

Brief Commentary

e **Peripheral and Neuraxial Chemical Neurolysis for the Management of Intractable Lower Extremity Pain in a Patient with Terminal Cancer**

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Disclaimer: There was no external funding in the preparation of this manuscript.

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We present the case of a 74-year-old man with Stage IV metastatic, multifocal, malignant fibrous histiocytoma (T2b, N1, M1, G4) invading the proximal area of the left lower extremity and resulting in intractable neuropathic pain along the distribution of the femoral nerve. He described the pain as being so severe to cause inability to ambulate without assistance or to sleep in a supine or prone position. After a spinal cord stimulation trial and a trial of intrathecal (IT) hydromorphone, both performed at an outside institution, had failed to achieve adequate pain relief, we decided to perform a femoral nerve chemical neurolysis with phenol under ultrasound (US) guidance. The intervention provided 6 months of almost complete pain relief.

With the tumor spreading in girth distally and proximally to the scrotal and pelvic areas as well as to the lungs, and pain returning back to baseline, we proceeded with a second femoral nerve chemical neurolysis. Unfortunately we were not able to achieve adequate pain relief. Therefore we opted to proceed with a diagnostic injection of local anesthetic under fluoroscopic guidance at the left L2, L3, and L4 nerve roots level. This intervention provided 100% pain relief and was followed, a few days later, by chemical neurolysis with phenol 3%. The patient reported complete pain relief with the procedure and no sensory-motor related side effects or complications. He was able to enjoy the last 6 weeks of life with his wife and family, pain-free.

With this report we add to the limited literature available regarding the management of intractable cancer pain with chemical neurolysis in and around the epidural space.

Key words: Cancer, pain, chemical neurolysis, peripheral, neuraxial

Pain Physician 2015; 18:E651-E656

Pain still represents a significant problem for many patients with a malignancy. Recent data show an overall prevalence of 53% in patients of all stages combined and 58% to 69% in those with advanced disease (1). Even though the implementation of the World Health Organization (WHO) guidelines has resulted in a significant improvement, still 15% – 20% of patients with cancer are not able to obtain satisfactory pain relief with escalating doses of systemic medications (2,3), particularly during the late stages of their disease (4). Moreover an increase in the dose of the pain medications is likely associated with the

development of unpleasant and disturbing side effects. Interventional pain management can be an appropriate option for these patients (3); many pain specialists advocate for the use of advanced interventional techniques early in the course of the disease (5).

Chemical neurolysis with alcohol and phenol has been reported to be effective for management of intractable cancer pain in various clinical situations (6- 10).

We present the case of a 74-year-old man with Stage IV metastatic multifocal malignant fibrous histiocytoma (T2b, N1, M1, G4) of the left lower extrem-

ity, resulting in intractable neuropathic pain along the distribution of the femoral nerve that was successfully controlled with a combination of peripheral nerve and neuraxial chemical neurolysis with phenol.

Consent for the publication of this case report has been obtained from the patient's wife. Both the patient and his wife have been actively involved in the decision-making process and their input has been invaluable in achieving a successful result at a time of significant physical and emotional distress

CASE REPORT

A 74-year-old man arrived with Stage IV metastatic multifocal malignant fibrous histiocytoma (T2b, N1, M1, G4) invading the proximal area of the left lower extremity and resulting in intractable neuropathic pain along the distribution of the femoral nerve. Tumor invasion of the underlying muscle structures, skin contractures with decreased range of motion, and post-radiation neuropathy also contributed to the pain syndrome. Because the pain intensity was very severe, the patient was not able to sleep in the supine position. He reported moderate leg weakness, but was able to walk with the help of a walker. Before the evaluation at our pain center, a spinal cord stimulation trial performed at another institution had failed due to the high intensity needed to achieve adequate pain relief, causing dysesthesia. An intrathecal (IT) trial of hydromorphone had also yielded no pain relief. Moreover the patient and his family were opposed to the idea of pain management with the help of an implantable device.

Upon presentation, his pain medication regimen included fentanyl patch 100 mcg/hr every 72 hours, oxycodone 30 – 45 mg twice a day as needed, morphine liquid 20 mg/mL, 100 mg every 2 hours as needed, amitriptyline 20 mg at bedtime, gabapentin 800 mg every 8 hours, clonazepam 0.5 mg at bedtime, and acetaminophen 1000 mg every 8 hours. Despite this medication regimen, pain was not well controlled, particularly when performing physical activities. In addition, due to the severity of the neuropathic pain caused by the compression of the tumor on the femoral nerve and surrounding structures, he was forced to sleep in a near seated position that, although being uncomfortable, was better tolerated than the supine position. The patient's goals were to be able to sleep supine, minimize the use of medications and mitigate their side effects.

The decision to proceed with a diagnostic ultrasound (US)-guided block of the femoral nerve was made. Risks and benefits of the intervention proposed

were discussed and the patient agreed to proceed. Positioning and optimal visualization of the femoral nerve proved to be challenging. The size and extension of the tumor and intolerable pain with the supine position obliged the patient to be in a nearly fixed hip flexion posture, not allowing a full extension of the proximal portion of the leg. Visualization of the anatomy was challenging due to the inability to extend the leg and to the displacement of the femoral nerve and the surrounding structures caused by the tumor and its neo-angiogenesis. However, despite these challenges, the procedure, performed with the patient in a seated position, provided almost 70% pain relief. Therefore we agreed to proceed with a neurolytic block to be performed, upon patient's request, under general anesthesia to allow for appropriate positioning and comfort.

The patient was brought to the operating room, and after general anesthesia was induced, he was placed in the supine position. Even under general anesthesia and with the patient in the supine position, full extension of the leg was not possible. The femoral nerve was identified with some difficulty under US guidance (Philips Sparq™ Broadband Sector Linear Array Transducer). Appropriate nerve stimulation was achieved utilizing a 22-gauge 50-mm echogenic Pajunk™ needle, and 8 mL of bupivacaine 0.5% and 10 mL of an aqueous solution of phenol 6% were injected. The patient tolerated the procedure well, and recovered from the anesthetic uneventfully. In the recovery room he noted a moderate burning sensation in the proximal thigh that subsided over the next 6 hours.

Chemical neurolysis of the femoral nerve provided 6 months of nearly 100% pain relief. The patient was able to sleep in the supine position and to perform physical activities relatively pain-free. The dose of fentanyl patch was decreased by 50% within the first few weeks after the procedure and eventually discontinued. He continued to use, occasionally, small doses of prn morphine. The patient reported only moderate to severe pain around the area where phenol had been injected. This increased painful sensation was likely due to the chemical irritation of the femoral nerve caused by the phenol solution and it resolved spontaneously in approximately 10 days. No other complications were reported. He continued to walk with the help of a walker.

With the tumor spreading in girth distally and to the scrotal and pelvic areas proximally, as well as to the lungs, pain eventually returned back to baseline in the distribution of the femoral nerve. The use of opioids gradually increased. Again the patient was not able

to sleep in the supine position nor was he able to perform physical activities such as walking or transferring to and from the toilet without assistance. He was re-evaluated at our institution and the decision to proceed with a second femoral nerve chemical neurolysis under general anesthesia was made. Unfortunately we were not able to achieve adequate pain relief with this intervention. Visualizing the femoral nerve under US guidance, already challenging the first time, proved to be more challenging the second time; the increased size and the anatomical derangements caused by the tumor made the identification of the target impossible. This was discussed with the patient and his wife in the recovery room. The inability to adequately spread phenol around the nerve was the likely reason for the procedure failure.

During a subsequent follow-up visit at the pain center to discuss further options for pain management, the possibility to proceed with another IT trial using local anesthetic was discussed. Again the patient and his wife declined this option. Therefore we decided to proceed with a diagnostic injection of local anesthetic under fluoroscopic guidance at the left L2, L3, and L4 nerve root levels, in preparation for a possible chemical neurolysis. The patient and his wife clearly understood risks and benefits of the intervention suggested, including the possibility of permanent paralysis, and agreed to proceed.

The diagnostic block of the left L2, L3, and L4 nerve roots was performed under general anesthesia. The transforaminal approach with fluoroscopic guidance was utilized. Three 22-gauge 3.5" Quincke spinal needles were used. After appropriate contrast spread was achieved (Fig. 1) and digital subtraction angiography (DSA) demonstrated no intravascular penetration of the contrast medium, a small amount of local anesthetic (ropivacaine 0.5% 1 mL) was injected at all 3 levels. After an uneventful recovery the patient reported 100% pain relief for several hours.

Chemical neurolysis of the left L2, L3, and L4 nerve roots was performed several days later in a similar fashion. One mL of an aqueous solution of phenol 3% was injected at the 3 levels under fluoroscopic guidance with DSA (Fig. 2). Almost complete pain relief was achieved for the remainder of the patient's life. He reported no sensory-motor related side effects or complications and was able to travel and visit with family and friends before peacefully passing away.

DISCUSSION

In spite of the appropriate implementation of the WHO guidelines (2) and the utilization of multimodal approaches to decrease pain, many cancer patients continue to suffer from inadequate management of their pain. Often in order to achieve adequate pain control,



Fig. 1. Digital subtraction angiography demonstrating no intravascular penetration of contrast medium.

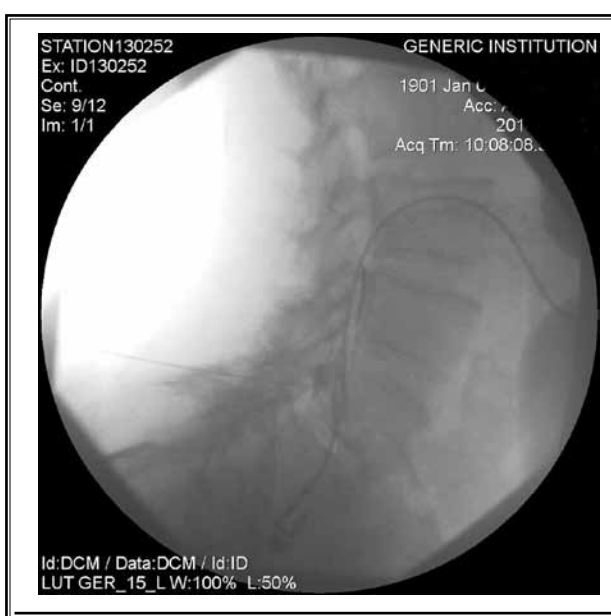


Fig. 2. Image showing chemical neurolysis of the left L2, L3 and L4 nerve roots.

high doses of opioids and other medications are necessary. Furthermore side effects such as constipation, pruritus, respiratory depression, sedation, and mental status deterioration may develop, causing disruption to the quality of life of patients and their families. High doses of opioids have also been reported to have a negative effect on cellular immune response (11); they may, potentially, play a role in neoplastic recurrence and the development of metastasis (12,13). Patients with a pain syndrome secondary to a neoplastic disease and who have had pain managed with appropriate interventional techniques such as intrathecal delivery systems or neurolytic blocks have been reported to live longer (14,15), suggesting that adequate pain control achieved with the minimal use of opioids is paramount when managing patients with cancer at any stage of the disease.

Chemical neurolysis with alcohol or phenol in combination with other treatment modalities has been reported to be effective especially in patients with refractory epigastric abdominal pain related to pancreatic cancer (15,16) and in patients with intractable pelvic pain (17).

At low concentrations (< 2%) phenol can be used as a short-term anesthetic with minimal nerve injury (18). At higher concentrations, phenol causes nerve destruction by inducing protein precipitation, loss of cellular fatty elements, separation of the myelin sheath from the axon, and axonal degeneration (19). Data indicate that at concentrations of ~5 – 7% phenol may cause a minimum of second degree nerve injury with minimal to no loss of the endoneurial nerve structure (20). At higher concentrations (7.5% – 10%), permanent anesthesia and muscle weakness have been reported, indicating an almost complete disruption of the nerve architecture (21).

Neurolysis with phenol is associated with a lower incidence of neuritis than ethanol, causes less pain on injection (4) and less local tissue irritation (5), and has an immediate local anesthetic effect due to its activity on smaller sensory nerve fibers while sparing larger motor fibers (19). These characteristics make the use of phenol more appealing when the neuraxial use of the medication may become necessary because pain is very severe, all other treatment modalities have failed, the patient refuses to proceed with the implantation of an IT delivery system, or when significant side effects from the use of opioids and other medications have developed (10).

Although side effects and complications from chemical neurolysis with phenol are rare, persistent

paraplegia after phenol intercostal neurolysis, resulting from the diffusion of phenol into the epidural space (22), or as a result of vascular ischemia of the spinal cord during the performance of a celiac plexus (23) and intercostal nerve blocks (24) has been reported. Severe systemic complications such as acute respiratory and renal failure have also been described (25).

Even though previous reports of phenol neurolysis performed within the intrathecal space or at the nerve root level have been associated with the development of motor weakness, bladder and bowel dysfunction, loss of sensation, and spinal cord infarction (26-28), our patient did not report any side effects or complications from the procedures performed. It is possible that the relatively low concentration of the phenol solutions used (6% and 3%) and low volume (10 mL for the femoral neurolysis, 1 mL at each level for the L2, L3, and L4 roots neurolysis) may have contributed to the achievement of adequate sensory analgesia and no motor paralysis.

Spread of small volumes of aqueous solutions of local anesthetic and phenol after single nerve injections has been reported (29). However in spite of this well-documented phenomenon that can be associated with the development of disturbing side effects and complications, our patient reported only a moderate to severe increase in pain for a few days after all neurolytic procedures, likely due to the chemical irritation of the femoral nerve and lumbar nerve roots. The increased pain eventually subsided, and sustained pain relief allowed a progressive tapering of the opioids and other medications.

Some authors advocate for the use of phenol in combination with glycerin 50% if injections are performed in areas close to the spine in order to limit the extension of the medication in the dorsal epidural space and minimize the bathing of the ventral motor nerve roots with local anesthetic and phenol (10,30,31). We decided to inject only phenol in our patient. He had no previous history of spine surgery causing disruption in the continuity of the ligamentum flavum and posterior longitudinal ligament; furthermore during the procedures we always observed spread of contrast medium along the dorsal nerve roots with no bathing of the ventral nerve roots nor penetration in the epidural space. We felt confident that the small volume and concentration of the phenol solution used and the appropriate spread of the solution along the dorsal root ganglions was enough evidence to warrant performing the injection without the addition of glycerin

to the solution. That also allowed us to use a smaller 22 gauge Quincke spinal needle compared to the larger size needles that may be necessary when injecting phenol with glycerin (29). The use of small size needles may also, in part, have limited the spread of phenol into the epidural space.

The neuraxial procedures (diagnostic and neurolytic) were performed on our patient with fluoroscopic guidance and DSA technology. Inadvertent penetration of contrast medium and medication into the vascular tree supplying the spinal cord and other vital structures, potentially causing devastating complications has been reported (32-35). Even though the inadvertent injection into a vessel can be perceived with traditional fluoroscopy, the addition of DSA technology to real-time fluoroscopy when performing interventional pain procedures improves significantly the detection rate of intravascular injection (36,37). Although the use of DSA technology is by no means fool-proof (38), we advocate for its use in interventional pain management, especially in patients, like ours, who may need heavy sedation or general anesthesia in order to tolerate positioning for the proposed intervention.

Finally, after a careful disclosure of the risks and benefits and upon the patient's request after the diagnostic femoral nerve block had been performed with him being awake, all procedures were performed under general anesthesia. Although performing regional anesthesia blocks and interventional pain procedures

with the patient awake or only lightly sedated may be preferable, the intensity of the pain experienced by our patient was so severe that he could not tolerate the recumbent position for the performance of the femoral nerve block nor the prone position needed for the lumbar nerve root blocks. We believe that in the hands of providers who are familiar with the procedures to be performed, and with the availability of the appropriate technology (US and fluoroscopic guidance with DSA), still being cognizant of the potential limitations of these technologies, chemical neurolytic procedures can be performed under heavy sedation or general anesthesia, particularly in patients with intractable pain who may not be able to cooperate with the operator to allow for optimal positioning and visualization of the target.

CONCLUSIONS

Chemical neurolysis with phenol is an effective option for the management of intractable cancer pain. With careful selection, appropriate coaching, and in the hands of experienced practitioners familiar with the techniques and the procedures to be performed, it can provide excellent results with minimal side effects and complications, and result in sustained relief with subsequent improvement of patients' quality of life.

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