Scoliosis and spinal muscular atrophy in the new world of medical therapy: providing lumbar access for intrathecal treatment in patients previously treated or undergoing spinal instrumentation and fusion

Luca Labianca and Stuart L. Weinstein

This study describes a new procedure for a safer and easier access for the intrathecal injection of the recently approved nusinersen therapy in spinal muscular atrophy. This therapy changed the natural history of the disease, but, to date, scoliosis surgery was an excluding criteria for nusinersen therapy. The bone mass, due to the posterior spinal fusion of the scoliosis surgery, prevents the needle for the nusinersen administration from intervertebral access. This is a single-center, single-surgeon case series descriptive study. A laminotomy at the L3–L4 level was performed to provide safer access for the intrathecal injection. The procedure was carried out during the scoliosis surgery in patients who underwent posterior spinal fusion (PSF) after the nusinersen therapy was introduced, whereas for those who underwent PSF earlier, a second procedure was necessary to perform a laminotomy. A fat grafting was used to prevent bone overgrowth in the laminotomy. Markers were applied as radiographic references for the intrathecal injection. Five patients were enrolled, four females and one male. The mean age of the patients was 11 years. Three patients underwent PSF before the introduction of the nusinersen therapy. Two patients underwent PSF after the nusinersen therapy was available. All of them underwent a laminotomy with a fat grafting at the L3–L4 laminotomy level and received nusinersen therapy without complications. The procedure described is simple and effective in providing safe intrathecal access to make these patients eligible for such important therapy. *J Pediatr Orthop B* **28:393–396**

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Department of Orthopedics, University of Iowa, Iowa City, Iowa, USA

Correspondence to Luca Labianca, MD, Via del Casale Sansoni, 98, 00135 Rome, Italy
Tel: +39 328 655 6092; fax: +39 063 377 5818;
e-mail: luca.labianca@uniroma1.it

Introduction

Spinal muscular atrophy (SMA) is the second most common fatal autosomal recessive disease after cystic fibrosis. The nusinersen is a modified antisense oligonucleotide that modulates the splicing of the SMN2 mRNA transcript. It is the first approved drug for all types of SMA and its efficacy has been reported in several studies [1]. This type of therapy is dispensed by an intrathecal injection with four lumbar punctures and administered with four loading doses on the first, 15th, 30th, and 60th day. Afterwards, patients are administered regular (also called maintenance) doses every 4 months.

According to Rodillo *et al.* [2], scoliosis in SMA patients progresses between 5° and 15° per year. Curvature worsening often leads to loss of stability when sitting, with a negative impact on everyday activities [2–8]. Bracing is tolerated poorly and cannot halt the progression of scoliosis in SMA [2–11].

Definitive posterior spinal fusion (PSF) is an effective treatment [12]. However, often, surgical treatment is necessary at a young age. Currently, SMA children are being treated by growing rods (magnetic or traditional) to delay the time of definitive fusion and to allow for spine growth [13]. Many children with SMA have undergone extensive spinal instrumentation and fusions before the introduction and availability of medical therapy. This condition has been considered an excluding criteria for lumbar intratechal injection for drug administration.

There are no reports in the literature, to our knowledge, describing a surgical procedure to provide a lumbar access window for patients who have previously undergone spinal fusion and instrumentation (luque rodding or segmental instrumentation). Few studies propose alternatives for effective nusinersen administration, and none for lumbar injection [14–17].

In this paper, we describe the approach that we used in patients with SMA who underwent access procedures in the face of previous spinal fusion surgery. We also discuss our current approach to previously unoperated patients with SMA who are undergoing definitive fusion and how we preserve access for drug treatment.

Patients and methods

Approval was obtained from the institution's human participants review board. This is a single-center, single-surgeon

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case series descriptive study. The population is of SMA patients with scoliosis. Patients' data have been collected from their records, complications described, and number of intratechal injections recorded.

In patients who underwent PSF before December 2016, the senior author performed a laminotomy as a second procedure. He opened a window in the bone mass at the L3–L4 level. A free fat graft was then applied to the above-mentioned opening to preserve it from bone overgrowth and a dot was tattooed on the skin as a reference for safer future injection access.

In patients who underwent definitive PSF as their primary surgery, after December 2016, the senior author performed the laminotomy during the scoliosis surgery itself. The same fat graft was applied to avoid the bone window from filling in with bone and hemoclips were affixed on the spinous processes above and below the laminotomy to provide easier reference for future injection access.

Results

From the beginning of nusinersen treatment (2016) to June 2018, five patients have undergone L3–L4 laminotomy and fat graft transplant, by the senior author (S.L.W.), to be eligible for nusinersen injections after PSF. In two patients, the laminotomy was performed during the scoliosis surgery, whereas in three patients, it was a second procedure after the previous PSF, depending on whether they underwent scoliosis surgery earlier than the nusinersen introduction or later. They were two females aged 8 and 12 years at the time of the procedure (Table 1).

The two patients underwent PSF and T2-pelvis instrumentation as the first spinal procedure; the laminotomy procedure was performed during the scoliosis surgery.

The other three patients underwent the laminotomy of the posterior spinal fused mass as a second procedure, two females (age at surgery 10 years) and one male (aged 15 years at surgery). The male patient had Luque instrumentation. The two females had pedicle screws and rod construct.

The main follow-up was performed for 6 months. All patients received at least one intrathecal injection and in two patients, the loading dose was completed without any complication. There was one wound dehiscence that was treated with vacuum-assisted closure therapy, and was resolved completely.

The lumbar laminotomy during scoliosis surgery was performed in patients who underwent definitive posterior spinal fusion after the nusinersen introduction. The laminotomy was performed in the central spine area within L3 and L4. This included partial removal of the superior half of the lamina and the spinous process of L4 and the inferior half of the lamina and the spinous process of L3 with complete excision of the intervening ligamentum flavum. A large fat graft, harvested from the subcutaneous tissue, was placed in the defect to prevent bone chips from entering the canal and to prevent arthrodesis across the gap. Large hemoclips were used as proximal and distal markers (Fig. 1) to enable future fluoroscopic identification of the open area for lumbar puncture.

In patients who had undergone a previous PSF, a second surgery was necessary to provide access for the lumbar puncture. In these cases, fluoroscopy was used to identify the area of the laminectomy. A skin incision between L1 and L4 was used with dissection carried down through the previous scar exposing both the right and the left side of the spine and hardware. Fluoroscopy was then used to identify the optimal boundaries for the laminotomy. The periosteum was stripped off of the fusion mass and screws (or wires in the case of Luque rods) and rods over a 2×2 cm area. Using a fluted burr, the superficial layer of the fusion mass was removed. All of the cancellous bone of the fusion mass was curetted away gently, leaving only the deep cortex overlying the spinal canal. A nondural cutting burr was then used to make a small opening in the deep cortex of the fusion mass overlying the dura. Then, using small Kerrison rongeurs, all of the deep cortical bone (usually a very thin shell of bone) was removed along with remnants of the ligamentum flavum, taking great care not to injure the dura or create a dural leak. Pedicle screws and Luque wire remained intact (Fig. 2). The extension of the Luque wires in the twist tie posterior to the rods had to be moved lateral to the canal opening in some cases. A large fat graft was placed in the defect as mentioned above.

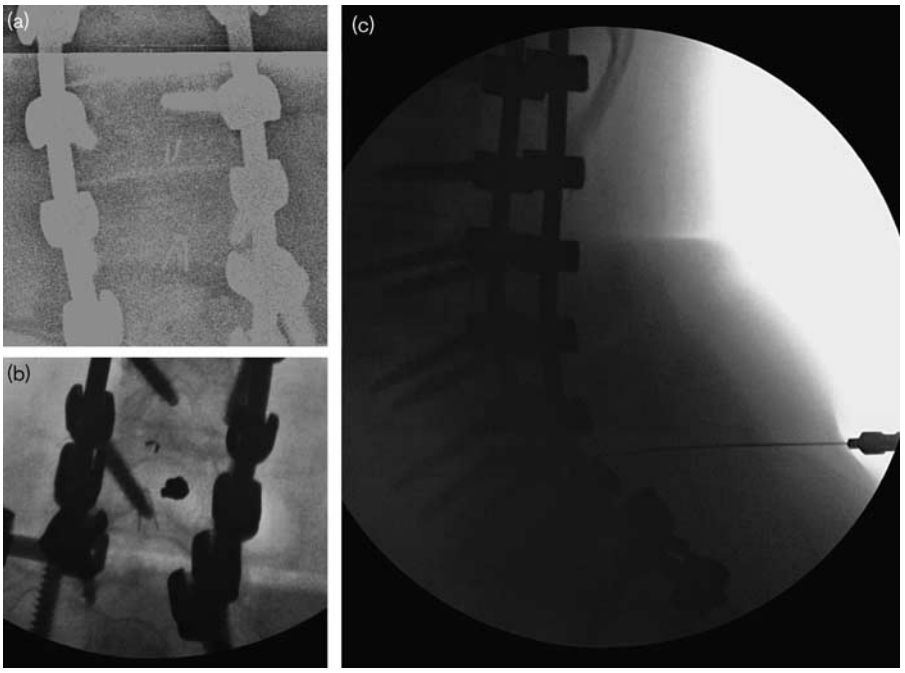
After skin closure, using fluoroscopy, in all patients, a small skin dot tattoo was made with the aid of fluoroscopic control (Fig. 2) in the operating room before

Table 1 Details of the series with complications

Case procedures	Age at surgery	PSF as first surgery (yes/no)	Sex	FU months	Injections at FU	Complications
Postspine fusion + laminotomy/fat transplant/markers	12	N	F	10	2	Wound treated with VAC resolved
Laminotomy/fat transplant/markers	10	Y	F	8	3	None
Laminotomy/fat transplant/markers	10	Y	F	6	4	None
Laminotomy/fat transplant/markers	15	Y	M	4.5	4	None
Postspine fusion + laminotomy/fat transplant/markers	8	N	F	3.5	3	None

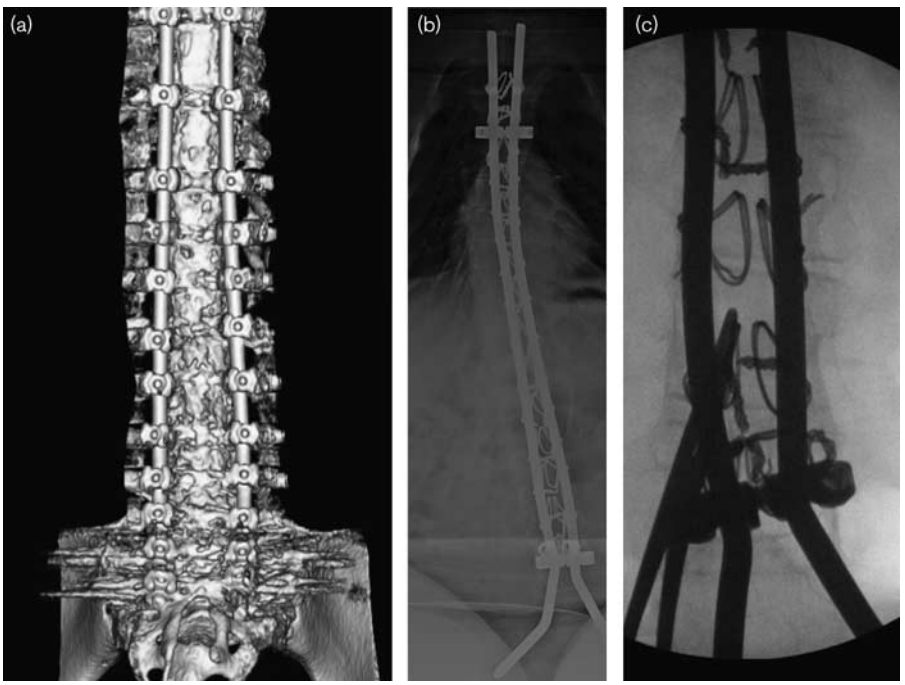
FU, follow-up; N, no; PSF, posterior spinal fusion; VAC, vacuum-assisted closure therapy; Y, yes.

Fig. 1



Patient underwent posterior spinal fusion (PSF) after the introduction of nusinersen therapy: the magnification shows hemoclips applied to provide a fluoroscopic reference for the injection (a). The anteroposterior and lateral views of the injection procedure are shown (b, c).

Fig. 2



Patients underwent posterior spinal fusion (PSF) before the introduction of nusinersen therapy: the three-dimensional computed tomography shows the fusion mass after PSF with a hybrid implant (a). Patient who received Luque instrumentation (b): the pickup shows the center of the laminotomy area (c).

application of wound dressings. This was to guide the neurologist or radiologist at the time of lumbar puncture in the future. Patients were indicated for intrathecal infusion after the 6-week postoperative orthopedic visit.

Discussion

Nusinersen treatment is an innovative therapy that completely changed the natural history of SMA [18]. The intratechal injection is almost impossible after scoliosis surgery due to the intervertebral bone mass. For this reason scoliosis surgery was, to date, an excluding criteria for the nusinersen therapy [15].

The procedure described here, to our knowledge, is undescribed. It could be considered for a standard protocol in patients who are undergoing PSF due to scoliosis. It is even safer, from the surgeon point of view, than skipping 1 or 2 level of fusion in the lumbar spine, to avoid bony mass fusion formation. It is also the standard, safer, approach for the intrathecal injection (lumbar). The other proposed procedures described in the literature (such as cervical puncture or thoracic laminectomy and durotomy, with an intrathecal catheter plus Ommaya reservoir) seem to be more challenging [16,17].

All of our patients have undergone successful injections to date, with just one complication that did not affect the final goal. The laminotomy as a second procedure was well tolerated by the patients. The use of the fat grafting to avoid bone growing seemed to be effective in preventing arthrodesis across the gap at this stage.

The limitations of this study include a small sample size, the limited number of procedures performed, and the short follow-up. Further experiences in children with SMA are needed to add to this knowledge.

Overall, given the promising early results of nusinersen therapy, referral for lumbar puncture administration of the drug is expected to increase. Hence, surgeons treating patients with SMA must adjust their surgical technique to allow for lumbar puncture access in the future and in addition, access must be gained in patients with previously fused spines who might benefit from drug treatment. Our experience may prove useful for guiding the development of best practice strategies for safe and effective intrathecal delivery of nusinersen and/or other promising emerging therapies for SMA.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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