

## Case Series


**Brachial Plexus Block for Cancer-Related Pain: A Case Series**

Nantthasorn Zinboonyahgoon, MD<sup>1</sup>, Kamen Vlassakov, MD<sup>1</sup>, Christ R. Abrecht, MD<sup>1</sup>, Suresh Srinivasan, MD<sup>2</sup>, and Sanjeet Narang, MD<sup>1</sup>

From: <sup>1</sup>Department of Anesthesiology, Perioperative and Pain Medicine, Brigham and Women's Hospital, Boston, MA; <sup>2</sup>Department of General Surgery, Creighton University Medical Center, Omaha, NE

Address Correspondence: Nantthasorn Zinboonyahgoon, MD  
Department of Anesthesiology, Perioperative and Pain Medicine  
Brigham and Women's Hospital,  
75 Francis St.  
Boston, MA  
E-mail:  
nantthasorn@gmail.com

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Neoplastic brachial plexopathy (NBP) is caused by a cancerous infiltration into the brachial plexus, presenting often as severe pain in the affected upper extremity. Such pain can be resistant to medical treatment. Invasive interventions such as brachial plexus neurolysis with phenol or cordotomy may result in severe complications including permanent neurological damage and death. Continuous brachial plexus and paravertebral block with local anesthetic have been reported to successfully control pain from NBP, but these techniques are logistically challenging and frequently have catheter-related complications.

We report a series of patients who received single-shot brachial plexus blocks with a mixture of local anesthetic and corticosteroid (bupivacaine 0.25% with methyl-prednisolone 20 – 120 mg) for the treatment of refractory cancer-related pain in the brachial plexus territory, mostly from NBP. Theoretically, such blocks could provide immediate analgesia from the local anesthetic and a longer-lasting analgesia from the slow-release steroids.

Responders reported a sustained decrease in their pain (lasting from 2 weeks to 10 months), a significant decrease in their opioid and non-opioid (ketamine, gabapentin) consumption, overall satisfaction with the block, and unchanged or improved function of their limb. The ideal candidate for this procedure is a patient who has pain that is predominantly neuropathic from a lesion within the brachial plexus and with anatomy amenable to ultrasound-guided nerve block.

Our case series suggests that, in the appropriately selected patient, this technique can safely and effectively alleviate pain from NBP. The procedure is simple, spares limb function, and can be diagnostic, predicting response to more complex procedures. To the best of our knowledge, this is the first report using this technique for NBP.

**Key words:** Brachial plexus block, neoplastic brachial plexopathy, intractable pain, cancer pain, pain intervention

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**N**eoplastic brachial plexopathy (NBP) is caused by a cancerous infiltration into the brachial plexus, usually originating from a lung or breast malignancy. It often presents with Horner's syndrome as well as numbness, weakness, and severe unrelenting pain in the affected upper extremity (1,2). Although malignant invasion of the brachial plexus occurs in only 3% of lung cancers and less than 0.5% of breast cancers, it accounts for intractable pain in 31% of lung cancer patients and 37% of breast cancer patients (2-4).

Pain from NBP can be resistant to medical treatment with oral non-steroidal anti-inflammatory drugs (NSAIDs), steroids, antidepressants, opioids, or even intrathecal opioids (3,5). Radiation therapy can provide significant pain relief, but 10% of patients do not respond to treatment and the typical course takes 2 – 4 weeks to complete – in addition, radiation has serious side effects and a dose limitation for each body area (6). Other invasive interventions to alleviate pain from NBP include brachial plexus neurolysis with phenol (7)

and cordotomy (3,8). These techniques, however, are not always effective and may result in permanent neurological damage (3,7). Spinal cord stimulators may be beneficial for treating neuropathic pain, but the evidence for their use in NBP is scarce. Furthermore, the presence of an implanted spinal cord stimulator is often a contraindication for magnetic resonance imaging (MRI), a test many cancer patients must undergo. Continuous brachial plexus block and continuous paravertebral block with local anesthetic have been reported to successfully control pain for NBP (9,10). However, continuous indwelling catheter techniques present inherent logistical challenges and catheter-related complications (11).

We report a series of 8 patients who received brachial plexus blocks with local anesthetic and corticosteroid mixtures for treatment of cancer-related pain originating from within the brachial plexus or from an adjacent region. Seven of these patients received single-shot injections and in one patient, a successful continuous block was followed 6 days later by the placement of a tunneled brachial plexus Port-a-Cath™ (Smiths Medical, Dublin, OH). Our case series explores the effectiveness, safety, and feasibility of these techniques. It also discusses a possible mechanism and the next steps for this treatment modality.

## METHODS

The medical records of 8 patients who underwent brachial plexus blocks for cancer-related pain from 2007 to 2015 were reviewed with Institutional Review Board approval. The collected data included patient de-

mographics, procedure notes, pain scores, opioid consumption, limb function, global physical performance (e.g., ECOG score), and complications related to the procedures. Data were collected from the time of cancer diagnosis through last documented clinical encounter, transfer to hospice, or death note.

## Procedure

The brachial plexus blocks were performed at the bedside or in a procedure room at the pain clinic, after obtaining written consent and the application of standard American Society of Anesthesiologists (ASA) monitors. The patients were positioned supine. Their block sites were prepped with chlorhexidine and linear 10 – 12 MHz ultrasound probes with standard sterile covers were applied. After obtaining optimal images via either a supraclavicular (Fig. 1) or an interscalene approach (Fig. 2), the block needle was inserted and advanced in-plane under real-time ultrasound guidance towards the brachial plexus. After negative intermittent aspiration for blood, a mixture of 0.25% bupivacaine or 0.5% ropivacaine and methylprednisolone was incrementally injected perineurally. From the series, the volume of local anesthetic varied from 6 – 22 mL, based on the spread of the injectate surrounding the target nerve structures to a satisfactory sonoanatomy end-point and amount of methylprednisolone varied from 20 – 120 mg. For the average-sized patients, the suggested optimal volume of local anesthetic is approximately 10 – 12 mL containing 60 – 80 mg of methylprednisolone.

Of note, one patient (patient 2) underwent a concurrent nerve block and catheter insertion for continu-

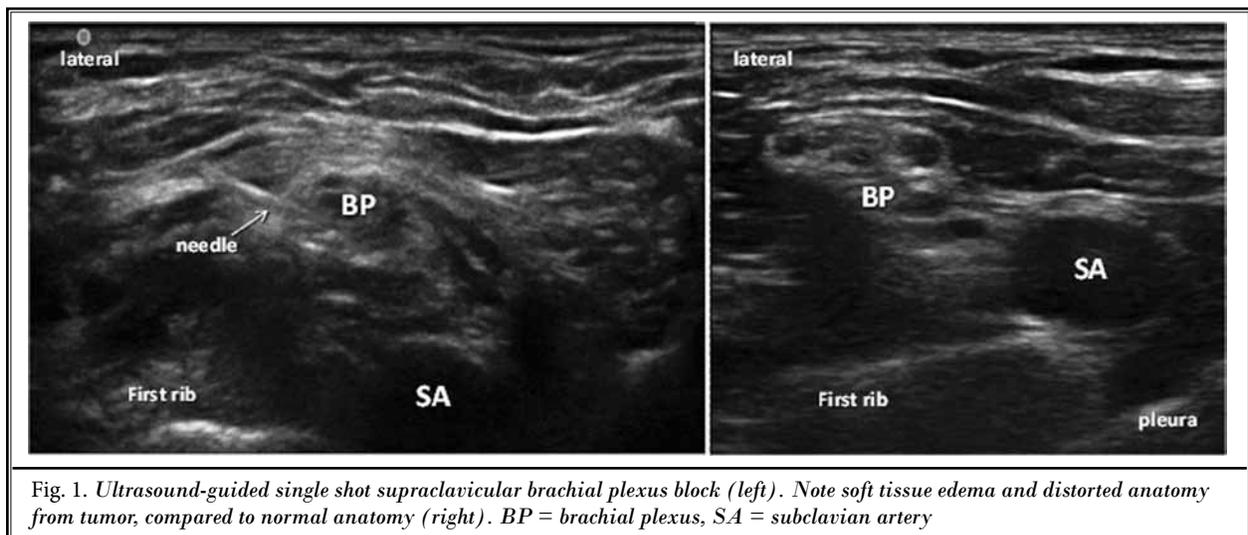


Fig. 1. Ultrasound-guided single shot supraclavicular brachial plexus block (left). Note soft tissue edema and distorted anatomy from tumor, compared to normal anatomy (right). BP = brachial plexus, SA = subclavian artery

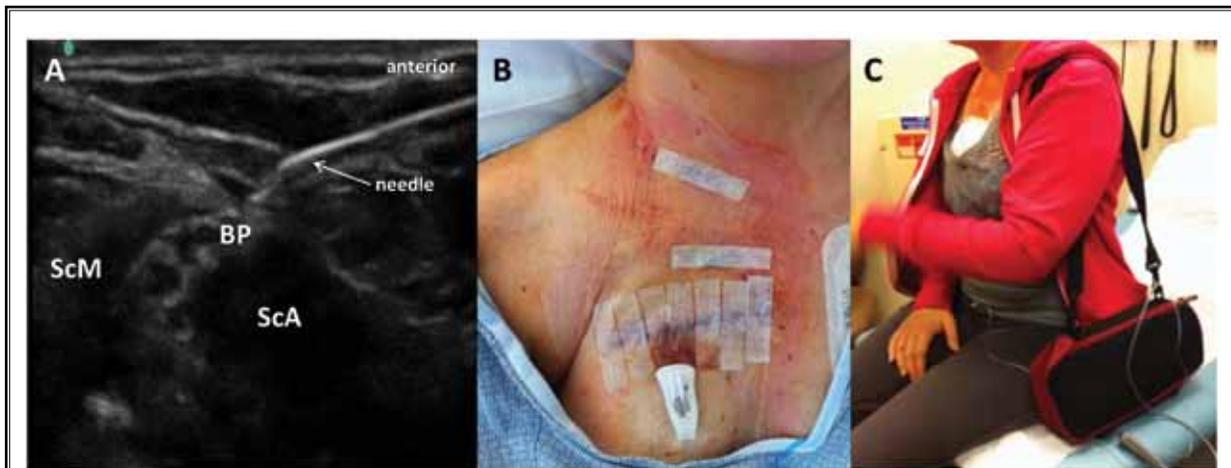


Fig. 2. Implantation of permanent interscalene catheter in patient 2. A. Ultrasound-guided anterior approach for interscalene block with catheter. Note that the block needle (second procedure in this patient) is inserted from anterior to posterior in order to minimize the kinking of the tunneled catheter. B. Accessed Port-a-Cath on patient's right chest for permanent attachment of interscalene catheter. C. Patient at the pain clinic for a follow-up appointment, with a travel case containing bupivacaine reservoir. ScA = Scalenus anterior, ScM = Scalenus medius

ous infusion. After 6 days of adequate pain relief with the continuous infusion, the original catheter was removed and this patient underwent a second brachial plexus block and insertion of a tunneled catheter and implanted Port-a-Cath (Fig. 2). All these procedures were supervised by the same attending physician from the interventional cancer pain service. Details of the procedures performed on each patient are listed in Table 1.

## RESULTS

The primary complaint of all 8 patients was severe upper extremity pain, refractory to medical treatment. Seven of these patients had symptoms consistent with brachial plexopathy. In addition to this neuropathic pain, patients 4 – 6 had nociceptive pain in chest wall and lower back. In contrast, patient 7 had only nociceptive pain, from invasion of the humeral head (Table 1).

The ages of these patients ranged from 40 to 76 years. Their primary malignancy varied, but the mass causing the pain was in the axilla and/or the pulmonary apex in all patients, except patient 7. All patients received palliative chemotherapy or radiotherapy or both along with pain treatment.

No complications related to the brachial plexus blocks were observed. Notably, no further sensory or motor deficits resulted; in fact, patient 3 reported improved strength and functionality of his affected limb (Table 2).

Patients 1 – 5 reported a sustained decrease in their

pain scores, unchanged or improved function of their limb, and overall satisfaction with the block. Opioid and non-opioid (ketamine, gabapentin) consumption were significantly decreased or stopped among the responders. According to the medical records, the pain relief lasted from 2 weeks (in which case the pain score had been recorded only once after the block prior to the patient's death at 4 weeks after the block) to 10 months. We considered these patients responders.

Two patients reported a long-lasting effect from the blocks and received a second block. Patient 3 reported reduction of pain from a 3/10 to a 2/10 after the first block as "significant." He received an additional block 2 months after his initial block due to pain from a worsening tumor burden. He was then pain free and off opioids until his death, 10 months after the second block. Patient 5 reported being initially pain free after the first block, but that the pain gradually increased over time. She received the second block 6 months later with significant pain relief.

Among responders, only one patient, patient 4, needed an additional intervention to cover pain outside the upper extremity. While she did report a decrease in pain from "severe" to "significantly improved" at one month, she ultimately underwent an intrathecal pump placement at 2 months after the block to cover pain in the chest wall related to worsening disease burden.

The only patient in this series who had improved performance score was patient 2, who also received a

Table 1. Patient demographics, pain characteristics, and description of nerve blocks.

	Age	Gender	Primary malignancy	Location	Symptoms	Initial block	Agents used in block
1	60	F	Breast adenocarcinoma	Left axilla, brachial plexus	Neuropathic pain: Left arm radiating to hand	Left supraclavicular, single shot	Bupivacaine 0.25% 17 mL and methylprednisolone 120mg
2	36	F	Synovial cell sarcoma	Right pulmonary apex, brachial plexus	Neuropathic pain: Right shoulder and arm, radiating to first - third digits	Right interscalene, then catheter for continuous infusion	Ropivacaine 0.5% 22 mL and methylprednisolone 80 mg, then bupivacaine 0.125% at 8 mL/hr
3	55	M	NHL	Left axilla, brachial plexus	Neuropathic pain: Left shoulder and arm, radiating to elbow	Left interscalene, single shot	Bupivacaine 0.25% 17 mL and methylprednisolone 120 mg
4	53	F	Breast adenocarcinoma	Left axilla brachial plexus, chest wall, pectoralis major muscle	Neuropathic pain: Left medial arm, radiating to elbow (the major pain source) Nociceptive pain: Left lateral chest wall	Left supraclavicular, single shot	Bupivacaine 0.25% 6 mL and methylprednisolone 80 mg
5	67	F	NSCLC	Right lung apex, brain, liver, spine	Neuropathic pain: Right shoulder and arm radiating to finger Nociceptive pain: Low back pain	Right interscalene, single shot	Bupivacaine 0.25% 10 mL and methylprednisolone 20 mg
6	76	F	NSCLC	Left pulmonary apex, brachial plexus Paraspinal mass left C6-T4, left chest wall	Neuropathic pain: Left arm, radiating to elbow Nociceptive pain: Left lateral chest wall pain	Left supraclavicular and intercosto-brachial block, single shot	Bupivacaine 0.25% 13 mL, methylprednisolone 80 mg for brachial plexus block and bupivacaine 0.25% 3 mL with methylprednisolone 20 mg for intercosto-brachial block
7	40	F	Carcinoid, pulmonary	Left humerus head	Nociceptive pain: Left shoulder and arm, radiating to elbow	Left interscalene block, single shot	Bupivacaine 0.25% 12 mL, methylprednisolone 120 mg
8	75	F	SCC of lung	Right pulmonary apex	Neuropathic pain: Right shoulder and arm pain, radiating to 1st-3rd digits	Right supraclavicular, single shot (technically difficult)	Bupivacaine 0.25% 17mL and methylprednisolone

Note: SCC is squamous cell carcinoma, NHL is non-Hodgkin's lymphoma, NSCLC is non-small cell lung carcinoma

brachial plexus catheter and reported an improvement in her ECOG score from 3 to 2, permitting the resumption of her chemotherapy. Unfortunately, during a subsequent chemotherapy-related neutropenic episode her Port-A-Cath wound dehiscd. Shortly thereafter, an intrathecal pump was implanted in lieu of the brachial plexus catheter due to worsening disease burden.

Not all of the patients experienced pain relief and were satisfied with the blocks. Patient 6 reported no changes in pain score, functional status, or opioid use. However, a subsequent thoracic epidural steroid injection did provide moderate pain relief before the patient transitioned to hospice. Patient 7, whose tumor was in the humeral head and was nociceptive in nature, reported complete relief of pain for 2 days but then return to baseline pain; an intrathecal pump implanted

prior to transition to hospice provided sustained relief. Lastly, the block for patient 8 was technically difficult and probably failed. The patient reported no improvement with the block but finally had some relief with a cervical epidural steroid injection performed prior to transition to hospice. See Table 2 for more individual details.

## DISCUSSION

This series demonstrates that single shot brachial plexus block with local anesthetics and steroids, with appropriate patient selection, is an effective treatment for NBP. To the best of our knowledge, this is the first report using this technique for NBP.

NBP is an uncommon condition of common cancers and usually presents as severe intractable neuropathic

## Brachial Plexus Block for Cancer-Related Pain

Table 2. Result of intervention and patient disease course.

ID	Pain score	Functional status	Analgesic requirement* (oral morphine mg/day)	Intervention after block	Disease course
1	9/10 → 4/10 at 2 weeks	ECOG 2 → ECOG 3 at 2 weeks	300 mg → 129 mg at 2 weeks	No	Despite improved analgesia, patient admitted to palliative care unit 2 weeks after block due to worsening disease burden; patient died in hospice one month after initial block.
2	severe → mild at 3 weeks	ECOG 3 → ECOG 2 at 3 weeks	Narcotics: 4,300 mg → 300 mg Ketamine infusion → off at 3 weeks	Intrathecal pump after 3 weeks	Due to improved functional status, patient restarted on chemotherapy. During a subsequent neutropenic episode, Port-a-Cath dehisced. An intrathecal pump was then inserted and provided pain relief until last follow-up, 7 months after initial block.
3	3/10 → 2/10 at 2 months	ECOG 2 → ECOG 2 at 2 months	180 mg → no opioids at 2 months	Repeat interscalene block at 2 months	Pain and range of motion were significantly improved, but due to worsening disease burden (transformation to follicular lymphoma) and reduced but persistent pain, patient received a repeat block 2 months later. Patient had minimal pain and was off opioids until time of death, 12 months after initial block.
4	severe → significantly improved at 1 month	ECOG 2 → ECOG 2 at 1 month	32 mg → 43 mg at 1 month	Intrathecal pump at 2 months	Due to worsening pain in arm and lesion in chest wall in setting of worsening tumor burden, intrathecal pump was placed 2 months after block. Patient died 4 months after initial block.
5	6/10 → 0/10 at 6 weeks	ECOG 1 → ECOG 1 at 6 weeks	Narcotic: 15 mg → no change Gabapentin 3600 mg → 1800 mg, at 1 month	Repeat interscalene block at 2 months	Patient reported pain free for 6 weeks, then the pain was gradually increased to 2 – 3/10, but able to stop narcotic. Finally pain increased to 6/10 at 6 months and patient received a repeat block. Patient had significant pain relieved after the second block.
6	8/10 → 8/10 at 1 month	ECOG 2 → ECOG 2 at 1 month	15 mg → no change at 1 month	TESI/ ICB at 1 month	Due to lack of response to BPB, TESI at T3-4 and repeat ICB at T2-T4 were performed a month later and provided moderate pain relief. Patient was transferred to hospice 10 months after initial block.
7	10/10 → 0/10 at 2 days, then returned to baseline	ECOG 2 → ECOG 2 at 2 days	240 mg → no change at 2 days	IT pump at 3 weeks	Due to lack of response to BPB and worsening disease burden, intrathecal pump was placed 3 weeks later. Patient died 3 months after initial block.
8	severe → severe at 3 weeks	ECOG 2 → ECOG 2 at 3 weeks	150 mg → no change at 3 weeks	CESI at 3 weeks	Due to lack of response to BPB, CESI was performed 3 weeks later and provided moderate pain relief. Patient was transferred to hospice, 3 months after initial block.

Note: Analgesic requirement\* (oral morphine equivalent, mg/day), not including prescribed breakthrough medications (PRN doses) (27). TESI is thoracic epidural steroid injection, CESI is cervical epidural steroid injection and ICB is intercostal block. ECOG is the Eastern Cooperative Oncology Group score, with 0 reflecting an asymptomatic, healthy patient, 2 reflecting a symptomatic patient spending <5 0% of the day in bed, 3 reflecting a symptomatic patient who is not bedbound but who spends > 50% of the day in bed.

pain. Invasive interventions such as brachial plexus neurolysis with phenol and cordotomy have been implemented to alleviate this pain but are often associated with severe complications. Cordotomy has been shown in a series by Watson and Evans (3) to successfully manage this pain syndrome, but it can also result in dysesthesia, permanent urinary retention, hemiparesis, respiratory arrest, and death. Brachial plexus block with phenol has been shown in a small series by Mullin (7) to provide significant pain relief with the initial block, but diminishing returns with subsequent blocks, likely

due to scar formation. In addition, that series noted an increase in arm weakness and sensory deficits after the blocks with phenol (7).

Regional anesthetic technique with local anesthetics is less likely to cause the aforementioned complications and has been employed to control pain in NBP. Vranken et al reported successful pain control with continuous brachial plexus block in Pancoast tumor with continuous axillary (9) and with cervical level brachial plexus catheters (10). Pelaez et al (5) also reported successful pain control with continuous cervical paraver-

tebral block. However, brachial plexus catheters, even for a period of only 24 hours, have catheter-related problems (e.g., dislocation, secondary pneumothorax) approaching an incidence of 6.7%, and the longer the duration of catheter, the higher the chance of complications such as catheter disconnection, obstruction, and infection (11). Moreover, catheters can make ambulation and some daily activities more difficult, and present logistic challenges of catheter care and medication refills.

To treat malignant pain while minimizing complications and problems, we performed brachial plexus blocks (7 single-shot and one continuous) with local anesthetic and depot-steroids to 7 patients with NBP and to one patient with pain in brachial plexus territory (patient 7). Most of our patients can be classified as responders (patients 1 – 5) – they were satisfied with the blocks and showed a significant improvement in pain and/or decreased opioid consumption. In contrast, patients 6 – 8 were considered non-responders because they did not meet any of these criteria and ultimately needed to pursue other pain management interventions.

We performed the brachial plexus blocks with a mixture of bupivacaine 0.25% (patients 1, 3 – 8) and methylprednisolone. Bupivacaine alone for brachial plexus block has an analgesic effect lasting 9 – 13 hours (12) and methylprednisolone, a particulate slow-release steroid cleared by local tissue esterases, usually has an effect lasting up to 8 weeks, depending on location (13). Theoretically, the ideal block would provide immediate anesthesia/analgesia from the local anesthetic and a longer-lasting analgesia from the slow-release steroids (13-15).

The mechanism of the corticosteroid effect on nerve blocks is not completely understood. A possible explanation in malignant nerve entrapment could be that the steroids may directly decrease the perineural inflammation from tumor compression and/or infiltration (13,16). Another possibility relates to the observation that nerve damage can cause both spontaneous neural discharge via derangement of voltage-gated sodium channels in injured nerves as well as upregulation of transient receptor potential V1 (TPRV1) in neighboring uninjured C fibers which results in spontaneous pain and hypersensitivity (14). Steroids suppress spontaneous ectopic discharge in injured nerves (15,17) and inhibit transmission of C-fibers, including in healthy nerves (18). These mechanisms may explain the benefit of local corticosteroid in treating neuropathic

pain and the inability to treat nociceptive pain, even if in the area innervated by the brachial plexus, as was the case with patient 7. Finally, the locally administered steroids are systemically absorbed, possibly producing systemic analgesia and a decrease in systemic inflammation (19,20).

Our series noted analgesic effect of the nerve blocks among the responders lasting from 2 weeks to 10 months. Patient 1, who reported pain relief at 2 weeks follow-up, could have had a longer analgesic effect but died before the next follow-up. Patients 3 and 5 reported pain relief for 10 and 6 months, respectively. The duration of pain relief outlasting the theoretical elimination half-life of methylprednisolone could be the result of chemotherapy or radiation therapy. Therefore, brachial plexus blocks may be used not only as a palliative pain control measure during the end-of-life stage, but also as a bridging technique, complementing the effects of chemotherapy and radiation therapy earlier in the disease course.

Among the responders, pain and opioid consumption were decreased, but improvement in performance status (as measured by the ECOG score) occurred only in one patient (patient 2), whose brachial plexus block was followed with a continuous infusion of local anesthetic. This result is consistent with the results of Vranken et al (10), demonstrating that a continuous infusion not only reduces pain but also improves functional status. Compared to single injection, therefore, continuous infusion may offer superior pain control, especially for pain with movement, and even improve functional status. Such a conclusion, however, cannot be made based only on the limited data of one patient in our retrospective study. Unfortunately, patient 2 ultimately developed complications related to her Port-A-Cath site during a neutropenic episode. Even if continuous infusions are shown in robust studies to provide better pain control and improvements in functional status, the potential complications of an implanted catheter in immunocompromised, malnourished cancer patients must be carefully considered.

All blocks in our series were performed at the bedside or in a procedure room, while the tunneled catheter and port placement (patient 2) was performed in the operating room. The blocks were performed either by an attending anesthesiologist or by supervised fellows or residents who had significant experience with peripheral nerve blocks. No immediate complications or new neurological deficits were observed, and patients in the responder group usually reported pain relief im-

mediately after the procedure. These procedures, then, proved to be safe, effective, and simple – able to be performed in any place where ultrasound and a skilled anesthesiologist was available. This simple procedure may be particularly useful at managing malignant pain in underserved areas.

Despite these encouraging results, patients 6 – 8 in this series did not respond to the brachial plexus blocks. Patient 6, with NSCLC, presented with pain not only in the brachial plexus distribution but also in the chest wall related to a paraspinal mass from C6 to T4. The lack of adequate relief from the brachial plexus block might have been due to the significant disease burden outside the plexus or proximal to the block site. The successful results reported from the subsequent thoracic epidural steroid injections support this hypothesis. Moreover, due to the dynamic nature of metastatic disease and cancer treatment, even some initial responders (such as patient 4) needed additional interventions. To cover pain outside the brachial plexus territory, epidural steroid injections, intercostal blocks, and intrathecal pumps remain useful options.

Patient 7, suffering from carcinoid in the left humerus head, failed to achieve lasting relief beyond the first 2 days. It could be argued that this patient did not suffer from NBP, since it was the humerus and not the brachial plexus that was affected. As discussed earlier, the nociceptive nature of this patient's pain may explain not only the initial relief from local anesthetic, enhanced by steroid, but also the lack of sustained analgesia from local steroid-mediated effects such as decreasing peri-plexus inflammation which are more apparent in neuropathic pain.

In patient 8, with SCC of the pulmonary apex, brachial plexus block did not produce pain relief, possibly because of failure to deliver the injected medications to the intended target. For patients with anatomical challenges from tumor compression, a more proximal approach such as a cervical root block or cervical paravertebral block or even a high interscalene block may be more successful.

In the setting of NBP pain, the "ideal responder" to a brachial plexus block would be a patient who has pain that is predominantly neuropathic from a lesion within the brachial plexus and with anatomy amenable to ultrasound-guided nerve block. However, not all patients chosen according to these selection criteria will have a good response. This case series did not focus on patients with other types of neuropathic pain in brachial plexus territory such as

deafferentation pain or radiation-induced brachial plexopathy (RIBP), conditions which have different pathophysiology and response to treatment (21,22). Indeed, patients with deafferentation pain will theoretically have a poor response to nerve block and may respond to neuromodulatory intervention such as spinal cord stimulation (23,24). Therefore, brachial plexus blocks could have diagnostic value to determine the cause of pain and prognostic value to predict the response to more complex intervention such as continuous blockade via indwelling perineural catheters (9) or nerve root ablation (25) or brachial plexus radiofrequency ablation (26).

Limitations of this case series include its retrospective nature, disparate pain measurement scales (numeric rating scale vs. verbal categorical rating scale), and clinically accepted, but non-standardized doses of agents administered. Further research is needed to evaluate the effectiveness and feasibility of single shot brachial plexus blocks in refractory cancer pain, as well as the optimal choice of case-specific techniques and medications.

## **CONCLUSION**

Single-shot brachial plexus blocks with local anesthetic and particulate steroid are effective interventions for the treatment of intractable neuropathic pain in properly selected patients who are suffering from NBP. The procedure is simple, safe, and spares limb function. It can be diagnostic and serve to predict response to more complex subsequent procedures.

## **Disclosure**

### **Author Contributions:**

Drs. Zinboonyahgoon, Abrecht, Vlassakov, and Narang have full access to all the study data and take responsibility for the integrity and the accuracy of the data and the data analysis. Dr. Narang and Dr. Srinivasan deigned the study protocol. Dr. Zinboonyahgoon and Dr. Abrecht managed the literature searches and summaries of previous related work and wrote the first draft of the manuscript. Dr. Vlassakov and Dr. Narang provided revisions of the intellectual content and final approval of the manuscript.

### **Conflict of Interest:**

All authors have no conflicts of interest to report. None of the authors of the manuscript received any remuneration. Further, the authors have not received

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