

Impact of Radiation Therapy on Pain Relief of Cancer Patients Affected by on Malignant Psoas Syndrome: 26 Years of Experience

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Abstract

Aim: The malignant psoas syndrome (MPS) is a rare and complex cancer-related clinical entity, with a significant impact on cancer patients' quality of life. The literature describing malignant infiltration of the psoas muscle as well as its management is limited. The primary endpoint of the study was the assessment of pain relief in symptomatic terminal-stage MPS patients. **Materials and Methods:** Patients underwent hypofractionated (two- or three-dimensional conformal) radiotherapy as palliative treatment. A dose of 42.5 Gy in 17 daily fractions (2.5 Gy/fraction) was prescribed. Pain response was measured before 3 and 6 months after radiation delivery. **Results:** Between May 1992 and April 2019, eight patients were treated. The median age was 75 years (range: 59–87 years). All patients had distant metastatic disease at the time of treatment. We found a significant pain relief (median duration of response of 105 days) and an improvement in health-related quality of life. **Conclusions:** Radiotherapy had a favorable outcome and can be considered an effective analgesic treatment in case of painful MPS.

Keywords: Malignant psoas syndrome, pain, radiotherapy

INTRODUCTION

Malignant psoas syndrome (MPS) represents a rare cancer-related clinical entity that was first described in 1990 by Stevens and Gonet^[1] It is associated with neoplastic infiltration either directly to the psoas muscle or extrinsically to the adjacent retroperitoneal (paraaortic and paracaval) lymph nodes that invade the psoas muscle and the lumbosacral nerve plexus.^[1]

The majority of MPS patients demonstrate neurological signs and symptoms. However, it is worth mentioning that asymptomatic psoas muscle malignant involvement can also occur. Its incidence has been reported to be <1% among persons with advanced-stage disease, although this value may not be representative of the real condition, since it is usually underestimated.^[2-4]

Carcinomas deriving from the breast, lung, stomach, pancreas, colon, cervix, ovary, endometrium, kidney, bladder as well as sarcomas, melanoma, and hematological malignancies (e.g., leukemia and lymphoma) may present MPS.^[5-7]

The literature describing the malignant infiltration of the psoas muscle as well as its management is limited. There is no

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standard treatment for the palliation of MPS. Various therapies can be used as opioids, nonopioids analgesics, antiepileptics, antidepressants, muscle relaxants, and irradiation.^[3,4,8]

This study was conducted to assess the role of radiotherapy in the pain control of MPS patients using hypofractionated (two dimensional [2D] or three dimensional [3D] conformal) regimens.

MATERIALS AND METHODS

Patient characteristics

Eighteen patients diagnosed with MPS, who were unsuitable for other therapies or who had failed a number of prior treatments, were eligible for radiotherapy. All patients submitted a written consent form before the treatment. The pretreatment evaluation included history taking, physical examination, histological confirmation of the primary tumor, and the characteristic radiological appearance on a dynamic computed tomography (CT) scan or a dynamic contrast-enhanced magnetic resonance imaging (MRI) scan of the abdomen. All patients had a poor (3–4) performance status according to the Eastern Cooperative Oncology Group Performance scoring.

Radiotherapy procedure

Each patient was immobilized in the supine position, with the use of a vacuum cushion to avoid any involuntary motion. The patients were treated with external-beam radiotherapy (2D- or 3D-conformal radiotherapy techniques). A planning CT scan was obtained for the 3D technique, with 0.5 cm spacing between the slices. The CT datasets were transferred to the contouring system through the DICOM network. The gross tumor volume (GTV) was the demonstrable tumor infiltrating psoas muscle. The clinical target volume (CTV) was made with a margin of 10 mm, for the microscopic spread of the disease. The planned target volume (PTV) provided a margin of 5–10 mm toward every direction to cover setup uncertainties. The uninvolved organs at risk (OARs) as small bowel and spinal cord, GTV, CTV, and PTV were outlined on all CT slices [Figure 1]. A total dose of 42.5 Gy/2.5 Gy per fraction was delivered to the PTV for

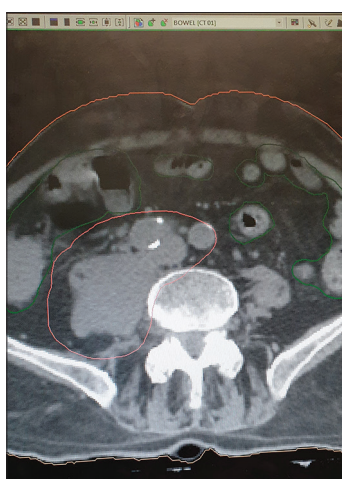


Figure 1: Three-dimensional conformal radiotherapy delineation in a case with malignant psoas syndrome

17 consecutive working days. The hypofractionation regimen was biologically equivalent to delivering 46.75 Gy in 2 Gy fractions, assuming a muscle α/β ratio of 3. To calculate the dose constraints for OARs, we used the European Organization for Research and Treatment of Cancer NSABP B-39/RTOG 0413 protocol and the Toxicity criteria of the Radiation Oncology Group corrected for hypofractionation.

Each patient had a clinical evaluation during and after the end of radiotherapy and every 3–6 months. Pain was assessed at baseline and then at month 3 and month 6 after the treatment. The evaluation of pain intensity was measured by the Visual Analog Scale together with the current pain medication. Patients underwent CT scans every 3 months following the completion of radiation to evaluate the tumor response.

Data statistical analysis

Data were analyzed through descriptive data analysis using the IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. (Armonk, NY: IBM Corp.).

RESULTS

From May 1992 to April 2019, a total of 18 consecutive terminal-stage MPS patients consented to be treated with palliative, external-beam radiotherapy (2D or 3D-conformal radiotherapy techniques). All patients had distant metastatic disease at the time of treatment, but the most painful site was related to MPS. Eleven patients were male and seven were female. The median age was 75 years (range: 59–87 years) [Table 1].

Patients had a persistent MPS of very long-lasting duration, which had failed a number of prior analgesic treatments. No patient had received prior radiation therapy in the same anatomic area before. No patient was treated in combination with concurrent chemotherapy during radiotherapy. The primary malignancies sites were the following: 4; colon, 2; ovary 2; bladder, 1 cervix, 1; gastric, 1; kidney, 1; sarcoma and 1; ureter. The patient primary cancer site distribution is summarized in Table 2 and Figure 2.

A significant pain relief and an improvement in overall health-related quality of life were observed in all the patients who received radiotherapy. Pain relief median response had duration of approximately 105 days. The median follow-up period was 5.5 months. Treatment compliance was very good, and no patient had an acute toxicity greater than or equal to Grade 2. The efficacy of treatment was assessed in terms of pain control, and all cases achieved an important pain relief.

DISCUSSION

MPS represents a rare clinical entity that can be presented in advanced-staged oncologic patients. A thorough understanding

Table 1: The age (mean, median, and range) of treated patients

	Mean	Median	Minimum	Maximum
Age	74.4	75	59	87

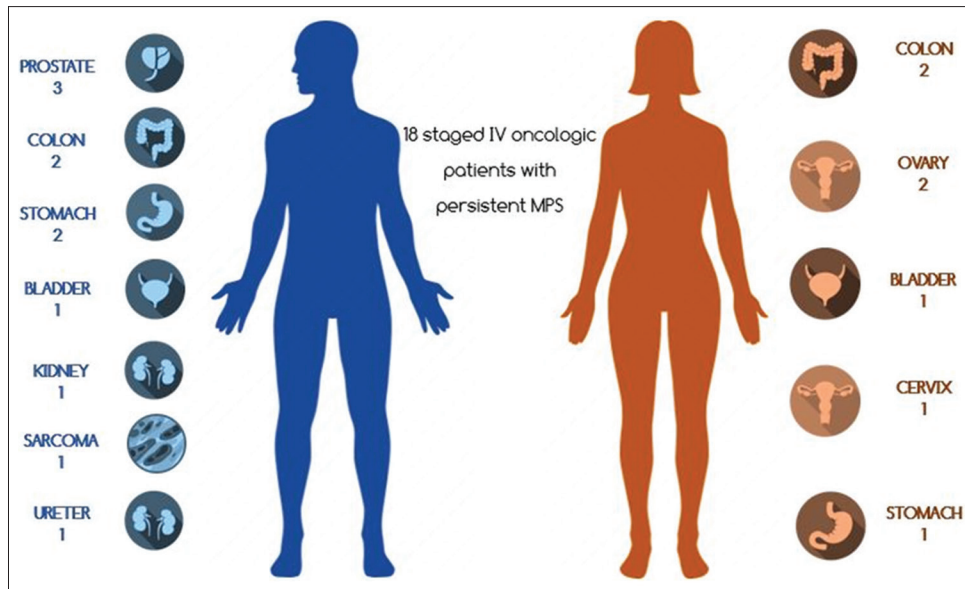


Figure 2: Distribution of primary cancer sites

Table 2: The distribution of the primary cancer sites

Sex	Number of cases
Female	
Colon	2
Ovary	2
Bladder	1
Cervix	1
Stomach	1
Male	
Prostate	3
Colon	2
Stomach	2
Bladder	1
Kidney	1
Sarcoma	1
Ureter	1

of the anatomy of the psoas muscle and lumbosacral plexus is needed to diagnose and treat this entity. The psoas muscle is the most powerful flexor of the body. It arises from the transverse processes and the lateral aspects of the vertebral bodies between the 12th thoracic and the 5th lumbar vertebrae, courses downward across the pelvic brim, passes deep to the inguinal ligament and anterior to the hip joint capsule to form a tendon that inserts into the lesser trochanter of the femur. Its role includes the maintenance of the lumbar lordosis while standing, the flexion of the trunk against resistance and the initiation of the thigh's forward swing during walking or climbing. In addition, the psoas is active in downhill ambulation.^[9]

The iliacus muscle joins the psoas to insert through the same tendon. The psoas and iliacus form the main hip flexors and are sometimes considered together as the iliopsoas muscle, located in an extraperitoneal space called the iliopsoas compartment. There is a close relationship between the psoas muscle and other important

anatomical structures such as the vertebral bodies, the abdominal aorta, the sigmoid colon, the appendix, the hip joint, and iliac lymph nodes. For that reason, a direct tumor-related infiltration of these tissues may activate the pathological symptoms of MPS. The lumbosacral plexus also has a rich vascular supply. It is fed by the five lumbar arteries that originate from the abdominal aorta, the deep circumflex iliac artery that branches from the external iliac artery and the iliolumbar and gluteal branches of the internal iliac artery. Taking under consideration this information, MPS may also be presented as a result of a distant hematogenous metastasis.^[10]

The diagnosis of MPS is made by the malignant infiltration of major psoas, as shown in imaging as CT scan and MRI, and one or more of the following clinical criteria: (a) ipsilateral nociceptive pain (location may be abdominal, back, hip, or thigh), (b) ipsilateral proximal (L1–L3) neuropathic pain, and (c) painful fixed flexion of the ipsilateral hip with positive psoas muscle stretch test.^[11] The above criteria can only be taken into consideration provided that there are no osseous metastases in the lumbar vertebrae and in the absence of other causes that could be responsible for lumbar plexopathy such as malignant infiltration of the nerve roots or nerve damage caused either by neurotoxic drugs or irradiation.

MPS is presented differently among different cancer patients. It may include the appearance of the asymmetric somatic nociceptive pain, painful fixed flexion of the hip ipsilaterally with positive psoas muscle stretch test, peripheral neuropathic pain and peripheral neuropathy-associated symptoms, and finally, the incidence of hydronephrosis (unilateral or bilateral). Patients that suffer from MPS describe their pain as a deep, continuous one, located in the abdomen, the back, or in the ipsilateral hip or thigh. Intra-psoas inflammation of a fixed hip may also result to hypoxia and muscle spasm. In addition, the peripheral neuropathy may be demonstrated as a sudden, burning pain which is associated with hyperalgesia. Neuropathic symptoms are conducted through six

important nerve branches that run in a common plane within the psoas muscle, the ilio-hypogastric (L1), the ilioinguinal (L1), the genitofemoral (L1–L2), the lateral femoral cutaneous (L2–L3), the femoral (L2–L4), and the obturator (L2–L4) nerves. The patients often mention focal weakness, numbness, dysesthesia, and or paraesthesia in multiple contiguous lumbosacral nerve root distributions.^[7]

The mechanistic link of MPS is a combination of somatic nociceptive pain and neuropathic pain due to lumbosacral plexopathy and muscle spasm. The referred pain is located in the groin, thigh, and anterior abdominal wall, as explained by L1–L4 involvement. McKay *et al.*^[8] suggested that nociceptive pain can be raised by chemical, mechanical, or thermal irritation of peripheral sensory nerve endings within skin-deep tissues. There is a further division into somatic (sharp, localized, and incident) or visceral (dull, cramping, and colicky) nociceptive pain according to the site of origin. On the contrary, it results from the direct injury of the nerves or dysfunction of the somatosensory system in response to uncontrolled pain. The neuropathic pain occurs in concert with the changes in nerve function such as motor deficits.

The literature describing the clinical presentation malignant infiltration of the psoas muscle as well as its management is scarce. This study aimed to report our 26-year experience, and to our knowledge, it is the first-reported larger experience on pain secondary to MPS treated with radiotherapy, although there is limited evidence to support this. Takamatsu *et al.*^[2] reviewed the English literature and identified 39 MPS gynecological cases. They noted that female genital tract malignancies accounted for 27% of the cases, followed by gastrointestinal (20%) and urinary tract malignancies.^[2]

McKay *et al.*^[8] suggest that since there had been no randomized controlled trials examining the role of radiotherapy in the neoadjuvant or adjuvant treatment of primary retroperitoneal sarcomas that are incriminated for MPS, the employment of radiotherapy was reliant upon observational data.

Le Pêchoux *et al.*,^[12] while investigating 110 patients with primary retroperitoneal sarcoma who underwent front-line aggressive surgery with or without adjuvant radiotherapy (to a median dose of 50 Gy) between 1994 and 2008, showed that relapse-free survival was 60% in the arm that combined surgery and radiotherapy, instead of 47% in the surgery arm alone. In addition, in the setting of MPS, symptoms were relieved with resection and radiotherapy improved failure rate in a way that the symptoms should be less likely to recur in the absence of recurrence disease.

In accordance with the authors, we suggest as well that radiotherapy may be useful in case of painful MPS because it was shown to have a good and durable effect.

CONCLUSIONS

MPS may be an underestimated and complex syndrome in oncologic patients. These cases illustrate the importance

of multi-modal treatment of pain which occurs in MPS. The improvement in the quality of life of these patients is critical and requires prompt diagnosis and an effective analgesic therapy because the median survival of patients with MPS ranges between only 5.5 and 10.7 months after the diagnosis.^[4,13-17] Our results suggest that radiotherapy is feasible and can be an effective method because it is associated with dramatic improvements in MPS pain.

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Conflicts of interest

There are no conflicts of interest.

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