Fractionated Focal Radiotherapy

for Intramedullary Spinal AVMs: Ten Years' Experience

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Abstract

Object: Radiosurgery for spinal AVM's is becoming a practical therapeutic option as methodology improves, but no comparative study has yet been published of focal fractionated radiotherapy. We report here our experience with conventional and hypofractionated radiotherapy for spinal AVM. **Methods**: Candidates for this study were patients who had symptoms due to an intramedullary AVM but were ineligible for embolization or surgery. Of 21 patients with spinal AVMs, there were 10 such cases in the past 10 years. Angiography and enhanced computed tomography (CT) were used for treatment planning in all cases. Fractionated radiotherapy with a linear accelerator, extra-cranial immobilization system and frequent orthogonal linacographic verification were used. The starting dose was 32 Gy in 2, 36Gy in 3, 40Gy in 2 patients, using a regime of 1.8-2.0 Gy daily which was recently changed to a hypofractionation schedule of 30Gy/8 in 1 and 20Gy/4 in 2 patients. **Results**: Follow-up ranged from 26 to 124 (median of 49) months. There were no hemorrhages nor any adverse reactions attributable to radiation. Of the seven patients who consented to follow up angiography, the nidus decreased in size in five, but none with complete obliteration. **Conclusion**: Since none of our study patients had adverse effects, the maximum tolerable dose for the spinal cord associated with an AVM could not be identified, though it presumably is higher than the doses administered. The absence of rebleeding in patients without complete angiographic occlusion

suggests that the natural history of spinal AVMs may be less aggressive than previously reported.

Running title: Stereotactic Irradiation for Intramedullary AVMs

KEY WORDS • spinal arteriovenous malformation • intramedullary • irradiation• subarachnoid hemorrhage

Introduction

Intramedullary AVM's haves a nidus within the spinal cord parenchyma, usually fed by both anterior and posterior spinal arteries and draining into both anterior and posterior spinal veins. Subarachnoid or intramedullary hemorrhage is the most common clinical presentation. Shephard, et al., [20] reported a high incidence of multiple hemorrhage in their series; 10 out of 22 patients showed multiple hemorrhage within 24 years and developed paraplegia or severe paraparesis.

The ideal treatment of intramedullary AVMs is complete occlusion of the nidus without any new neurological deficit. Direct surgical extirpation carries a high risk of serious complications, although some series have reported good result.[20, 28] Surgical interruption of feeding arteries is simple, but is effective only in the short-term because alternative feeding arteries develop. Embolization may be effective, but carries the risk of serious and irreversible neurological complications and may be only temporarily effective[6, 8, 12].

Stereotactic radiosurgery using single high dose or hypofractionated irradiation is an effective treatment for small intracranial AVMs.[1, 2, 17] By extrapolation, stereotactic radiosurgery for spinal AVMs may offer an attractive occlusion rate[7, 11]. However, rates of radiation-induced injury to the associated spinal cord may be less acceptable than in the brain, because the spinal cord is more vulnerable and injury more often permanent. Though fractionated irradiation

using conventional daily doses is thought to be less effective than radiosurgery, it seems to have a lower risk of complications while still offering a 20 to 30% rate of occlusion.[17] With the rate of spontaneous hemorrhage in spinal AVMs being high and their consequences devastating, a 20 to 30% occlusion rate may be an attractive option in those patients with limited alternatives. However, there has been no systematic study of the tolerance of the spinal cord associated with AVMs to even a conventional fractionation schedule.

Over 10 years we have carefully studied the management of spinal AVMs with fractionated irradiation in patients who were not eligible for treatment with other methods. Because this disorder is rare and requires a long observation period, our treatment techniques reflect the improvements and changes in dose scheduling that have occurred over the time of the study. Therefore, we present this retrospective analysis as a starting point which might be of benefit in the design of future clinical trials of single dose radiosurgery.

Methods

Since 1982, out of 89 patients with spinal AVMs treated in our hospital, 21 had intramedullary AVMs. Ten of these 21 cases, though symptomatic, were ineligible for embolization or surgery and were offered close follow-up or focal radiotherapy. All opted to enter the radiotherapy trial. All of these patients were diagnosed after an acute intramedullary or subarachnoid hemorrhage. Four patients had multiple hemorrhages before irradiation. There were 6 women and 4 men, from 15 to

50 years of age (median 25 years). Four lesions were in the cervical and 6 in thoracic spinal. Angiography demonstrated intramedullary AVMs fed mainly by the anterior spinal artery in all patients. Three patients had been treated with embolization and 2 with surgery prior to focal radiotherapy. Embolization was performed using polyvinyl alcohol (PVA) particles (Contour; Boston Scientific Co., Natick, MA). Informed consent was obtained from all patients before entry into the study.

Treatment methods changed during the period of the study. From 1982 to 1999, focal radiotherapy using relocatable localization devices was used. For cervical spinal AVMs, treatment center coordinates were calculated from angiography using external fiducial markers attached to the head ring, with an accuracy of ± 2 mm (Figure 1). For thoracic and lumber spinal AVMs, computed tomographic simulation (CT-simulator) was used without external fiducial markers, with an accuracy of ± 1mm[21]. Orthogonal-plane angiography and CT scanning were undertaken and the relationship of the AVM nidus to the corresponding vertebral bodies calculated. The thoracic and lumbar vertebrae were not fixed, but rather the vertebral bodies themselves were used as reference for the co-ordinates. Repositioning accuracy depended on the linacographic determination of the vertebral bodies, with the overall accuracy of this technique ~~was~~ estimated to be ± 3 mm. Because of this uncertainty, we chose irradiation ports consisting of either a single posterior field or two oblique fields. Patients remained supine on the table to minimize the effects

of posture and respiration on the position of the spinal cord. The clinical target volume was defined as the nidus of the AVM as shown by angiography, as delineated by a neuroradiologist, and registered on CT images using the vertebral bodies as landmarks. A 3-dimensional radiotherapy planning system was used for dose calculation. The initial 7 patients underwent fractionated radiotherapy with a linear accelerator and orthogonal linacographic verification. The doses were prescribed at the center of CTV. The initial dose given was 32 Gy, increasing to 40 Gy in 20 fractions using 1.8 – 2.0 Gy per day (Table 1).

In view of significant technical improvements during the period of the study, treatment of the 3 most recent patients included use of a real-time tumor-tracking radiation treatment (RTRT) system with localization accuracy of ±1.5 mm such that the dose to a part of the spinal cord in the same slice level can be reduced to less than 50 % of the prescribed dose. Details of such an RTRT system have been described elsewhere.[21, 22, 23] Three round gold markers (diameter 2.0 mm) were inserted transcutaneously or by open surgery onto the surface of the appropriate laminae. A linear accelerator was synchronized to irradiate the nidus only when the gold markers were located in the planned position ±1.5 mm (Figure 2). Rotational set-up error was also calculated from the three markers[15]. With such improvement in localization technique, dose fractionation was changed to a hypofractionated schedule and non-coplaner mutiple fields (Table 1). Thus the dose given to a part of the spinal cord in the same transaxial level can be reduced by the RTRT system without fear

of underdosing the AVM nidus (Fig 2).

Results

The follow-up period ranged from 26 to 124 months (median of 49 months). All 10 patients had a satisfactory neurological outcome. None showed any symptomatic or radiographic signs of hemorrhage after treatment. Leg strength was improved in 2 and stabilized in 8. There was no complication related to radiation. Seven patients agreed to follow-up angiography (Table 1). In 5 of 7 cases, angiography demonstrated a decrease in size of the nidus and its feeding arteries. MRI showed reduction of AVM size and/or decrease of flow void in these 5 patients. Complete AVM obliteration was not observed in any patient during this study period.

Illustrative cases

Case 1: A 34-year-old man experienced sudden numbness in his right hand in May 1984 which lasted for 1 month. In September 1985, he had sudden weakness of right hand with transient pain and numbness of right foot. In November 1985, he experienced weakness in his right leg, was diagnosed with spinal AVM and transferred to our institute. On admission, there was weakness and upgoing Babinski response in both the legs, hypalgesia and hypesthesia below the level of T5, diminished vibration sense below the iliac crest, dysesthesia of the right foot, bladder and bowel dysfunction and a spastic gait. MRI revealed multiple flow voids in front of, behind

and within the spinal cord (Fig. 3-A) associated with low intensity within the cord suggesting hemosiderin due to previous hemorrhage (Fig. 3-B). Angiography showed an intramedullary AVM fed by the right C7 segmental artery via the anterior spinal artery (Fig. 4-A). Trans-arterial embolization was performed using polyvinyl alcohol (PVA) powder. After embolization, the nidus was completely embolized and the patient's symptoms improved. However, recanalization occurred 6 months later, and required 2 more subsequent embolizations. The patient agreed to enter the radiotherapy trial in September 1991. Stereotactic irradiation was performed with an initial dose of 36 Gray followed by a daily dose of 1.8 Gray four times a week. Symptoms of numbness and dysesthesia in the right foot gradually decreased after irradiation. Angiography 3 years after radiation (Figure 4-B) showed marked reduction in size of the nidus. Ten years after radiation, MRI showed diminished flow void (Fig. 5-A, B), and DSA did remarkable reduction (nearly obliteration) of the AVM (Fig. 6-A, B). He has experienced no hemorrhage for more than 10 years and has been working normally after STI.

Discussion

The maximum tolerable dose of radiation for normal spinal cord has been reported to be 50 Gy using a conventional fractionation schedule,[3] but that for cord adjacent to an AVM is not known. Since the spinal cord may be compressed by the enlarged vascular components of an AVM, the maximum tolerable dose may be lower than that of normal cord. Our results showed

no injury to the spinal cord adjacent to an AVM after administration of 36 to 40 Gy using daily doses of 1.8 to 2.0 Gy. Wolkov, et al.,[23] reported two cases of spinal AVMs that were treated by conventional radiation therapy. Their patients underwent decompressive laminectomy followed by irradiation of 45 Gy and 50 Gy respectively which caused no radiation damage with a follow-up of more than 5 years. Their findings are consistent with the present study. Since that time, the use of hypofractionated irradiation for spinal AVMs has been reported by Stanford University using 21 Gy in 3 fractions.[19] Following their lead, we have been using hypofractionated irradaition and have experienced no complications to date. We must point out that while the results of these and our own studies are informative, the maximum tolerable dose of conventional or hypofractionated radiotherapy has not yet been reached and remains to be defined.

Because of their rarity, the incidence of hemorrhage from spinal AVMs and their natural history remain to be defined. Shephard, et al.,[19] reported that 10 (45%) of 22 patients experienced repeated hemorrhages. This incidence is much higher than the 5% annual bleeding rate (i.e. 18.5% cumulative bleeding rate over 4 years) for intracranial AVMs.[16] In our series, the incidence of hemorrhage was zero in 10 patients over 4 years, with clinical improvement in some. This incidence is lower than that that expected from Shephard, et al.'s report (4 of 10), and closer to that for cerebral AVMs~~,~~. This observation may simply be an artifact of small sample size (true

of all reports studying this disease), differences in patient populations, or an actual effect of radiation. Since it is known that partial occlusion of cerebral AVMs does little to reduce the risk of hemorrhage, [10] one would expect little protective effect of radiation against bleeding from spinal AVMs as well, though a therapeutic effect cannot be definitively ruled out in this study. Another possibility is that the natural history of spinal AVM may not be as aggressive as has been previously reported.

There have been several attempts to treat spinal lesion with radiosurgery[6, 10, 14, 19]. One may expect the effectiveness of radiosurgery for spinal AVMs to be comparable with that for cranial AVMs if dose distribution is optimally conformal. This study provides baseline~~ic~~ data about the risks and effects of low-dose fractionated radiotherapy for spinal AVMs. The present results~~,~~ do not warrant routine clinical use of fractionated focal radiotherapy for spinal AVMs, but do suggest that further studies may be worthwhile.

Recent innovations such as the fluoroscopic RTRT system and internal fiducial markers now allow stereotactic irradiation for spinal disease with real-time verification and an accuracy of ± 1 mm for every 0.03 seconds.[22, 23] Small-field radiation can be given with confidence in its accuracy and the ability to reduce radiation dose to the unaffected spinal cord. Image-guided radiation for spinal disorders is reported to be accurate by other investigators as well.[19]

Conclusion

We treated 10 patients with intramedullary AVMs using fractionated focal radiotherapy. Five out of 7 (71%) patients showed reduction of nidus size on angiography, but no complete obliteration was obtained. There was no rebleeding in the follow-up period nor any complication related to radiation. The rate of hemorrhage in the natural history of spinal AVM may be lower than previously reported.

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Figures and Legends

Figure 1 Relocatable immobilization device

Figure 2 Real-time tumour-tracking radiotherapy system

Figure. 3 A and B: MRI showed marked multiple flow voids ventral, dorsal and within the cervical spinal cord and parenchymal low intensity at C7.

Figure 4 A: Selective angiography of right C7 segmental artery, anteroposterior view, revealing intramedullary AVM via anterior spinal artery before fractionated focal radiotherapy. B: Angiography 3 years after radiation, anteroposterior view, showing marked reduction in size of the nidus.

Figure. 5 MRI 10 years after fractionated focal radiotherapy, (A: T1 weighted image, B: T2 weighted image) showing no flow void.

Figure 6 Selective angiography of right (A) and left (B) C7 segmental artery, anteroposterior view, showing nearly occlusion of the AVM 10 years after the radiation.

Table 1: Summary of Clinical data in patients with intramedullary AVMs treated with fractionated focal radiotherapy. M = Male, F = Female, Embo.= Embolization, Unchanged $^{\#}$ = Unchanged on MRI

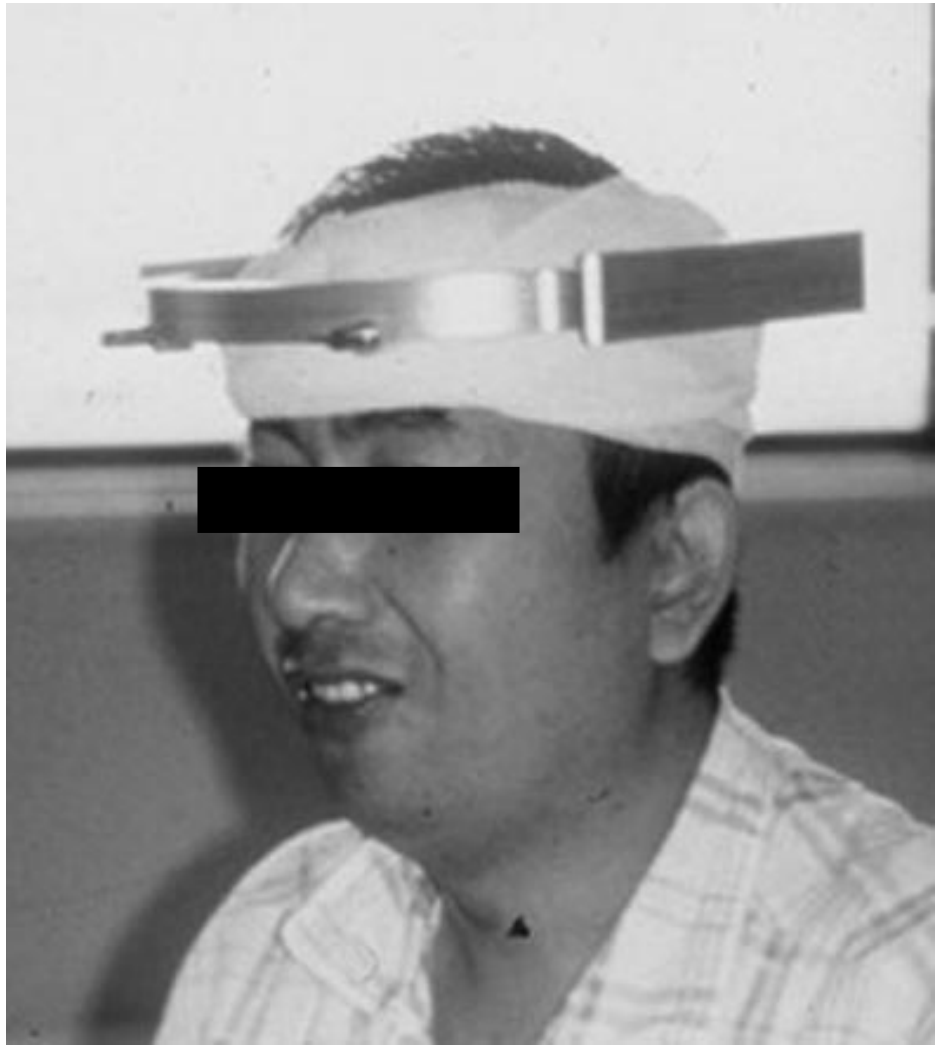


Fig. 1

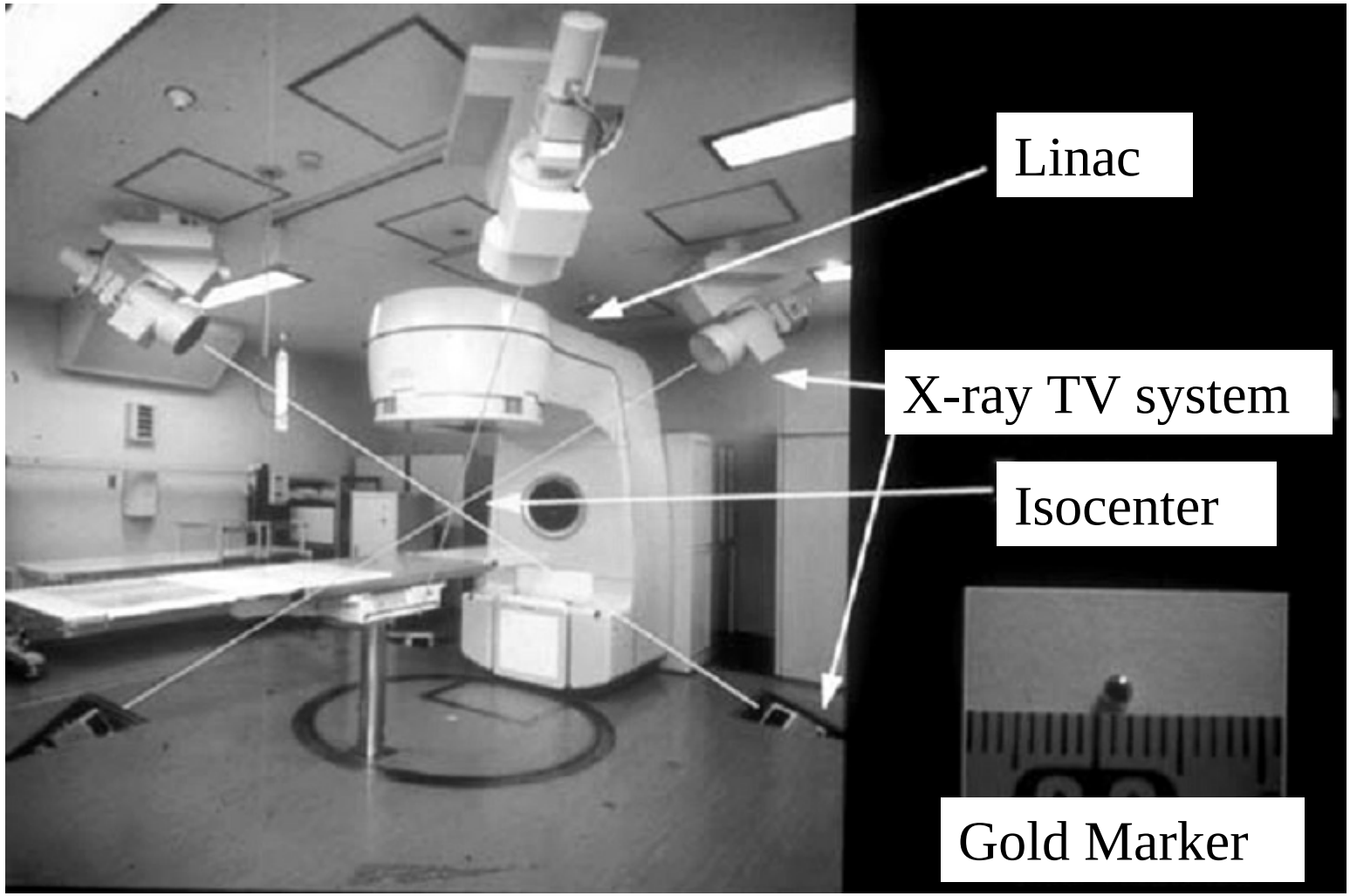
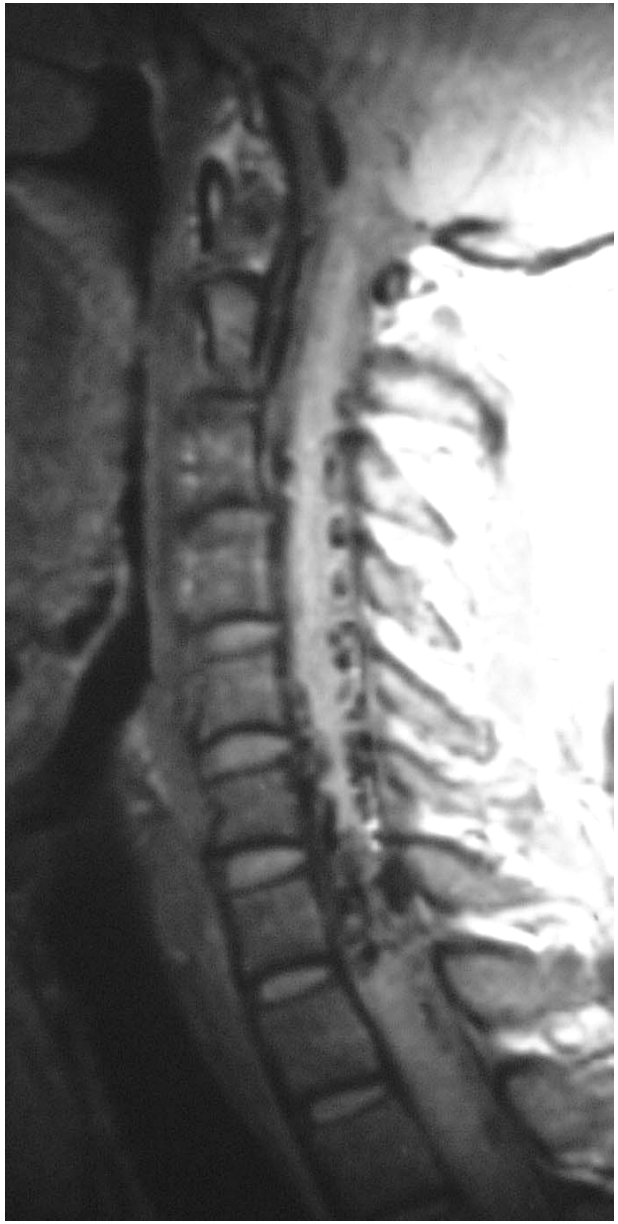


Fig. 2



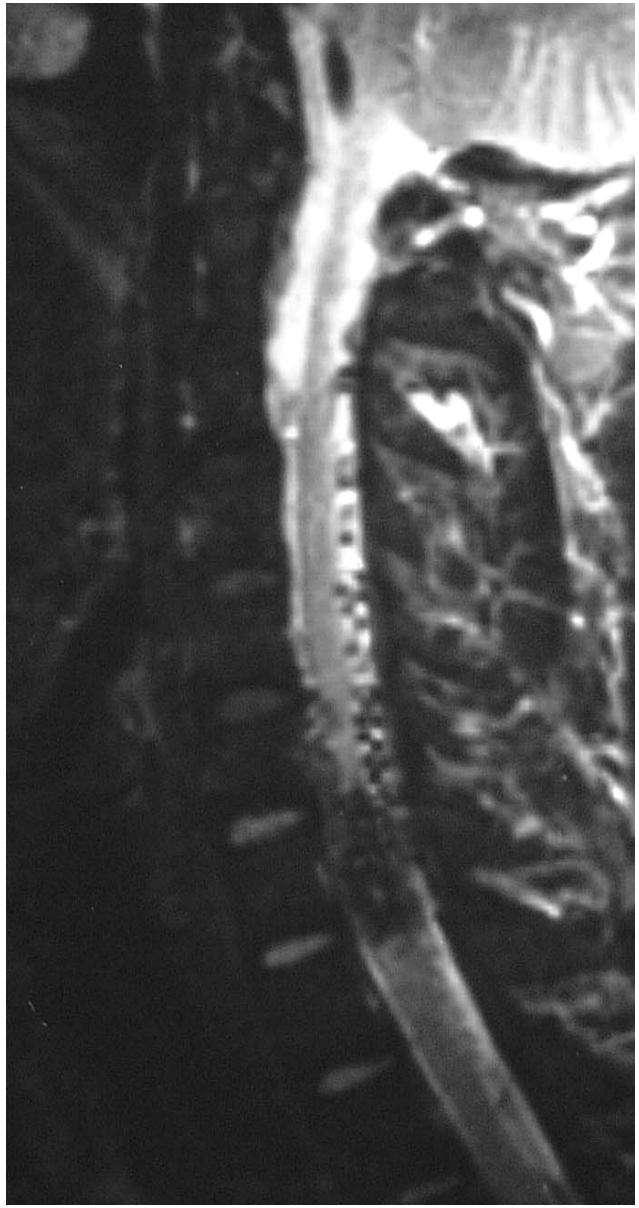
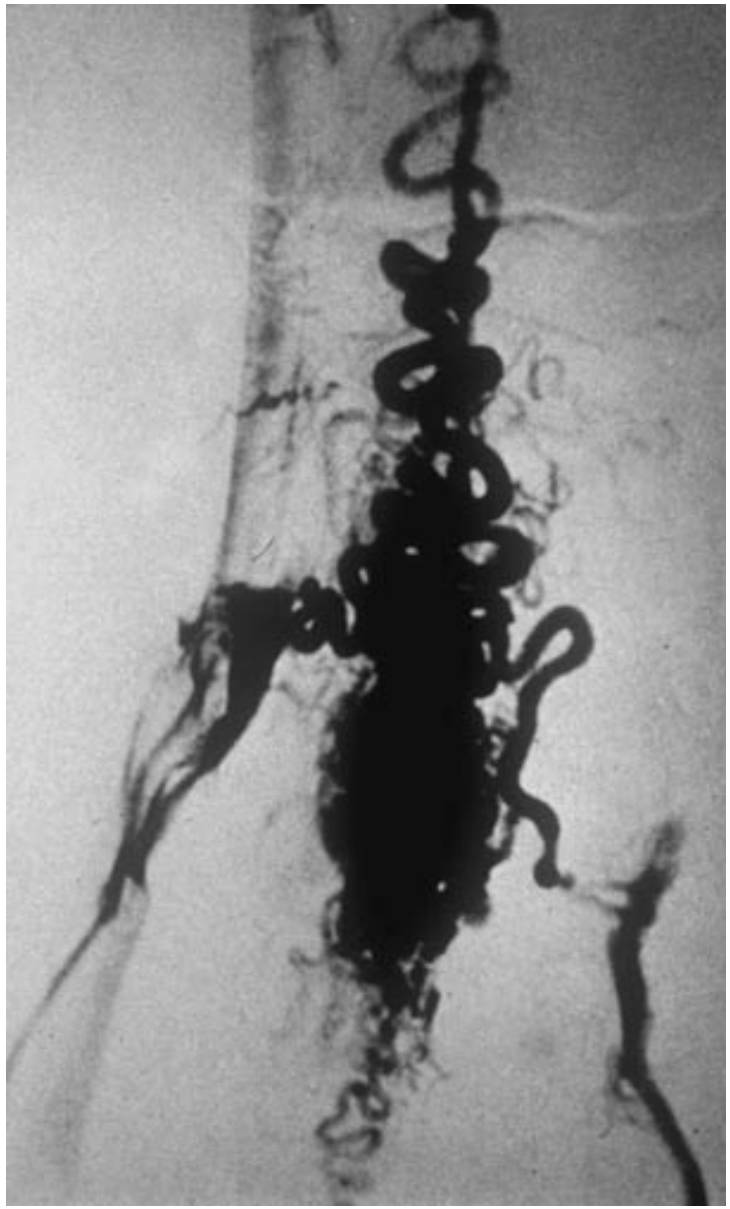


Fig. 3

A

B



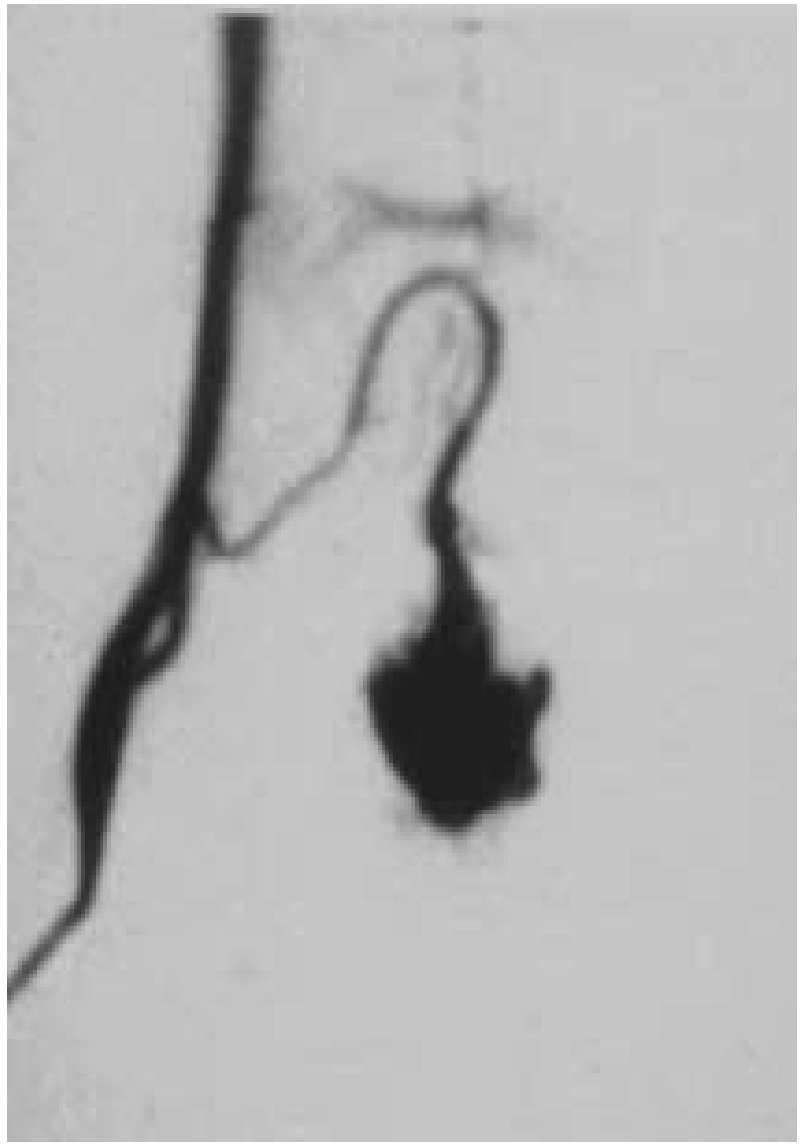
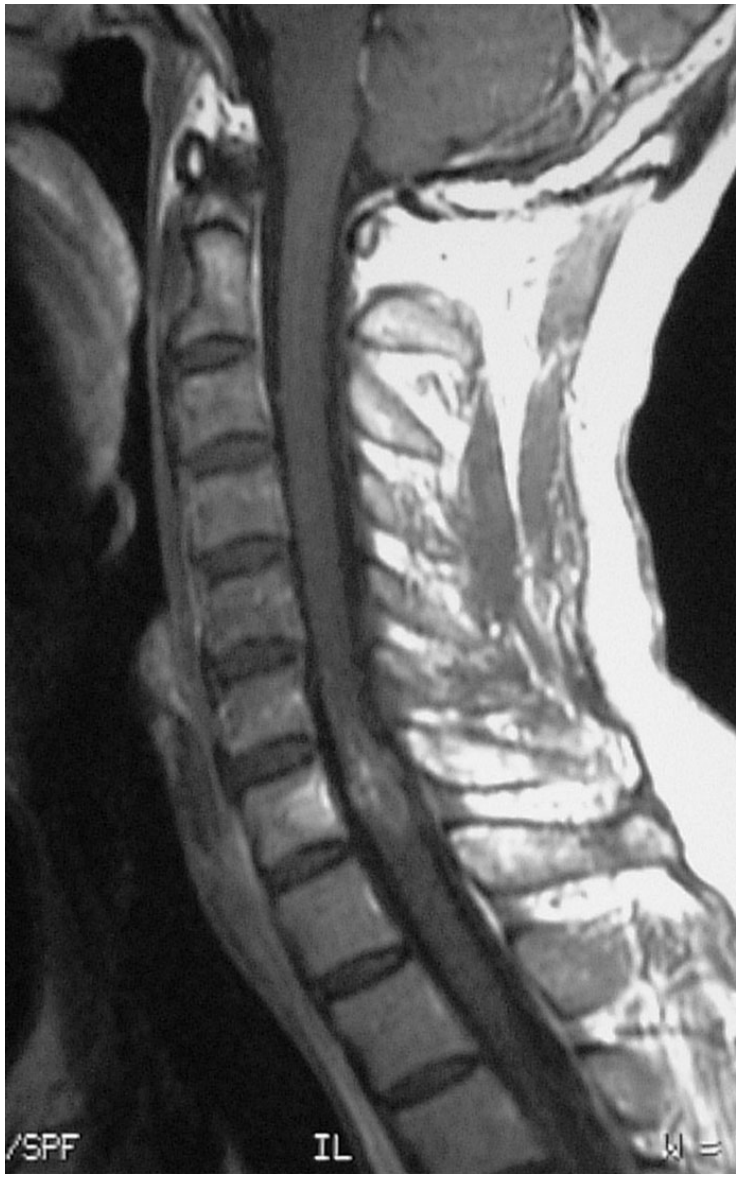


Fig. 4 **A** **B**



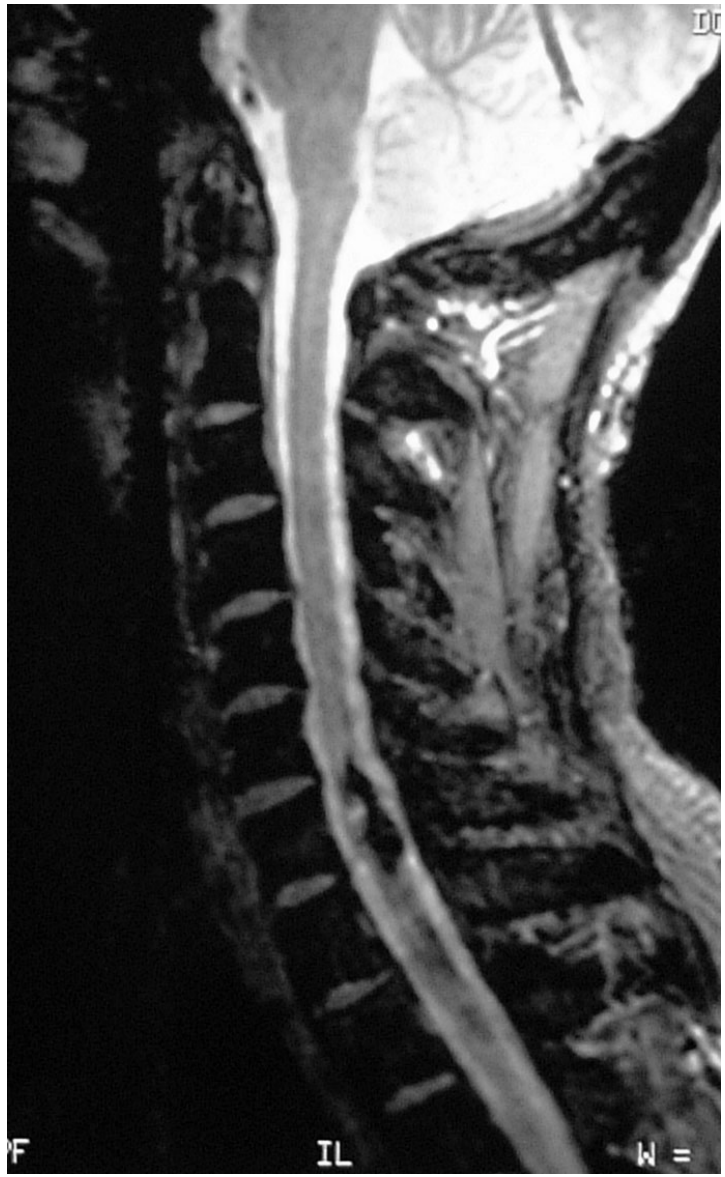
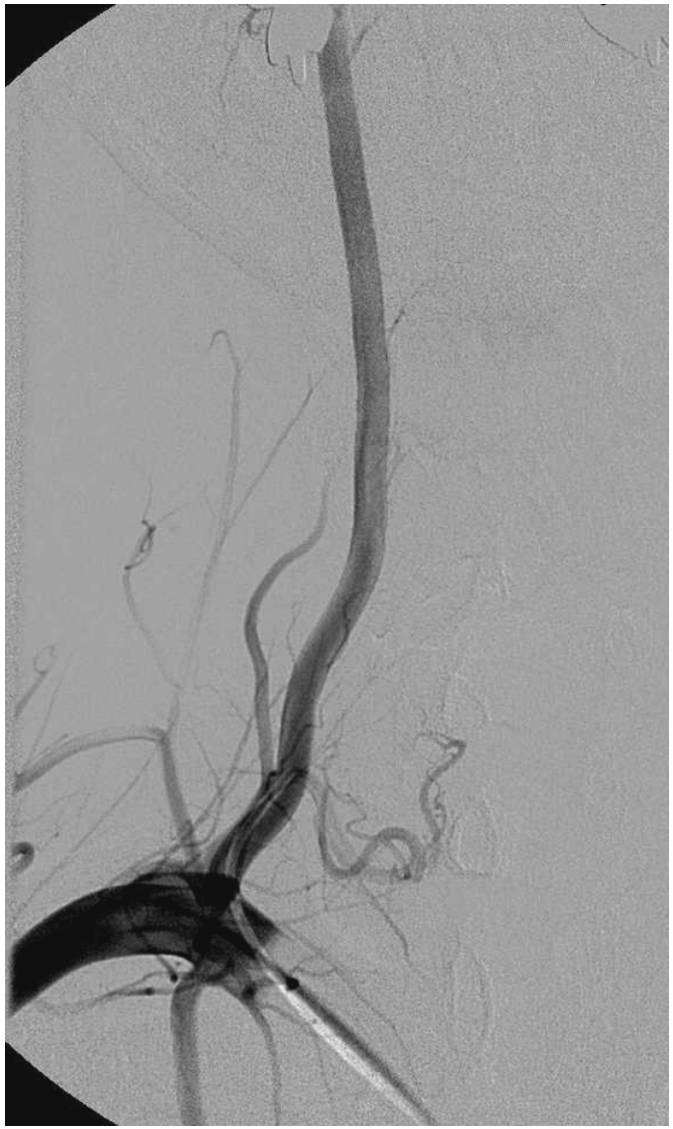


Fig. 5

A

B



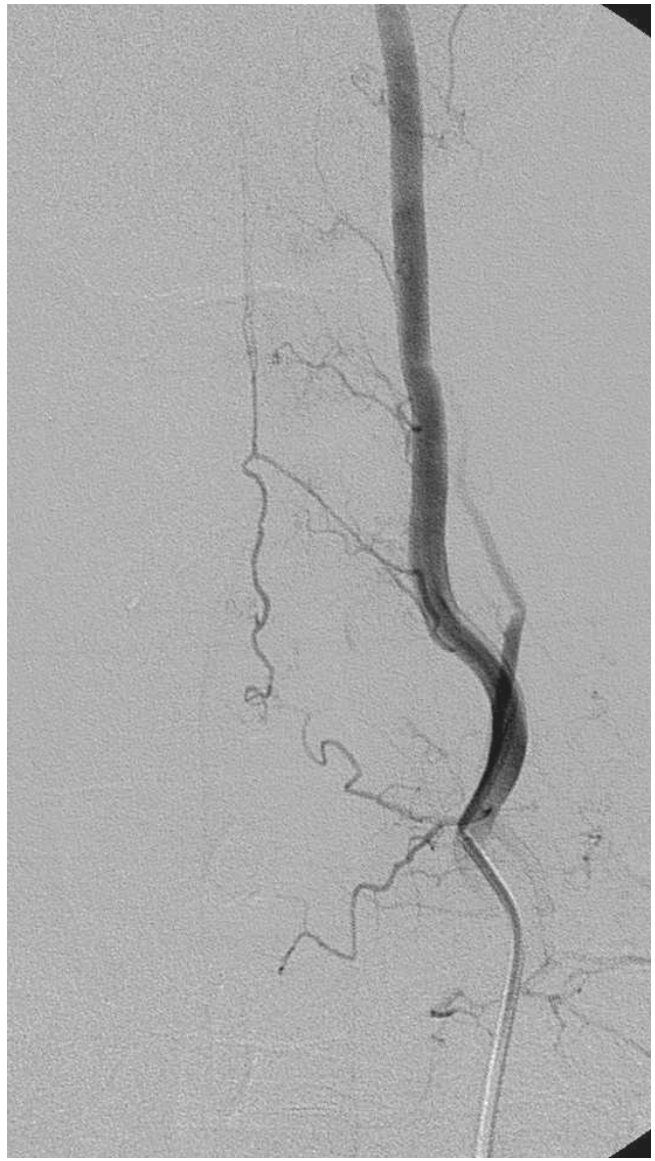


Fig. 6

A

B