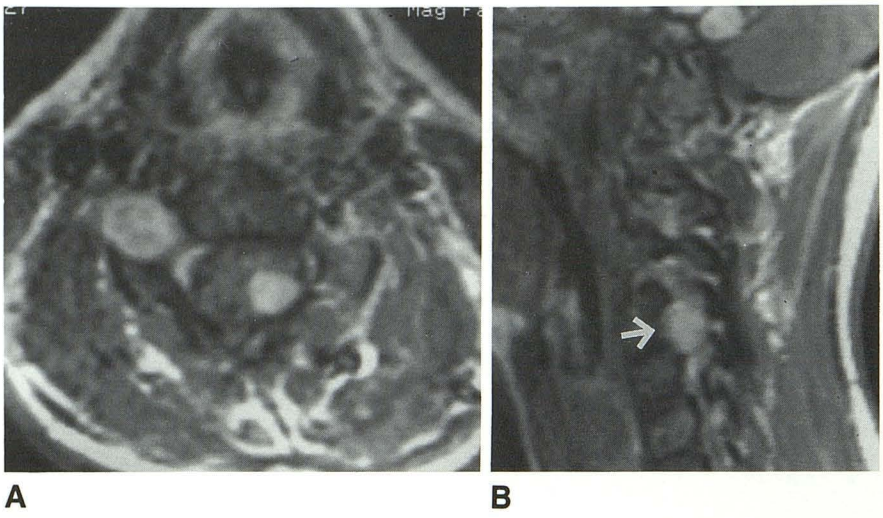


Fig. 4. A 20-year-old NF-2 patient who is asymptomatic relative to the cervical spine.

A, Axial T1-weighted (500/24) postcontrast image demonstrates an enhancing cervical dumbbell type mass (schwannoma) extending through the neural foramen on the right. Intradural, extramedullary mass is seen at the same level on the left (schwannoma).

B, Sagittal T1-weighted image (500/24) after contrast shows enlargement of cervical neural foramen (*arrow*) secondary to enhancing dumbbell mass (schwannoma). Enhancing acoustic schwannoma is noted in the posterior fossa.

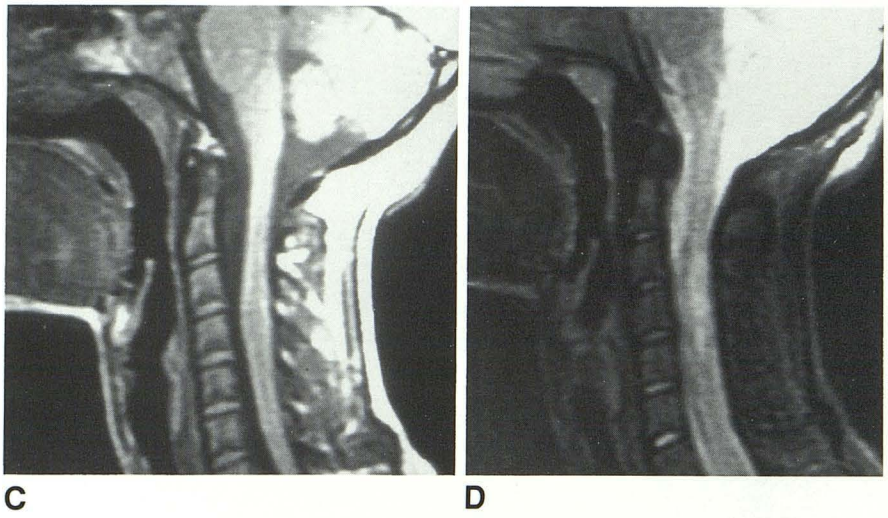


Fig. 5. A 15-year-old NF-1 patient with paresthesias of the upper extremities. Sagittal T1- (*A*) (600/20) and T2- (*B*) (2000/80) weighted images demonstrate an enlarged cervical cord (T1) with abnormally increased signal (T2). Biopsy revealed low-grade astrocytoma.

destroyed by a soft-tissue mass in one patient, which has not been biopsied. Three patients demonstrated scoliosis.

Discussion

Tilesius recorded the first description of neurofibromatosis in 1793, in which he noted the cutaneous lesions of molluscum fibrosum. Von Recklinghausen was the first to recognize the neural origin of the disease in 1882 when he described two patients with multiple skin and subcutaneous neurofibromas (9). More recently, the genetic basis of the disease has been established with NF-1 and NF-2, now recognized as distinct genetic entities (1, 2).

NF-1 is an autosomal dominant with the gene locus localized near the centromere on chromosome 17 (1, 10). Approximately 50% of cases represent new somatic mutations with penetrance approaching 100%. The mutation rate is among the highest observed in humans and the disease represents the most common genetic disorder of the nervous system affecting approximately 1/4000 individuals (2, 11, 12). It also accounts for greater than 90% of cases of neurofibromatosis (13).

NF-2 is also an autosomal dominant trait caused by a deletion in the long arm of chromosome 22. The mutation rate is uncertain but penetrance approaches 95% and the incidence is approximately 1/50,000 individuals. In 1988, the NIH Consensus Development Conference established clinical criteria for diagnosis of the two disorders (1, 2).

Tumors

Multiple intradural tumors are characteristic of NF-2 (nine of nine patients). Intramedullary

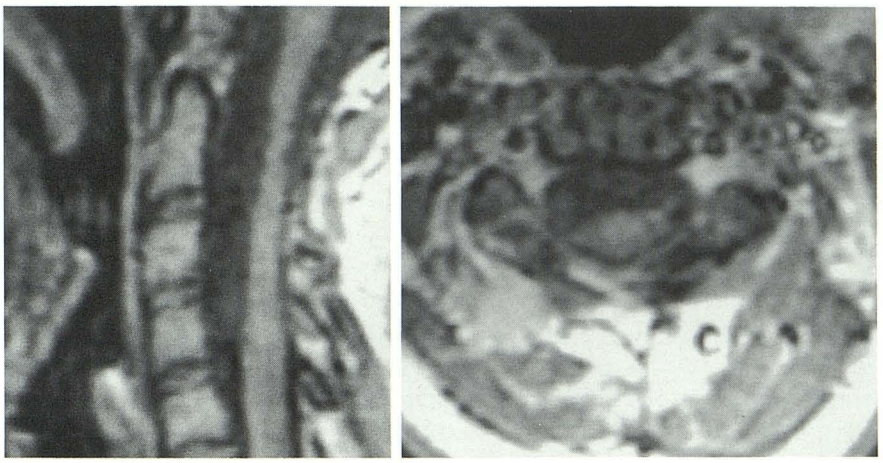


Fig. 6. Asymptomatic 20-year-old NF-1 patient.

A, Sagittal T1-weighted image (500/24) demonstrates posterior scalloping of cervical vertebral bodies (C3-C5) with large subarachnoid space. Findings compatible with dural ectasia.

B, Axial T1-weighted image (500/24) shows a large cervical subarachnoid space with spinal cord narrowed in anteroposterior dimension. No associated mass was present.

masses are common (five of nine patients), with a high frequency of ependymomas as previously noted by Rubinstein and confirmed by our study (five of five masses) (1, 14). These masses usually occur in cervicothoracic region (five of five masses) (Fig. 1). They often present in younger patients (in their 20's), may be multiple (two of five patients), and may be clinically silent (three of five patients). Syringomyelia can be associated with these intramedullary masses, but was not observed in our NF-2 patient population (15).

In contrast, intramedullary tumors are more unusual in the NF-1 population. One biopsy-proven, low-grade astrocytoma was found in 28 patients (Fig. 5), with three additional NF-1 patients having findings on imaging suggestive of intramedullary disease. The incidence of subtle intramedullary lesions in these patients, such as hamartomas of the spine, may be potentially underestimated in our study, as T2-weighted images were not obtained because of time constraints (16).

Intradural, extramedullary masses are also characteristic of NF-2 (nine of nine patients) with meningiomas and schwannomas most commonly found. Meningiomas are usually thoracic in location and tend to occur at an earlier age (20's) than the general population age (40's). Often more than 10 schwannomas are found (average 12) with a slight predominance in the lumbar region (Figs. 2 and 3). These masses are usually extramedullary in location, but can have both intra- and extradural components (dumbbell) as well. Large dumbbell-type masses are also relatively common in NF-2 (three of nine patients) and usually are found in the cervical spine (three of four masses) with a larger extradural component (Fig. 4) (17).

Intradural, extramedullary and extradural disease was also found in the NF-1 population, however, the incidence does not approach the NF-2 population. Intradural, extramedullary disease was found in five of 28 NF-1 patients and extradural disease in one of 28 patients. There was a relatively equal distribution of masses throughout the spine, which agrees with previous authors reports (15). Multiple asymptomatic masses were common in both NF-1 (eight of 10) and NF-2 (four of nine) patient populations (Figs. 3 and 4). Incidental soft-tissue masses (mediastinal, parapharyngeal, carotid sheath, neck schwannomas (NF-2); neurofibromas of the neck, bladder and paraspinal areas (NF-1)), not directly related to the spine, were seen in both patient populations.

The difference in incidence of pathology between the NF-1 and NF-2 populations may be partially related to the younger age of the NF-1 group (mean, 15) compared to the NF-2 group (mean, 23). Further studies evaluating spinal pathology in an older NF-1 population may be beneficial to allow an age-matched comparison of patient populations.

Bony Abnormalities

The incidence of bony abnormalities of the spine is similar in both populations occurring in 16 of 28 NF-1 patients, as compared to four of nine NF-2 patients. Enlargement of neural foramina and posterior vertebral scalloping may emanate from several causes, including dural ectasia, tumor, and arachnoid cyst (5–7, 18, 19). In the NF-1 group, eight patients had enlarged neural foramina, five of which were secondary to a mass lesion (extramedullary or extradural) and three

secondary to dural ectasia. Posterior vertebral scalloping was seen in four patients, with only one having an associated mass (arachnoid cyst) to explain this finding. The remaining three patients were felt to have dural ectasia (Fig. 6).

In the NF-2 group, enlarged neural foramina (Fig. 4) were seen in three patients and posterior vertebral scalloping in one patient, with masses present in all patients to explain these findings. Scoliosis was noted in three patients in the NF-1 group with no evidence of associated masses or dysplastic bony changes.

Our study indicates that overall frequency of bony changes of the spine are similar in NF-1 and NF-2. However, primary dysplastic bony changes may be confined to the NF-1 population whereas secondary bony changes associated with masses may be seen in both the NF-1 and NF-2 groups. Scoliosis was seen in the NF-1 group only, however, this may be secondary to the small number of patients in the NF-2 group.

The cranial MR findings in NF-1 and NF-2 have previously been described (3). In that study, it was found that patients with NF-1 had tumors of astrocytic (optic and parenchymal gliomas) and neuronal (neurofibromas) origin. Foci of abnormally increased signal intensity on T2-weighted images (thought to represent hamartomas) were the most common parenchymal abnormality. In contrast, patients with NF-2 developed tumors of the meninges (meningiomas) and schwann cells (schwannomas). Our findings corroborated the above conclusions with an intramedullary astrocytoma as well as multiple neurofibromas seen in the NF-1 group, and multiple meningiomas and schwannomas seen in the NF-2 group. Ependymomas were the only intramedullary tumor found in the NF-2 group, however, again, the overall incidence of intramedullary lesions in both of these groups may be potentially underestimated, as T2-weighted images were not obtained. Primary dysplastic bony changes and dural ectasia were found in the NF-1 group only in both studies.

Thecal Sac

Dural ectasia is an uncommon finding in the NF-1 population, seen in three of 28 patients. It does represent the most common cause of posterior vertebral scalloping (three of four patients) in this group and it may occur at any level. It usually affects multiple levels (4, 20). Dural ectasia was not seen in the NF-2 group.

In conclusion, we found a significant incidence of intradural disease in the NF-2 population. Intramedullary disease is common and often asymptomatic with multiple tumors presenting at a young age. Multiple intradural, extramedullary masses (meningiomas/schwannomas) should be expected in the NF-2 population. Intramedullary disease has an increased incidence in the NF-1 population compared to the general population. Intradural, extramedullary and extradural masses are seen in this group, however, the incidence does not approach the NF-2 population. Primary dysplastic bony changes and dural ectasia appear to be confined to the NF-1 population. Because of the significant incidence of symptomatic and asymptomatic intradural pathology in both NF-2 and NF-1 populations, screening of the entire spine with contrast-enhanced T1-weighted, as well as T2-weighted, images is recommended.

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