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CLINICAL CASE

Oncological triple primary and its impact on pain: A case report

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SOCIEDAD DE LUCHA CONTRA EL CÁNCER-ECUADOR.

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Abstract

Introduction: Cancer patients present pain in 40% of cases, and 38% of them describe it as moderate to intense. Almost 85% of patients with cancer pain can achieve reasonable control with conventional oral medications.

Clinical case: A 57-year-old male with metachronous triple primary malignancy associated with three types of pain with a progressive increase in intensity and requiring several lines of opioid analgesic treatment.

Conclusion: Triple primary malignancies are rare and are associated with complex pain, and opioids are the most appropriate therapeutic option.

Keywords:
MESH: Neoplasms, Multiple Primary; Receptors, Opioid; Cancer Pain.

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Introduction

Globally, more than 18 million new cancer cases were reported in 2020. It is estimated that by 2040, they will exceed 28 million. More than 50% of people who undergo cancer treatment experience pain. Cancer survivors experience pain in 40%, and 38% rate it as moderate to severe [1]. Almost 85% of patients with cancer pain can achieve reasonable control with conventional oral medications [2].

However, pain management can be considerably more difficult for patients with advanced or metastatic cancer. From 60 to 90% of this population reports that pain interferes with their functionality, mood, and sleep, affecting their quality of life [3]. Multiple primary malignancies (MPMNs) are clinically rare, comprising 0.52% to 11.7% of all cancers, the increase in which may be due to improved diagnostic techniques and treatment of cancer patients [4, 5].

No other cases of complex pain in PMN have been described, making it necessary to study this field in depth to find the best therapeutic option that provides the patient with adequate symptom control and better quality of life.

Clinical case

We present the case of a 57-year-old mixed-race man with no family history of significant diseases who reported type 2 diabetes mellitus, arterial hypertension, and hypothyroidism as a history. He was diagnosed with three malignant neoplasms, one hematological and two solid neoplasms. The first was papillary thyroid carcinoma, treated with thyroidectomy and radioactive iodine in 2015. Subsequently, POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin disorders) in 2017, associated with Castleman disease, was diagnosed by biopsy. Through thoracotomy with excision of a mediastinal tumor, he received chemotherapy, radiotherapy, and autologous hematopoietic progenitor transplantation. Finally, in 2021, a large tumor in the right kidney compatible with urothelial carcinoma of the renal pelvis was identified as the third primary tumor.

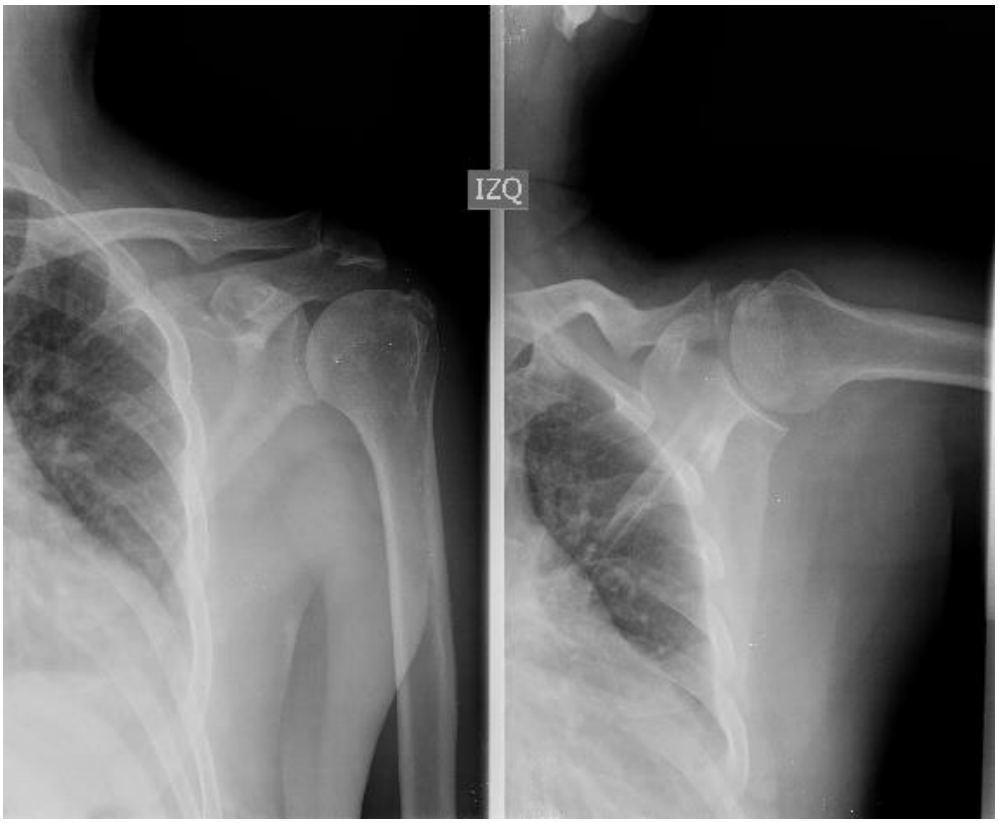
Initially, she consulted the palliative care service in March 2019 due to pain with a composite component (somatic-neuropathic) in the cervical region, an intensity of 5/10 on the Visual Analog Scale (VAS), characterized by tingling and burning sensation, which radiates to the right and left shoulders and causes moderate functional limitation of the upper extremities of several months' duration. A lipomatous mass was observed on physical examination without any other interesting data. Because it was neuropathic pain, he received local transdermal analgesia with 5% lidocaine plus oral paracetamol, which progressed favorably for approximately two months.

During the follow-up of the case, the patient evolved with muscular weakness of the lower limbs secondary to underlying pathology (POEMS syndrome), with the use of an orthopedic device (cane), which increased bilateral shoulder pain, presenting as intra-articular pain predominantly left, breakthrough, intense VAS 8/10, a simple shoulder X-ray shows sclerosis at the level of the coracoid process and tubercle (Figure 1) as a possible cause of increased pain, which translates into the need to escalate analgesia, in May 2019, starting with a weak opioid (tramadol 75 mg/day) combined with paracetamol for several weeks, without significant pain relief.

Transdermal buprenorphine was switched, which caused a skin hypersensitivity reaction, limiting this alternative. A new early rotation to oral oxycodone 15 mg/day was performed, progressing to 60 mg/day associated with a neuromodulator, gabapentin 900 mg/day, with adequate pain management for approximately nine months (November 2019 - July 2020). He underwent a hematopoietic progenitor cell transplant in August 2019, which facilitated the progressive weaning of the prescribed analgesic, maintaining adequate pain control.

Almost a year later, in May 2021, faced with the diagnosis of a third primary urothelial carcinoma of the renal pelvis, he debuted with acute nociceptive pain located in the right dorsal region, intensity 9/10 on VAS, with no favorable response to rescue with a weak opioid, requiring analgesia with transdermal fentanyl up to doses of 50 mcg/h and rapid-release oxycodone 5 mg rescues up to 25 mg/day.

Figure 1. X-ray of the left shoulder. Sclerosis at the level of the coracoid process and tubercle.



In August 2021, after an exploratory laparotomy with an attempt at radical nephrectomy ("open-close" due to an unresectable tumor with vascular involvement) (Figure 2), the pain in the immediate postsurgical period was managed with tramadol 300 mg in continuous intravenous infusion with a lousy answer. The palliative care service was consulted for outpatient analgesia, and 100 mg/day morphine plus 10 mg/day ketamine was prescribed in a programmable elastomeric infuser via the subcutaneous route, requiring up to 30 mg of additional morphine as rescue, achieving better pain control. Several weeks later, the oral route was restored with oxycodone 160 mg/day, maintaining recovery with subcutaneous morphine. Six months after using baseline oral analgesia and subcutaneous rescues, due to the progression of the oncological disease and more significant clinical deterioration, it was necessary to restart the elastomeric infusor subcutaneously with fentanyl at a dose of 0.5 mg/day until the end of life (Figure 3).

Figure 2. Simple abdominal tomography showing a tumor mass in the right renal pelvis

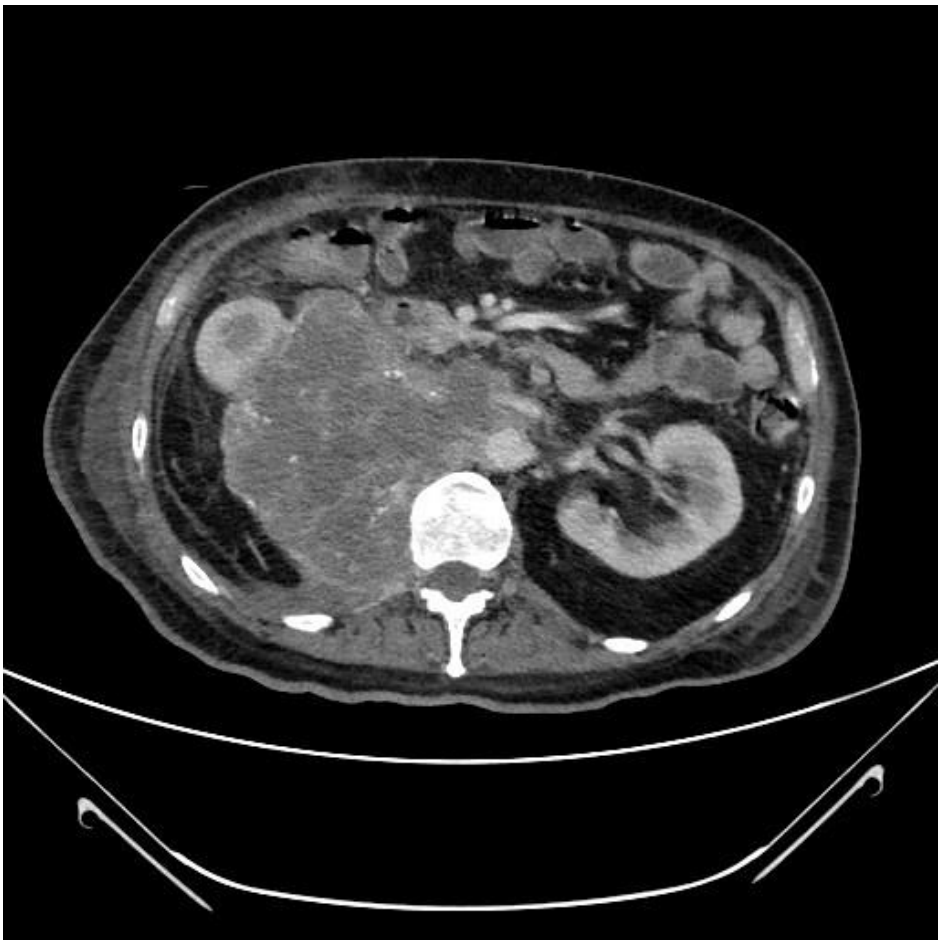


Figure 3. Timeline of analgesic treatment.

Discussion

The oncological triple primary can cause pain with a composite component that leads to a constant rotation of opioids and route of administration, whose purpose is pain relief.

This patient with papillary thyroid neoplasm received adjuvant treatment with radioactive iodine, a predisposing factor for developing second malignant neoplasms in a range of 6-31%[6, 7]. Although he did not report a family history of cancer, according to the literature, multiple primary malignancies may be related to genetic predisposition or a family history of cancer [8].

In this case, a monoclonal gammopathy with POEMS syndrome, associated with Castleman disease, occurred in approximately 11-30% [9]. Some studies report that approximately 50% of patients with this association report distal numbness and pain that progresses to weakness [10]. The characteristic that could be observed in the patient's evolution is documented as one of the main symptoms, directly affecting the quality of life and mood [11].

This patient, while receiving cancer treatment, presents with pain that progressively increases in intensity, depending on the progression of the disease and with characteristics specific to each of his diagnoses. It was necessary to use various analgesic treatment regimens, including opioids. Many drugs can be used individually or in combination to provide synergistic effects, considering their mechanism of action, side effects, dosage, drug interactions, and the characteristics of each patient [12]. However, scientific societies have disagreed on the preferred strategy for managing this pain phenomenon [13].

The European Society for Medical Oncology (ESMO) guidelines strongly recommend short-acting opioids (evidence level I, recommendation grade A). In contrast, the World Health Organization guidelines indicated that breakthrough cancer pain should be relieved with rescue medications based on clinical experience and the patient's need and recommended immediate or slow-release morphine. The European Association for Palliative Care (EAPC) guidelines indicate oral opioids as first-line treatment, although short-acting opioids are suggested when rapid-onset effects and shorter duration are needed [13]. This reinforces the therapeutic scheme proposed in this clinical case in which morphine and immediate-release oxycodone were used.

Urothelial carcinoma of the renal pelvis, corresponding to the third primary, is a rare neoplasm that represents 7% of all renal tumors [14, 15] associated with renal damage. In this case, the large right tumor mass partially impaired renal function. preserving the part of the left kidney, for which reason fentanyl infusion was considered, which is one of the noblest opioids in the renal context [16].

It is important to emphasize that before changing the opioid or route of administration, the analgesic response or tolerance must be constantly evaluated to consider the respective rotations. In palliative medicine, subcutaneous infusions are used frequently and with good results for administering drugs, especially opioids, and changes must be motivated mainly by their efficacy and adverse events [2, 3].

Conclusions

Triple primary malignancies are infrequent and are associated with complex pain depending on the progression of the disease, which represents a real challenge for medical personnel who seek to ensure an adequate quality of life and alleviation of suffering. The use of opioids suggests being the most appropriate therapeutic option, with necessary rotation or adaptation, according to the characteristics of each patient.

Abbreviations

IASP: International Association for the Study of Pain
MPMN: Multiple primary malignant neoplasms
POEMS: polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin disorders
VAS: Visual Analog Scale
SNMP: Second Primary Malignancies
ESMO: European Society for Medical Oncology
EAPC: European Association for Palliative Care

Administrative information

Additional Files

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7. Validation: Mariana Vallejo Martínez
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10. Writing - proofreading and editing:

All authors read and approved the final version of the manuscript.

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The studies, images, and medications constituted the regular activity of the service and were not an additional cost to the patient.

Availability of data and materials

Data are available upon request to the corresponding author. No other materials are reported.

Statements

Ethics committee approval

It does not apply to review studies, database studies, or clinical cases.

Consent for publication

The authors have the corresponding publication permission for this clinical case.

Conflicts of interest

The author declares that they have no conflicts of competence or interest.

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