Usefulness of FDG-PET/CT in the diagnosis and follow-up of mucinous adenocarcinoma of the colon

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ABSTRACT

Mucinous adenocarcinoma (MAC) accounts for 5-20% of all histologic variants of colorectal cancer (CRC). This variant is associated with worse oncological outcomes, is often diagnosed at more advanced stages, and typically presents with multiple metastatic sites compared to conventional colorectal adenocarcinoma. Several studies indicate fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) is more effective than computed tomography for staging metastatic or recurrent CRC. However, the routine use of FDG-PET/CT for follow-up remains controversial, particularly in cases of MAC. This is because FDG-PET/CT may not have the same sensitivity for detecting metastases and recurrence in these tumors, which exhibit decreased FDG uptake due to their relative hypocellularity. We report on two patients diagnosed with colorectal MAC who experienced recurrence, in whom FDG-PET/CT yielded false-negative results.

Keywords: *Colorectal Cancer; Mucinous Adenocarcinoma; FDG-PET/CT*

INTRODUCTION

Worldwide, colorectal cancer (CRC) is the second most common cancer in women and the third most common in men.[1] Among all its histological types, approximately 5-20% are mucinous adenocarcinoma (MCA), a variant with poor oncologic outcome. MCA has been shown to exhibit higher metastatic rates and is often diagnosed at a more advanced stage and with multiple metastatic sites compared to classic colorectal adenocarcinoma.[2]

The presence of lymph node metastases is one of the most important prognostic factors for CRC. Survival is directly related to the presence of residual metastatic nodes after surgery for the primary tumor.[1]

Multiple studies suggest fluorodeoxyglucose positron emission tomography (FDG-PET/CT) is more accurate in staging metastatic or recurrent CRC than computed tomography (CT) and other standard diagnostic modalities. However, the routine use of FDG-PET/CT remains controversial.

According to the National Comprehensive Cancer Network (NCCN) guidelines, positron emission tomography/computed tomography (PET/CT)-fluorodeoxyglucose (FDG) is not routinely indicated and does not replace computed tomography (CT) or magnetic resonance imaging (MRI). PET/CT-FDG has an 88% sensitivity and specificity for diagnosing recurrent metastatic disease. However, lesions must be larger than 1 cm, as subcentimeter lesions are below its detection level.[4] Consequently, its utilization is predominantly observed in scenarios where CT or MRI results are non-specific or when there is a clear contraindication to intravenous contrast and/or gadolinium. Another potential indication is for selected patients in whom, based on prior imaging, metastatic disease is suspected. This study evaluates the possibility of curative surgical resection, or targeted therapy, such as thermal ablation or radioembolization, in hepatic metastatic disease. It also serves to assess the response to treatment.

Concerning postoperative follow-up of patients with CRC, CT is indicated in stages II and III at intervals of 6-12 months for a period of 5 years, and in stage IV at intervals of 3-6 months for 2 years, followed by intervals of 6-12 months for 5 years. PET/CT-FDG can be used to evaluate hepatic recurrence following targeted therapy or in sustained increases in CEA levels during follow-up. However, its utilization as a standardized follow-up imaging modality is not recommended.[4]

Despite the challenges posed by PET/CT-FDG due to its high uptake of FDG resulting from physiological causes, it remains a valuable diagnostic tool. This approach provides a comprehensive view of the body, enabling the identification of abnormal glucose metabolism before morphological changes associated with lesions are identified.[1] However, its sensitivity and specificity for detecting metastases in lymph nodes in patients with recently diagnosed CRC are low. This method is only useful for confirming metastases in lymph nodes when the results are positive.[1] Furthermore, it can be concluded that sensitivity decreases even more when detecting mucinous adenocarcinoma metastases, likely due to the relative hypocellularity that characterizes these tumors.[3]

Based on the above and the popular belief that FDG-PET/CT is the most sensitive study for the follow-up of patients with potential tumor recurrence, we present this publication, which illustrates two distinct cases of macroscopic tumour relapse accompanied by false negative results using this complementary tool in patients diagnosed with mucinous adenocarcinoma of the colon.

CASE 1

A 52-year-old male patient underwent a Hartmann's procedure for a perforated tumor in his sigmoid colon. During the procedure, nodules on the peritoneum consistent with peritoneal carcinomatosis were identified and removed. Pathological analysis of the primary lesion revealed mucosecretory adenocarcinoma of the colon that had infiltrated the entire wall and parietal peritoneum, with negative nodes (0/18). The final staging was T4aN0M1.

Because he was K-Ras wild type, he received adjuvant treatment with capecitabine, oxaliplatin, and bevacizumab. Eighteen months after surgery, a CT scan during oncological follow-up revealed a hypodense, pseudonodular image in the right paramedian mesenteric topography, suggesting tumor recurrence (Fig. 1A). PET/CT-FDG showed lack of pathological uptake (Fig. 1B). After discussion with the multidisciplinary team, surgical intervention was decided upon. A mucinous mesenteric tumor implant was found in the first jejunal loop, measuring 51 x 34 mm. Bowel resection and *en bloc* resection of the implant were performed.

The pathological anatomy revealed bowel infiltration of mucinous adenocarcinoma and a macrometastasis in the mesenteric implant.

The authors declare no conflicts of interest. **Camila Rodriguez.** rodriguezc1232@gmail.com
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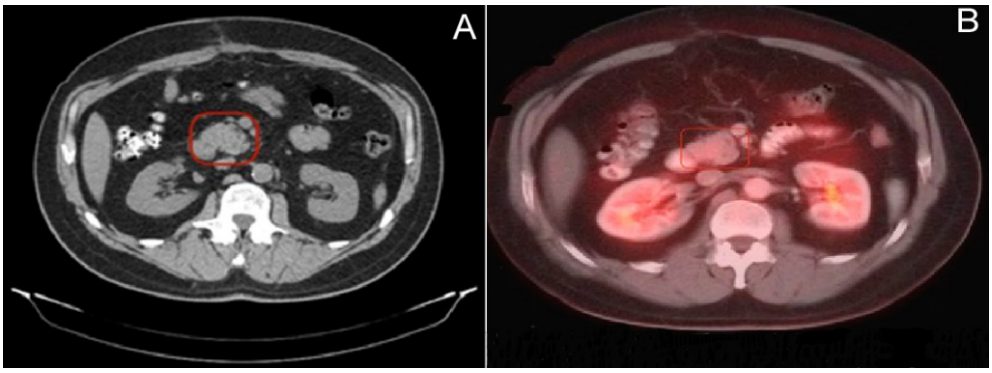

Figure 1. A. *Contrast-enhanced CT scan, axial section. A nodular image is visible to the right of the superior mesenteric artery, indicating lymph node metastasis.* ***B.*** *PET/CT-FDG axial section. Same image without abnormal uptake.*

CASE 2

A 49-year-old female patient underwent an extended right hemicolectomy with ileo-transverse anastomosis and a segment VI hepatic resection due to an ascending colon tumor with hepatic infiltration. Subsequently, an anastomotic dehiscence required a loop ileostomy.
The pathological anatomy revealed a mucinous adenocarcinoma with spread to nearby structures and 0/16 positive lymph nodes. Stage T4b N0 M0.
She underwent adjuvant treatment with capecitabine, oxaliplatin, and cetuximab. During oncological imaging monitoring two years after the procedure, two nodular images of soft tissue density in the mesentery at the central abdomen, measuring 25 x 19 mm and 15 x 14 mm (see Fig. 2A), were identified. The study was completed with PET/CT-FDG, which showed no pathological uptake (Fig. 2B).
Due to complications associated with the ileostomy, the decision was made to close it. Mesenteric lymphadenectomy was also performed during the intervention.
The pathological anatomy report showed a lymph node with macrometastasis of mucinous adenocarcinoma.

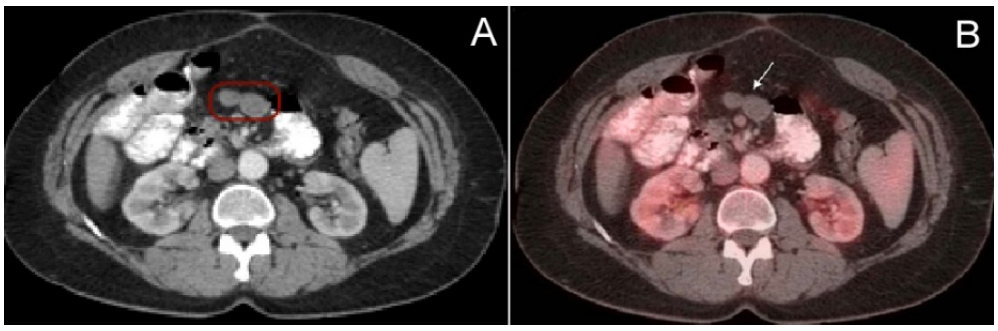

Figure 2. A. *Axial CT scan. Centroabdominal image suggestive of mesenteric lymph node metastasis.* ***B.*** *PET/CT-FDG, axial section. Same image without abnormal uptake.*

DISCUSSION

Por otro lado, un estudio realizado por la NCCN para el manejo de enfermedad metastásica sincrónica, mostró que si bien el uso de la PET/TC-FDG no genera impacto en la supervivencia, puede inducir un cambio de la conducta quirúrgica en hasta un 8% de los casos.
The main objectives of oncologic follow-up imaging are to detect lesions, determine their extent, stage malignant lesions, and assess therapeutic response.
Several imaging modalities are used for this purpose. Some authors consider PET/CT-FDG more accurate for preoperative diagnosis than other methods.[5]
Whiteford et al.,[3] in 2000 compared contrast-enhanced CT and PET/CT-FDG as diagnostic studies for CRC metastases and recurrences. The study found that PET/CT-FDG had a higher sensitivity for detecting loco-regional recurrence when compared to CT associated with colonoscopy.
However, in 5 out of 12 cases of true disease, PET/CT-FDG failed to detect or significantly underestimate the tumor burden. Consequently, it was concluded that the sensitivity of PET/CT-FDG for mucinous adenocarcinoma metastases was inferior to that for non-mucinous adenocarcinoma metastases, with statistically significant findings.
In contrast, it should be considered that up to 8.4% of PET/CT-FDG scans yield false-positive results.[4]
On the other hand, a study conducted by the NCCN for the management of synchronous metastatic disease found that PET/CT-FDG has no impact on survival. However, it can lead to changes in surgical procedures in up to 8% of cases.

CONCLUSION

Given the relatively hypocellular nature of mucinous adenocarcinoma and its association with 18-FDG under-uptake, FDG-CT PET would not be as sensitive as it is for classical CRC in detecting metastases and recurrences.

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