The potential for this side effect should be noted when administering gabapentin for neuropathic pain.

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References

The Impact of Transcatheter Arterial Embolization on Pain Scoring and Analgesic Dosing in a Patient with Metastatic Renal Cell Carcinoma

To the Editor:

We report an account of transcatheter arterial embolization (TAE) as a means of achieving relief from refractory bone and neuropathic pain in a patient with metastatic renal cell carcinoma in the last weeks of life, specifically, detailing changes in pain scores and analgesic dosing after the procedure. Although this technique has previously been described as reducing pain caused by hypervascular tumors, evidence for its use solely as a pain-relieving procedure, including detail of pain scoring or analgesic use, is limited. We believe ours to be the first published account to include such detail.

Case

A 68-year-old woman with metastatic renal cell carcinoma was admitted to hospital with increasing neck pain. She had been diagnosed with a G3pT2 tumor of the right kidney two years previously, managed by nephrectomy alone (ineligible for adjuvant interferon therapy because of her history of vasculitis and steroid use). Eight months post-nephrectomy, she received radiotherapy to her mediastinum for nodal recurrence and was commenced on medroxyprogesterone acetate. Ten months after this, she presented with neck pain and was found to have an expansile mass causing T2 vertebral destruction and early cord compression. She was treated with radiotherapy (40 Gy to C7-T3). When pain returned two months later, and worsening spinal instability was noted on repeat magnetic resonance imaging (MRI), she underwent surgical decompression by means of thoracic laminectomy.

Unfortunately, her pain continued to escalate, exhibiting both bony and neuropathic features. MRI indicated that the T2 mass was now circumferential, with partial destruction of the neck of the second rib. Further, neurosurgical intervention was not considered appropriate given her poor prognosis. Her pain was managed with upward titration of oxycodone and a variety of adjuvants (dexamethasone, gabapentin, topical lidocaine, and ketamine), but three weeks later, pain was no better, and she was extremely drowsy secondary to her large opioid dose. Hospice transfer was arranged. Her analgesic regimen on hospice admission was as follows: oxycodone, 120 mg subcutaneous infusion/24 hours; ketamine, 200 mg subcutaneous infusion/24 hours; gabapentin, 600 mg three times daily; dexamethasone, 6 mg twice daily; lidocaine, 5% patch, and oxycodone, 40 mg orally as needed.

Given her opioid-induced sedation and her desire to be cognitively clear, embolization of the T2 deposit was proposed as an alternative to either increasing the ketamine or switching to methadone. The patient was fully informed of potential risks and benefits of the procedure and decided to proceed, returning to the acute
hospital where TAE was performed under general anesthesia. On waking from the anesthetic, she described a reduction in her pain score, which further reduced to zero over the next 96 hours (Fig. 1). She suffered no complications from the procedure. By Day 27, post-TAE, her analgesic doses had reduced significantly (Fig. 1), down to oxycodone slow release 30 mg every 12 hours (25% of original oxycodone dose) and gabapentin 300 mg twice daily. The ketamine and lidocaine were discontinued. She was, consequently, much more alert, remaining both alert and comfortable up until the time of her death, 46 days post-TAE.

Comment

Deliberate vascular occlusion by means of TAE was first described in the treatment of a spinal cord angioma in 1967.1 Interventional radiology advances have seen its use in the management of a variety of both benign2–4 and malignant conditions, where it has been reported to successfully reduce hemorrhage, pain, tumor bulk, hormone production and hypercalcemia.5–8 For bone metastases, it has been used to alleviate pain5–11 and to minimize neurological deficit caused by spinal cord compression.12,13 It also can be part of a preoperative strategy to reduce intraoperative blood loss, particularly with hypervascular metastases, such as in renal or thyroid carcinomas.14,15 The proposed analgesic mechanism of TAE is to decrease vascular supply to the tumor, thereby impeding growth and causing necrosis. Shrinking the tumor may reduce pressure on the nerve fibers of the periosteum and any spinal nerve roots involved.10

TAE is usually performed by transfemoral access, which allows selective catheterization of most of the arterial system.16 The tumor is identified by the characteristic “tumor blush” generated by the capillary tumor bed feeding the tumor. For spinal lesions, it is also important to identify any supplementary arteries of the vertebrae originating from the tumor-feeding arteries, as embolization of these may induce cord infarction. Embolization is performed once a safe catheter position is found. The goal is to eliminate the capillary tumor bed, demonstrated by the absence of “tumor blush” on follow-up arteriography (Fig. 2). For many patients, local anesthesia is sufficient, but more technically difficult lesions may necessitate a general anesthetic, with attendant risk.

There are no randomized controlled trials of TAE for the palliation of painful bone metastases. Several case series indicate positive results, documenting an improvement in postprocedure pain in most of the cases.10,16,17 Nagata et al. published a series of 29 patients with painful bone metastases, and using the Radiation Therapy Oncology Group pain scoring (severity [0–3] × frequency [0–3]), identified a decrease in postprocedure scores in 76% of cases at two weeks.18 However, the embolization particles used were infused together with chemotherapeutic agents; hence, the impact of vessel embolization alone is difficult to determine. Other studies have used TAE in combination with treatment modalities, such as radiotherapy, surgery, and radioactive iodine.19 Although it is impossible in these
situations to ascribe a direct effect for any one treatment, subgroup analysis did support an association between TAE and improvement in pain, while also indicating that additional therapies increased the duration of successful pain relief achieved.\textsuperscript{19}

The duration of the analgesic effect achieved by TAE alone would appear to be difficult to estimate for any given individual, varying widely between studies. Eustatia-Rutten et al. suggest a median duration of pain relief of six months for TAE alone,\textsuperscript{19} which would potentially make this a definitive procedure for someone with a short prognosis, as was the case with our patient. If prognosis is longer, TAE may be used to supplement the effect of other treatment modalities, affording longer duration of pain relief; it may be repeated when pain recurs (possibly a sign of development of a collateral circulation). Uemura et al., when comparing TAE with radiotherapy for the treatment of bone metastases from hepatocellular carcinoma, found that both offered a similar degree of analgesia, although the time interval to the onset of pain relief from TAE was much less (4.7 days) compared with radiotherapy (15 days).\textsuperscript{20} This study also suggested that combining the two modalities increases the duration of analgesia achieved.

Possible complications of TAE include cardiac arrest, permanent neurological deficit, and skin or muscle necrosis, depending on the vascular territory affected. Severe complications appear rarely in published series,\textsuperscript{18,19} but there is no way of calculating risk for any given individual. More commonly reported is the “postembolization syndrome,” with increased pain, fever, and malaise the week after the procedure, potentially because of postembolization edema, causing a transient increase in tumor size and local pressure, together with tissue necrosis. This was not something encountered by our patient.

In summary, this case demonstrates the safe use of TAE for the relief of refractory bone and neuropathic pain caused by a high thoracic hypervascular tumor deposit. The beneficial effect, as demonstrated in the patient’s pain scores, allowed significant reduction of analgesics and elimination of opioid side effects. Although this may represent a relatively unique situation, it highlights the potential role for invasive procedures even at the end of life and the consideration of TAE as a tool in the management of complex pain relating to hypervascular tumors and their metastases.

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References


Re: Complex Regional Pain Syndrome After Infliximab Infusion

To the Editor:

We read with interest the letter, “Complex Regional Pain Syndrome After Infliximab Infusion,” by Chahine et al.,1 which described a 36-year-old woman who developed symptoms of edema and severe pain in her right leg. These symptoms occurred after a routine intravenous infusion of the anti-tumor necrosis factor alpha antibody, infliximab, into the right arm. These symptoms occurred after a routine intravenous infusion of the anti-tumor necrosis factor alpha antibody, infliximab, into the right arm. The criteria for complex regional pain syndrome (CRPS)2 allow the diagnosis of CRPS in this case despite the absence of symptoms or an identifiable trauma in the limb where the infliximab was infused. Although CRPS can occur in a limb unaffected by an initiating trauma, it more commonly occurs in a limb that mirrors a limb that has been subject to trauma.3 It is also interesting to note that, in the case of infliximab, there is the suggestion that “burning, tingling, numbness or pain in the hands, arms, feet, or legs” is a side effect whose occurrence, although presently not fully revealed, is acknowledged.4

Our concern is that the current criteria for CRPS may lead to inappropriate diagnoses. Moreover, given that the knowledge of CRPS is very much in its infancy, we would suggest that there needs to be caution before concluding that a set of symptoms are, in fact, indicative of CRPS.

For those patients who present with symptoms where there is no apparent trauma to