# Spinal Deformity in Neurofibromatosis: Classification and Management

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## Abstract

The effects of treatment of scoliosis in neurofibromatosis type 1 are less satisfactory than other scoliotic types due to the particular pathogenesis and clinical characteristics. Surgical treatment usually included 360 degrees fusion with instrumentation, but optimal strategies are different according to the degree of deformity. High incidence of pseudarthrosis, extensive bleeding and curve progression even after solid spinal fusion are also major concerns of neurofibromatosis type 1 associated spinal deformity surgery. With advance of technology, cobalt-chrome rod with dural rod technique, tranexamic acid, recombinant human bone morphogenetic protein-2 and electrophysiologic monitoring were used in neurofibromatosis deformity surgery to get better outcome. Searching from PubMed, we reviewed overall about neurofibromatosis spine deformity surgery.

**Keywords:** Neurofibromatosis; Scoliosis; Kyphosis; Deformity

## Introduction

Neurofibromatosis (NF) type 1, peripheral neurofibromatosis, having a global prevalence of one in 3000 individuals and published reports of prevalence of scoliosis varied from 10% to 30% during childhood [1-5]. Spinal deformity is the most common osseous complication of NF-1 and many of these patients will eventually require surgery for curve progression [6-9]. Further, several studies also report poor bone quality of dystrophic change with decreased bone mineral density [10,11]. In this paper, we reviewed almost all paper from PubMed search, from management methods of the NF spinal deformity to additional strategies to overcome this challenging disease.

## Search Strategy and Selection Criteria

We searched PubMed (September 1, 1965 to September 1, 2015) using the search term 'neurofibromatosis' with 'deformity, scoliosis, and kyphosis'. Publications were reviewed and selected predominantly from the last 10 years. Greater emphasis was placed on selecting high quality research and review articles published in the last 10 years. Reference lists of articles identified by this search strategy were reviewed and our reference list was also modified on the basis of comments from Corresponding Author to ensure no significant publications were missed.

## Classification of Spinal Deformity

Coronal spinal decompensation is classified into non-dystrophic and dystrophic types based on the absence or presence of skeletal dysplasia [12]. Characterization of the curve should be based on a combination of MRI and radiological findings [13-16]. Clinical and radiologic findings, treatment, and complications of non-dystrophic type are similar to idiopathic scoliosis [2,17-20]. However, patients with NF-1 associated non-dystrophic scoliosis are historically affected earlier in life, have a worse prognosis, and have a higher pseudarthrosis rate or failure to obtain spinal fusion after surgery than their idiopathic counterparts [2,18]. Vertebral scalloping, rib penciling, spindling of the transverse processes and wedging of vertebral bodies, paraspinal or intraspinal soft tissue masses, a short curve with significant apical rotation are typical feature of dysplastic type [12,21]. These could lead to subluxation or dislocation of vertebral bodies [22]. Dystrophic changes are thought to be intrinsic in origin or associated with intraspinal anomalies, such as dumbbell shape neurofibromas causing foraminal enlargement, dural ectasia causing posterior vertebral scalloping and lateral thoracic meningocele [13-16,20]. Anterior and lateral scalloping was commonly the result of primary mesodermal dysplasia [16]. Even in tremendous angular deformity, if dural ectasia (Figure 1) is the reason of canal expansion, it may not be accompanied by spinal cord compromise and neurologic deficit [23]. On the other hand, if an intraspinal neurofibroma is related to the development of canal widening, it can provoke cord compression easily [23]. Generally, the more severe the dystrophic changes identified, the higher the likelihood that the scoliotic curvature will find out. When a combination of three or more dysplastic features was present in NF-1, the risk of curve progression was significantly increased in 85% of the patients, while rib pencilling was the only singular dystrophic factor statistically influencing risk of scoliosis deterioration [24].

## Radiological Evaluation

Postero-anterior and lateral radiographs of the entire spine should be obtained in all NF-1 patients. If there is any suspicion of instability, computed tomography (CT) and/or flexion-extension plain radiographs are indicated. The dynamic or supine radiographs are helpful to evaluate flexibility of the curve. Magnetic resonance imaging (MRI) of the entire spine will illustrate the intraspinal and extraspinal contents that might interfere with any attempt for surgical correction of the deformity [13-16]. A thorough search for evidence of dysplastic changes on plain radiograph and MRI is essential and will clarify prognosis and management options even if there were no neurologic

deficit [2,5,9]. MRI is also helpful to find out spinal neurofibromas, closely associated with an increased incidence of scoliosis [13-16]. In contrast, other investigators do not advocate routine MRI and emphasize that MRI should be indicated by clinical necessity [5,14,15].



**Figure 1:** Dural ectasia from posterior scalloping. 54 year old female patient spine magnetic resonance imaging shows dural ectasia causing canal expansion without any neurological deficit.

## Non-Dystrophic Curves Management

Non-dystrophic curves can be managed similarly to idiopathic scoliosis and shows comparable response to treatment [2,17,18,25,26]. If the degree of the scoliotic deformity is less than 20–25°, it may be observed with a regular follow up [9]. Brace can be applied for curves between 20° and 40° if the patient still has remaining growth. When bracing is selected as the preferred management option, compliance should be considered, because child patients with NF-1 often have cognitive dysfunction, intellectual handicap and great degree of psychological problems [9,19,27,28]. If the deformity exceeds 40°, it should be treated surgically by a posterior spinal fusion and segmental instrumentation. The use of autologous iliac crest graft is recommended to enhance a bony fusion, especially since there is evidence of a higher incidence of nonunion comparison to those with idiopathic scoliosis [2,18,25,26]. Circumferential fusion including discectomy and instrumentation is necessary to achieve restoration of spinal curvature in patients with deformity more than 55–60° [2,18,25,29].

When observing patients with NF-1 initially classified as having non- dystrophic curves over an extended period of time, there is a higher propensity for developing progressive deformity compared to the idiopathic scoliosis population [2,18,25,12]. Close observation of the evolution of deformity is critical due to the possibility of modulation of spinal deformity from non-dystrophic to dystrophic curves. Modulation rate of non-dystrophic to dystrophic scoliotic curvatures is outstanding to children before 7 years. Dystrophic changes may develop with growth as part of the modulation phenomenon, but does not show a consistent pattern [24].

## Dystrophic Curves Management

The presence of a combination of three or more dystrophic features on radiographs and MR image was highly predictive of the need for surgery. Individual features most predictive of need for surgery were the presence of vertebral scalloping followed by the presence of dural ectasia [23]. Apart from the presence of dystrophic changes, other factors that increase substantially the risk of curve deterioration include a young age and a high magnitude of deformity at initial presentation, pathological kyphosis of greater than 50°, location of the apex of the curvature in the mid to caudal thoracic region of the spine, severe apical vertebral rotation of more than 11°, and a severely notched anterior vertebral body [2,12,18,20,25,26,30,31]. The dystrophic type of scoliosis is more resistant to treatment. The natural history of untreated dysplastic curves, particularly between the ages of 6 and 18 years, is that of relentless deterioration [32]. Brace therapy has been ineffective and the need for early surgery is well documented even in young children [19,33]. The need for early fusion for dystrophic NF spinal deformity is now a well-known and widely accepted method [2,9,17,18,20,24,25,26,31,34-41]. Early spinal fusion does not lead to loss of height since the developing curves limit the growth potential [9]. Dystrophic scoliotic curves less than 20° should be closely observed with short intervals to identify sudden and rapid progression [6]. For patients with 20–40° scoliosis with less than 50° of kyphosis, posterior spinal arthrodesis using segmental fixation with either multiple sublaminar wires or dual rod-multiple hook constructs and the application of plentiful bone graft is strongly indicated [2]. Apart from this selective group of patients that can be treated with isolated posterior instrumented fusion, for most dystrophic NF spine, corpectomy and circumferential fusion shows high fusion rate, good curve correction, and good functional outcome [36,42-45]. Most authors recommend circumferential fusion and instrumentation as the most reliable surgical option in patients of thoracic kyphosis that exceeds 50° [26,46,47]. Structural auto bone graft, rib or fibula, could reinforce the vertebral column followed by posterior instrumentation with copious amount of autologous iliac crest bone [38,42].

Kyphosis, by creating a pathological spinal flexion, produces excessive attenuation and deformation of the spinal cord parenchyma and gives rise to neurological symptoms more easily than scoliosis [48-51]. If the cord is compressed due to the development of a progressive kyphotic deformity, treatment should consist of anterior decompression through a vertebrectomy in the concavity of the deformity followed by combined anterior and posterior fusion with instrumentation [38,42]. Laminectomy has been shown to be ineffective to release pressure in a sharply angulated spinal cord [38]. In the presence of an angular kyphotic deformity, if it is flexible on dynamic plain radiographs, with associated mild neurologic involvement, preoperative halo-dependent traction may be considered, in order to maximize curve correction during the anterior decompression and facilitate placement of the strut graft [37]. The development of thoracic lordosis is relatively infrequent in patients with NF-1. However, it is often associated with significant respiratory compromise and mitral valve prolapse [52].

## Strategies for NF-1 Spinal Deformity Surgery

Primary goal of NF deformity surgery is to stabilize the vertebral column and halt further progression of the deformity rather than perform perfect correction that could result to permanent neurologic sequelae [9]. During the posterior exposure of the spine, the surgeon should be particularly careful to avoid invading the spinal canal and

injuring the cord in areas where the posterior bony elements are weakened (Figure 2) due to the presence of intraspinal tumors or dural ectasia [9].
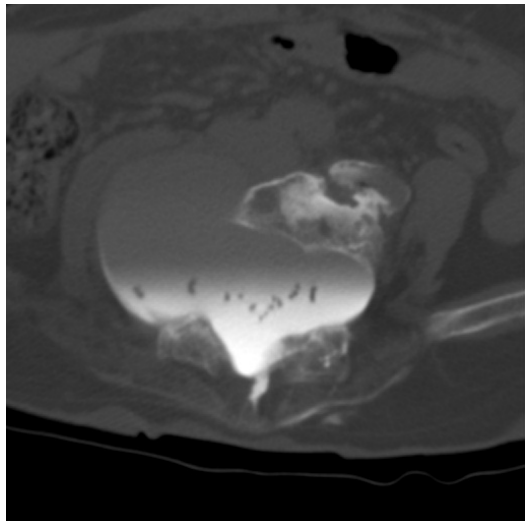


**Figure 2:** Weakened posterior body element from dural ectasia. Spinal computerized tomographic scan with myelogram shows weakened posterior bony elements due to the presence of dural ectasia.

If excessive angular kyphosis is present or if the vertebrae are weak due to the bony dysplasia, postoperative orthotic immobilization is recommended even if instrumentation has been successfully applied, in order to remove excessive strains at the proximal hook sites and prevent dislodgement of the instruments [2,26]. Moreover, because the pedicles were too hypoplastic (Figure 3) to install pedicle screws, obtaining adequate fixation points was very important.

Patients with type-1 NF are known to be osteopenic, predisposes the instrumentation construct to screw pullout, and have high pseudarthrosis rates of up to 60% [40]. Some authors recommends posterior re-exploration and augmentation of the fusion in 6 months if there were possibility of fusion failure [20,26,38]. Use of recombinant human bone morphogenetic protein-2 (rhBMP-2) has been studied extensively to enhance fusion and has demonstrated equivalent or better fusion rates than autologous iliac bone graft [53]. Despite the demonstrated efficacy of rhBMP-2, there were possibility of heterotopic ossification, radiculitis and the promotion of tumor formation in animals [54,55]. Nevertheless, there is no report of rhBMP-2 induced cancer in humans yet, interaction of the rhBMP-2 with hyperproliferative neurofibroma is a potential concern, especially in young patients [56]. Both the risks and the benefits of off-label use of rhBMP-2 should be carefully considered on a case-by-case basis.

The usual reason for failure of spine surgery is inadequate anterior procedures, such as performing a short fusion or using a limited amount of bone graft. Dystrophic curves should be treated aggressively, as there is a strong tendency for curve progression even after spinal fusion [35]. All grafts should have direct contact with the spine and with each other, while any intervening soft tissue should be meticulously excised. The fusion should be extended to include the neutral vertebra above and below the curve. Segmental instrumentation can occasionally be challenging, since severely deformed vertebrae constitute poor anchorage points for fixation. If internal fixation is not technically feasible because of poor bone stock, in situ fusion with bone autograft and application of a postoperative cast or brace is necessary [7].



**Figure 3:** Iliac screw with Wisconsion wiring technique. Lumbar pedicles are too hypoplastic to install the pedicle screws, multiple iliac screws were inserted instead of lower lumbar pedicle screws with modified Wisconsin wiring technique.

Extensive bleeding is another major concern. Excessive bleeding can hamper particularly anterior approaches to the vertebral bodies for corpectomy or vertebrectomy and can occur due to rigorous bone bleeding or the presence of paraspinal neurofibromas and plexiform venous channels in the soft tissues surrounding the spine. Meticulous hemostasis and wound drainage are absolutely needed. As potent antifibrinolytics, tranexamic acid (TXA) and aminocaproic acid are helpful to decrease intraoperative and postoperative blood loss in adult as well as pediatric patients [55-57]. Low dose TXA to adults and high dose TXA to pediatric patients is recommended [57].

## Conclusion

NF-1 associated spinal deformity requires early recognition and aggressive surgical intervention according degree of deformity with regular follow-up. With effort to reduce bleeding loss with TXA, surgeons should utilize modern technologies of instrumentation and consider new potent biologic materials like rhBMP-2 to get better outcome.

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