Ganglion Impar Neurolysis in the Management of Pelvic and Perineal Cancer-Related Pain

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Keywords
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Abstract
Cancer-related pain is a very prevalent problem in all stages, with 10\% of patients requiring invasive techniques for adequate pain management. Ganglion impar neurolysis has been used in the treatment of pelvic-perineal pain with efficacy and rare complications, but only a few case or series reports in cancer patients have been published. We report the case of a patient presenting with an ovarian carcinoma (FIGO stage IIIC), who had several disease relapses at the colorectal transition and need for palliative colic prosthesis. She presented later with ano-rectal pain associated with a rectovaginal fistula, which had an important impact on the activities of her daily life. She was submitted to two ganglion impar neurolyses, which resulted in improved pain control for a total of 5 months, an important improvement in her quality of life, and reduction of opioid consumption. The authors aim to alert to the importance of pain control and to address the fourth step of the WHO analgesic ladder as an option for cancer patients, including palliative patients.

Introduction
Cancer-related pain is a problem that affects a large proportion of cancer patients. It is estimated to be present in approximately 60\% of patients undergoing targeted treatment, more than 60\% of the patients in advanced stages, and more than 30\% of the survivors [1, 2]. Studies show poor pain control in 56–82\% of cases, including patients at the end of life [3, 4].
Pain is associated with a reduced ability to tolerate treatments, a higher incidence of depression, and an important decrease in the quality of life of patients and caregivers [1].

It is estimated that adequate pain control with conventional analgesia is not achieved in 10–20% of patients. Therefore, invasive procedures (such as neurolytic blocks, locoregional anaesthesia or spinal analgesia) were proposed as a fourth step in the analgesic ladder of the World Health Organization (WHO) [1]. Its use is advocated by the leading worldwide associations of medical oncology and present in clinical guidelines of the European Society of Medical Oncology (ESMO), National Comprehensive Cancer Network (NCCN), and American Society of Clinical Oncology (ASCO) as an option for patients resistant to conventional analgesic therapies or with intolerable adverse effects related to these therapies [4–6]. There is increasing evidence of the benefit of these techniques in early cancer stages and they should also be considered in survivors with pain which is associated with the targeted treatments previously performed and which is difficult to control [2, 4]. They should not be considered if it is against the will of the patient, if the life expectancy is very low, or in the case of major coagulopathies or infections [1].

Neurolytic blocks consist of the destruction of nervous tissue usually through the injection of alcohol at 50–100% or phenol at 6–12%. The coeliac plexus, the superior hypogastric plexus, and the ganglion impar are the most common neurolysis sites for the treatment of upper abdominal, pelvic, and pelvic-perineal pain, respectively [1, 2]. The ganglion impar, or ganglion of Walther, consists of a semi-circular retroperitoneal median structure, anterior to the coccyx or the sacrococcygeal junction. Its neural network is formed by several neurological fibres but it is not yet fully understood: it is believed to include not only the nociceptive and sympathetic fibres of the perineum, distal portion of the rectum, anus, distal urethra, lower third of the vagina, and vulva/scrotum [1, 2], but also sympathetic branches innervating the pelvic organs [7, 8]. Ganglion impar neurolysis was first described in 1990 by Plan-carte et al. [9] for the treatment of pain related to perineal cancer. The neurolysis can be performed according to four techniques: anococcygeal, coccygeus-transverse, intercoccygeal and trans-sacrococcygeal, the latter being the most common. In all techniques, the positioning of the needle is confirmed by the injection of radiological contrast by fluoroscopy, followed by the administration of local anaesthetics and then the neurolysis with alcohol or phenol [1, 2]. All techniques can also be guided by ultrasound, tomography or magnetic resonance imaging [7, 8]. Pain relief usually lasts for 3–6 months, although the response is variable, given tumour burden and nerve regeneration. Complications are rare but may be related to local infection or haemorrhage, perforation of the rectum, injection of the periosteum, epidural injection, or autonomic/motor dysfunction caused by dispersion of the neurolytic substance [1, 2, 8].

Case Report/Case Presentation

The authors present the case of a 75-year-old female patient, diagnosed in 2008 at age 66, with high-grade bilateral serous ovarian adenocarcinoma with peritoneal carcinomatosis at presentation, corresponding to a FIGO (Fédération Internationale de Gynécologie et d’Obstétrique) stage IIIC (2014 classification). She initially underwent a total hysterectomy, bilateral adnexectomy and omentectomy, and completed adjuvant chemotherapy with paclitaxel and carboplatin.

In 2012, the disease relapsed in the rectosigmoid transition, presenting as intestinal sub-occlusion. Therefore, she was submitted to the endoscopic placement of a colic prosthesis (Fig. 1) and palliative chemotherapy with paclitaxel and carboplatin was started, achieving a partial response. In 2015, there was new progression of the colonic disease, presenting again
with intestinal sub-occlusion, and a new prosthesis was placed. At that time, the patient started referring to intermittent anorectal pain that radiated to the lower limbs, with breakthrough pain that scored 10/10 on the visual analogue scale. The pain had an important neuropathic component described by the patient as a feeling of an electric shock, burning or a biting sensation. She also referred to the seated position, certain movements, and intestinal elimination as factors of aggravation. Although medicated daily with hydromorphone 32 mg and pregabalin 25 mg, with fentanyl sublingual 200 μg as a rescue medication for breakthrough pain, she continued to have uncontrolled pain, which had an important impact on her daily life. She was then referred to the Pain Unit of the Hospital Prof. Dr. Fernando Fonseca. An initial improvement was achieved with an opioid rotation to transdermal fentanyl and a combination of corticosteroids, but after a couple of months a constant dose increase was needed and soon she was medicated with transdermal fentanyl 175 μg/h associated with pregabalin 400 mg/day, prednisolone 20 mg/day, and sublingual fentanyl 400 μg as rescue medication.

At the end of 2017, there was a new increase in pain intensity associated with the appearance of a rectovaginal fistula. By this time, palliative chemotherapy with cyclophosphamide was initiated with good tolerability but no effect on pain control, needing constant rescue medication. Since this patient was collaborative, had a good performance status, had good family support, and had undergone extremely frequent analgesia adjustments with little or no effect, it was suggested to her that she should undergo an invasive technique for pelvic and perineal pain management. Therefore, in January 2018, she was submitted to a ganglion impar neurolysis guided by fluoroscopy, with the administration of 5 mL of 0.5% levobupivacaine and 3 mL of alcohol at 70%, which was done without problems (Fig. 2, 3). One week after the procedure, the patient already reported 10-h periods without pain, tolerance of longer periods in a seated position, and improved sleep patterns, with a reduction in the need for rescue medication from 9–10 pills of sublingual fentanyl 400 μg/day to 1–2 pills. This improvement in pain control was maintained for about 3 months, with an important gain in the quality of life. After this period, there was new disease progression and an increase in the number of episodes of breakthrough pain per day. Since the patient had benefited before from the ganglion impar neurolysis, a second procedure was suggested to her, this time with a complementary blockade of the superior hypogastric plexus, which allowed pain control for about 2 months. During this time, the patient maintained palliative chemotherapy with cyclophosphamide. She maintained a good quality of life and independence in the activities of her daily life till July 2018. At this point there was disease progression refractory to the systemic therapy and the patient died in early August.
Discussion/Conclusion

The available data in the literature suggest that ganglion impar neurolysis is a safe procedure with few adverse effects and which is effective in the treatment of pain [1, 7, 8]. It has been shown to be effective in the treatment of pelvic pain of malignant or benign origin, with most of the studies including patients with different pain aetiologies [7]. Most published papers included a follow-up of 2–3 months, showing maintained efficacy of treatment in this period in most patients.

Plancarte et al. [9] described reduction of more than 60% of the intensity of perineal pain in half of the patients. Several studies have reported cases of patients with pelvic tumours with baseline pain relief of 50% or more after the procedure, with reduction of baseline visual analogue scale scores of 9–10 to mild pain levels that persist after more than 2 months of follow-up and with a significant reduction of opioid use [10–12]. Studies with a longer follow-up show pain relief durations that reach 3 years [13]. In the largest study with patients submitted to this procedure, which included 15 oncology patients from a total of 43, the intensity of pain reduction was more prominent in the group with pain of oncological aeti-
ology [14]. Favourable results of combined neurolysis of the ganglion impar and superior hypogastric plexus in the reduction of pelvic oncological pain are also reported, since the latter includes neural afferent fibres of pelvic viscera [9, 15].

The reported case refers to a cancer patient whose quality of life was significantly affected by pelvic-perineal pain, which made it impossible or difficult to perform simple daily tasks. Pain control was achieved for 3 months with the first ganglion impar neurolysis, which is consistent with the median duration of benefit reported in the literature. The second procedure was less effective, but coupled with superior hypogastric plexus neurolysis, it allowed pain control for another 2 months. Of note is the significant gain in quality of life, quality of sleep, accomplishment of daily tasks, and improvement of social interaction during this period.

With this article the authors aim to alert to the importance of pain control in cancer patients and to address the fourth step of the WHO analgesic ladder as an option for these patients. The importance of the collaboration between medical oncology departments and pain units as a multidisciplinary approach also needs to be emphasized. Invasive techniques should be used as part of a multimodal therapy, together with conventional analgesia, in order to enhance pain control and decrease possible adverse effects [1, 2, 5]. These techniques might be indicated in palliative patients, as in the case presented, provided that the patients are expected to have a benefit in their quality of life with the approach, it is justified by their life expectancy, and the risk-benefit is balanced accordingly. Careful patient selection as well as control of expectations and appropriate post-procedure care are essential [1].

**Statement of Ethics**

The authors have no ethical conflicts to disclose. Informed consent was obtained from the patients for this report.

**Disclosure Statement**

The authors have no conflicts of interest to declare.

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**Author Contributions**

Filipa Ferreira is the principal and corresponding author, responsible for the idea of the article and its writing. Ana Pedro is the second author, specialized in pain medicine and revisor of the article. There are no other contributors.

**References**

1. Sindt J, Brogan S. Interventional treatments of cancer pain. Anesthesiology Clin. 2016;34:317–39.
2. Beuken-van Everdingen M, et al. Prevalence of pain in patients with cancer: a systematic review of the past 40 years. Ann Oncol. 2007;18:1437–49.
3. Christo P, Mazloomdoost D. Interventional pain treatments for cancer pain. Ann NY Acad Sci. 2008;1138:299–328.
4 Management of cancer pain: ESMO clinical practice guidelines. Ann Oncol. 2012;23(Suppl 7):vii139–vii154.
5 National Comprehensive Cancer Network. Clinical practice guidelines on adult cancer pain. Version 1. 2018.
6 Paice JA, Portenoy R, Lachetti C, et al. Management of chronic pain in survivors of adult cancers: American Society of Clinical Oncology clinical practice guideline. J Clin Oncol. 2016;34(27):3325–45.
7 Scott-Warren J, Hill V, Rajasekaran A. Ganglion impar blockade: a review. Curr Pain Headache Rep. 2013;17:306.
8 Gunduz O, Kenis-Coskun O. Ganglion blocks as a treatment of pain: current perspectives. J Pain Res. 2017;10:2815–26.
9 Plancarte R, et al. Presacral blockade of the ganglion of walther (ganglion impar). Anesthesiology. 1990;73:A751.
10 Toshniwal G, Dureja G, Prashanth S. Transsacrococcygeal approach to ganglion impar block for management of chronic perineal pain: a prospective observational study. Pain Phys. 2007;10:661–6.
11 Eker H, et al. Transsacrococcygeal approach to ganglion impar for pelvic cancer pain: a report of 3 cases. Reg Anesth Pain Med. 2008;33:381–2.
12 Bhatnager S, et al. Early ultrasound-guided neurolysis for pain management in gastrointestinal and pelvic malignancies: an observational study in a tertiary care center of urban India. Pain Pract. 2012;12:23–32.
13 Malec-Milewska M, et al. Neurolytic block of ganglion of Walther for the management of chronic pelvic pain. Videosurg Miniminv. 2014;9(3):458–62.
14 Agarwal-Kozlowski K, et al. CT-guided blocks and neuroablation of the ganglion impar (Walther) in perineal pain: anatomy, technique, safety and efficacy. Clin J Pain. 2009;25:570–6.
15 Ahmed D, Mohamad M, Mohamed S. Superior hypogastric plexus combined with ganglion impar neurolytic blocks for pelvic and/or perineal cancer pain relief. Pain Phys. 2015;18:E49–E56.