

## Review article

Rare Tumors of the Rectum. Narrative Review<sup>☆</sup>José Errasti Alustiza,<sup>a,\*</sup> Eloy Espín Basany,<sup>b</sup> Ángel Reina Duarte<sup>c</sup><sup>a</sup>Unidad de Coloproctología, Servicio de Cirugía General, Hospital Universitario de Álava, Universidad del País Vasco, Vitoria-Gasteiz, Spain<sup>b</sup>Unidad de Coloproctología, Servicio de Cirugía General, Hospital Universitario Valle de Hebron, Universidad Autónoma de Barcelona, Barcelona, Spain<sup>c</sup>Unidad de Cirugía Colorrectal, Complejo Hospitalario Torrecárdenas, Almería, Spain

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## A B S T R A C T

Most rectal neoplasms are adenocarcinomas, but there is a small percentage of tumors which are of other histological cell lines such as neuroendocrine tumors, sarcomas, lymphomas, and squamous cell carcinomas, which have special characteristics and different treatments. We have reviewed these rare tumors of the rectum from a clinical and surgical point of view.

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## Neoplasias de recto poco frecuentes. Revisión de conjunto

## R E S U M E N

La mayoría de los cánceres de recto son adenocarcinomas, pero existe un pequeño porcentaje de tumores de otras estirpes histológicas, como neoplasias neuroendocrinas, sarcomas, linfomas y carcinomas de células escamosas, que tienen unas características y tratamientos diferentes. Hemos efectuado una revisión de estos raros tumores del recto desde un punto de vista clínico y quirúrgico.

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## Palabras clave:

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Revisión de la literatura

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\* Corresponding author.

E-mail address: jose.errastialustiza@osakidetza.net, joseerrasti@yahoo.es (J. Errasti Alustiza).

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## Introduction

Rectal cancer is typically adenocarcinoma. Nonetheless, there are other types of tumors that are much less common, such as neuroendocrine neoplasms, lymphomas, sarcomas, and squamous-cell carcinomas, which can also be located in the rectum.<sup>1-4</sup> The incidence of each of these tumors is difficult to calculate. According to the data from 2005 to 2009 from the National Cancer Institute's Surveillance Epidemiology and End Results (SEER),<sup>5</sup> out of 183 000 colorectal cancers (not including lymphomas), 94.3% were adenocarcinomas, 1.7% other carcinomas, 3.3% carcinoid tumors, 0.5% epidermoid carcinomas, 0.1% sarcomas, and 0.1% other types.

All these tumors present very different characteristics from adenocarcinomas, which also makes their treatment and prognosis very different (Table 1). In addition, there have been recent modifications in the diagnosis and treatment of some of the types. This all causes doubt and controversy in their clinical management, and it is recommended that they be treated by a multidisciplinary team including surgeons, oncologists, pathologists, and radiologists.<sup>6-8</sup>

The objective of this article is to review the clinical and surgical management of these uncommon rectal neoplasms. We used PubMed to review the literature from 1997 to 2012 using the key words related to a colorectal location stated at the beginning of this article.

## Neuroendocrine Neoplasms

Neuroendocrine neoplasms are epithelial and present neuroendocrine differentiation.<sup>9</sup> They can be located in different organs.

They are classified<sup>10,11</sup> by their degree of differentiation (well or poorly differentiated) and their histologic grade (G1, G2

and G3), based on the number of mitoses and the Ki67 index.<sup>9,12-14</sup> Three different groups are defined: neuroendocrine tumors (NET), neuroendocrine carcinoma (NEC), and mixed adenoneuroendocrine carcinoma (MANEC).<sup>7,12</sup>

### Neuroendocrine Tumors

NET are well-differentiated neuroendocrine neoplasms made up of tumor cells that express neuroendocrine markers (chromogranin A, synaptophysin) (Fig. 1) and hormones.<sup>12</sup> Cellular atypia and proliferative activity are low. By definition, they are grade G1 or G2 tumors. This category includes lesions that were previously called "carcinoid tumors", a denomination that is now criticized and is no longer included in the gastrointestinal NET classifications, but is still widely used. The rectal location represents 18% of all NET and 27% of all digestive tract tumors.<sup>12,15</sup>

The annual incidence of rectal NET, according to the SEER,<sup>5</sup> is 0.86 per 100 000, which has experienced a large increase in recent decades.<sup>7</sup> The incidence is higher in Asians,<sup>12</sup> and mean age is 56.<sup>16</sup>

NET usually present as small polypoid lesions or submucosal nodules.<sup>4</sup> 45% measure 10 mm or less, while only 17% measure more than 20 mm.<sup>17</sup> These tumors are frequently asymptomatic<sup>12,18</sup> or accompanied by mild symptoms such as bleeding, tenesmus or discomfort.<sup>17,18</sup>

49% of the NET only affect the mucosa and submucosa, 24% infiltrate the muscularis propria, and 15% extend to the perirectal fat.<sup>17</sup> 75%-85% are located in the rectal wall.<sup>12</sup> Tumor size and lymphovascular invasions are risk factors for lymph node involvement.<sup>16,17,19,20</sup>

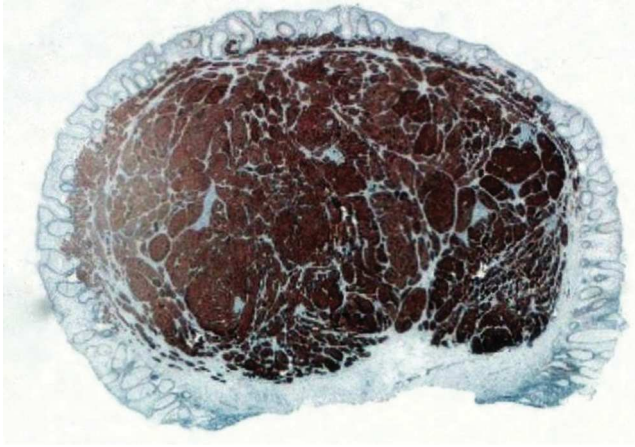
Liver metastases become more frequent as tumor size increases.<sup>16</sup> These are present in 1.7% of the NET $\leq$ 1 cm, in 15% of those between 1 and 2 cm and in 50% of those >2 cm.<sup>20</sup>

The majority of NET are diagnosed endoscopically.<sup>12</sup> Endorectal ultrasound seems to be the best method for

**Table 1 – Particularities of Each Type of Tumor.**

Tumor type	Cells of origin	Risk factors	Prognostic factors	Usual treatment	Adjuvant treatment	5-year survival %
NET	Kultschitzky cells	Unknown	- No. of mitoses - Ki67	<1 cm: local resection >2 cm: oncologic resection	-	90
NEC, MANEC				Oncologic resection	CTx	15
GIST	Interstitial cells of Cajal	Unknown	- Size - No. of mitoses - Tumor rupture	Resection with free margins	Imatinib	70
Other sarcomas	Rectal connective tissue	- Previous RT	- Differentiation - Tumor necrosis	Resection with free margins	RT	50
Lymphomas	Rectal lymphoid tissue	- HIV - IBD - Immunosuppression	- No. of mitoses - Histologic type - Histologic grade	Oncologic resection	CTx	30-60
Squamous carcinoma	Rectal epithelium	- HPV - Chronic rectal inflammatory processes	-	CRT Oncologic resection	-	30

IBD: inflammatory bowel disease; GIST: gastrointestinal stromal tumor; HIV: human immunodeficiency virus; HPV: human papilloma virus; MANEC: mixed adenoneuroendocrine carcinoma; NEC: neuroendocrine carcinoma; NET: neuroendocrine tumor; CRT: chemoradiotherapy; CTx: chemotherapy; RT: radiotherapy.



**Fig. 1 – Rectal neuroendocrine tumor treated with endoscopic polypectomy with disease-free resection margins (macro-micro photo); immunohistochemistry for synaptophysin.**

assessing the size and invasion depth of these tumors.<sup>16,18,20,21</sup> In NET measuring less than 1 cm and without risk factors, no further studies are necessary. MRI and CT are indicated in larger tumors in order to study the pelvis and to rule out liver metastasis.<sup>12</sup> OctreoScan seems to have high sensitivity, but it is not often used<sup>20</sup>; it is mainly used in cases with suspected metastatic disease.<sup>12,18</sup>

Less than 1% of the colorectal NET produce serotonin or other hormones; therefore, the routine analysis of serotonin and 5-HIAA is not recommended.<sup>18</sup> Chromogranin A may be elevated and is useful as a tumor marker in the follow-up of surgically treated patients in stages II and III or in metastatic disease.<sup>7,12,18</sup>

Tumor size predicts its behavior and the type of treatment necessary.<sup>12,16,17</sup> Other factors must also be taken into account, such as invasion of the muscularis propria, lymphovascular invasion, atypia, and mitotic rate.<sup>12,20,22</sup> The treatment of a localized NET is complete resection.<sup>12-14</sup>

NET measuring less than 1 cm can be treated with local resection<sup>12,18,19,21</sup> as they present a risk of less than 3% for lymph node metastasis.<sup>12</sup> Previously, infiltration of the muscularis propria needs to be ruled out with ultrasound.<sup>23</sup> Resection can be performed with standard (Fig. 1) or dual-channel endoscopic ultrasound,<sup>22-27</sup> through transanal surgery,<sup>17,21</sup> or even with band ligation.<sup>28</sup>

The treatment of NET from 1 to 2 cm in diameter is not clear because between 10% and 15% will have lymph node metastasis.<sup>12,18</sup> Local resection is indicated in cases where no involvement of the muscularis propria and lymph nodes has been detected by ultrasound<sup>18,21</sup> and the mitotic rate is low.<sup>12</sup> If atypia and high mitotic rate are identified, radical surgery should be considered.<sup>12</sup>

Tumors that are more than 2 cm in size have a risk of between 60% and 80% for lymph node metastasis.<sup>12,18</sup> NET larger than 2 cm, with invasion of the muscularis propria or lymph node involvement should be treated with either anterior resection of the rectum or abdominoperineal

resection, depending on the distance to the anal margin.<sup>12,18</sup> There is no evidence for adjuvant treatment after surgery.<sup>12</sup>

Curative surgery should be proposed in patients with operable liver metastasis, since 5-year survival reaches 60%–80%.<sup>29</sup> Subsequent adjuvant treatment is not recommended.<sup>29</sup> Liver transplantation can be carried out in selected cases in which surgical removal is not possible.<sup>29</sup>

In metastatic disease, long-acting release (LAR) octreotide and interferon- $\alpha$  have been used.<sup>7,18,21,29</sup> Recently, radiotherapy has been applied with peptide receptor radionuclide therapy using somatostatin analogs, providing responses of 30% in patients with tumors that express somatostatin receptors.<sup>7,18</sup> On rare occasions, chemotherapy is indicated in NET G1 or G2. When used due to disease progression, streptozotocin is most often administered in combination with 5-fluorouracil±doxorubicin, but the response is less than 25%.<sup>7,12</sup>

Five-year survival is 91% in localized disease, 49% in regional disease and 32% in metastatic disease.<sup>15</sup>

Follow-up is not necessary in NET <1 cm that present with no other data for poor prognosis.<sup>13</sup> In the remainder, follow-up includes endorectal ultrasound, rectoscopy, MRI or CT, and chromogranin A<sup>13</sup> for 10 years.<sup>12</sup>

### **Neuroendocrine Carcinomas and Mixed Adenoneuroendocrine Carcinomas**

NEC are poorly differentiated high-grade malignant neoplasms of tumor cells that express neuroendocrine markers (chromogranin A, synaptophysin) and have marked cellular atypia, frequent necrosis and high proliferative activity.<sup>12,30</sup> NEC and MANEC are G3 tumors by definition. There are 2 categories of NEC: small-cell and large-cell. Due to their histologic characteristics, they behave much more aggressively than NET.<sup>31,32</sup>

The annual incidence of these colorectal carcinomas is 2 cases per 1 000 000 inhabitants.<sup>2</sup> Symptoms are similar to those of rectal adenocarcinomas, but they differ because many have already metastasized at diagnosis (Fig. 2a and b) and have a poorer prognosis.<sup>32</sup> Mean survival is 11 months.<sup>31,33</sup>

In NEC, chromogranin A is usually negative, but neuron-specific enolase can be used as a marker.<sup>15</sup>

There is no standardized treatment.<sup>30</sup> The usual treatment is surgical: amputation or anterior resection depending on the location, with total mesorectal excision.<sup>30</sup> Nonetheless, it seems that surgery alone is curative on few occasions, so adjuvant chemotherapy is recommended in most cases.<sup>30</sup> The same chemotherapy is used as in neuroendocrine lung cancer, which is a combination of cisplatin or carboplatin and ectoposide.<sup>7,29,30</sup> Radiotherapy can be indicated in cases at risk for local recurrence.<sup>30</sup> There have been cases described with good evolution after chemotherapy alone, without surgery.<sup>34</sup>

### **Sarcomas**

Up until the 1990s, most intestinal mesenchymal tumors were leiomyomas or leiomyosarcomas, but with the development of immunohistochemistry techniques it was seen that the



**Fig. 2 – (a, b) Locally advanced rectal neuroendocrine carcinoma with liver metastases.**

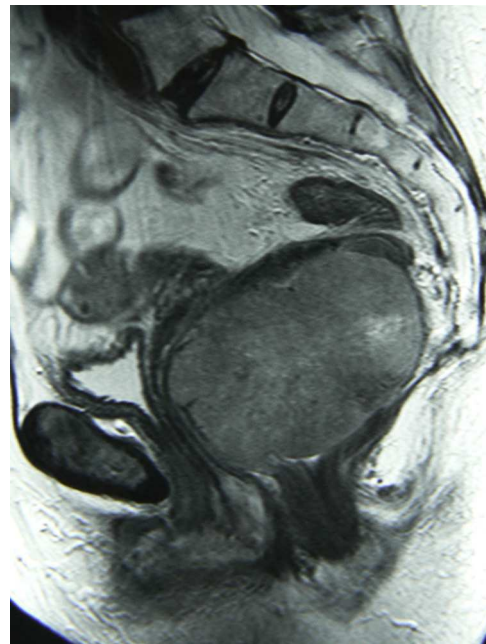
majority of these tumors belonged to a different group: gastrointestinal stromal tumor (GIST).<sup>35,36</sup>

### Gastrointestinal Stromal Tumors

GIST originate in the interstitial cells of Cajal, which are intestinal pacemakers. They are characterized by having specific markers, such as CD117 (c-KIT) in more than 95% and CD34 in 70%, which differentiate them from leiomyomas and leiomyosarcomas.<sup>37</sup> The annual incidence is estimated at 1.5 per 100 000.<sup>6</sup> The most common locations are the stomach and small bowel; however, 10% of GIST are situated in the rectum.<sup>35</sup>

GIST are submucosal tumors, most of which measure between 4 and 15 cm. They can present central necrosis and ulcerate to the rectal lumen. The most frequent symptoms are tenesmus and rectal bleeding.<sup>38</sup>

Diagnosis is reached with CT, MRI, and endorectal ultrasound. Rectal GIST are visualized as eccentric masses with well-defined tumor margins (Fig. 3), which can have areas of hemorrhage or necrosis.<sup>39,40</sup> MRI seems to be the preferred test for rectal localization.<sup>41</sup> Ultrasound is able to confirm that the tumor originates in the muscle wall and not in the mucosa.<sup>40</sup> The histologic diagnosis can be difficult with unaffected mucosa.<sup>38</sup> In cases of extensive or risky surgeries, or in cases of doubtful diagnoses with processes



**Fig. 3 – Rectal GIST.**

that require other treatments, endoscopic ultrasound biopsy is recommended, which has a success rate of 80%–90%.<sup>42</sup>

Standard treatment of localized GIST is surgical resection with free margins,<sup>6,36,43,44</sup> and, as lymph node metastases are infrequent,<sup>6,37</sup> lymph node dissection is not required if the nodes are clinically negative. These tumors have a pseudocapsule and are friable, so they should be manipulated with care to avoid rupture,<sup>37,42,43</sup> which would worsen the prognosis.<sup>45</sup>

In the rectum, the size and location of the GIST determine the type of surgery. Small tumors can be treated with local resection, involving either the abdominal or transanal approaches.<sup>46</sup> There should be no tumor cells in the resection margins.<sup>6</sup> It is not clear whether asymptomatic tumors <1 cm should be removed or have strict follow-up and only be resected if they increase in size.<sup>6,42</sup> Large tumors, which are generally larger than 5 cm, are usually treated with anterior resection and without the need for mesorectal excision, or by means of abdominoperineal resection.<sup>38,44,47,48</sup> There have also been reports of large tumors removed using the transsacral<sup>49,50</sup> or transvaginal<sup>51</sup> approaches.

The most important prognostic factors are tumor size, number of mitoses, and their location.<sup>6,36,43,52,53</sup> Rectal tumors have a poorer prognosis than gastric lesions.<sup>6,45</sup> Furthermore, tumor rupture is another adverse factor.<sup>45</sup>

GIST are resistant to chemotherapy but sensitive to imatinib, a tyrosine-kinase inhibitor that has demonstrated important clinical benefits in patients with advanced disease or recurrence.<sup>37</sup> It is also effective for increasing survival in patients at risk in an adjuvant treatment.<sup>54–56</sup>

Disease-free survival after 5, 10, and 15 years is 70%, 63%, and 60%, respectively.<sup>45</sup> Adjuvant therapy is indicated in

patients at risk for recurrence.<sup>6,43</sup> In rectal GIST >5 cm with any number of mitoses/50 fields, in those of any size with >5 mitoses/50 fields or in those with rupture,<sup>45,57</sup> the recommended dose is 400 mg/day for 3 years.<sup>54,58</sup>

Given the good response of GIST to imatinib, it is being used as neoadjuvant treatment to be able to resect initially unresectable tumors and to avoid abdominoperineal resection in large distal tumors.<sup>37,42,59-62</sup> After neoadjuvant therapy decreases tumor size and increases resectability,<sup>60,62-64</sup> there may even be a complete response.<sup>62,63,65</sup> These indications are not supported by randomized studies and are based on short series or isolated cases. A recent multicenter study<sup>44</sup> confirmed that neoadjuvant treatment reduces tumor size and increases resectability, but it does not avoid mutilating surgery; it also concluded that surgery continues to be the treatment of choice in primary resectable GIST. Before neoadjuvant therapy, there should be histologic confirmation.<sup>66</sup> The optimal duration of preoperative treatment is unknown.<sup>63,66,67</sup> For some, maximum tumor response is achieved after 3-6 months of treatment,<sup>40,68</sup> while others consider 6-12 months reasonable.<sup>63</sup> Treatment should be maintained until the maximum response is reached, defined by non-improvement between 2 CT or MRI studies.<sup>63,66,67</sup> The use of PET can predict the response to treatment 2 weeks after initiation since functional results become evident before morphological results.<sup>66</sup>

For patients with inoperable metastatic tumors, the standard treatment is imatinib.<sup>40,41,68</sup> Treatment should be continued indefinitely because its interruption is generally accompanied by rapid tumor progression.<sup>6,68</sup> In cases of progression during treatment with imatinib, other substances can be used such as second-line sunitinib or third-line regorafenib.<sup>6</sup>

There are no data to recommend a follow-up protocol in patients operated on due to localized GIST, but it seems logical for the follow-up to be done in line with patient risk.<sup>6</sup> Most recurrences arise within the first 5 years and rarely do so after 10 years.<sup>45</sup>

### Other Sarcomas

Soft tissue sarcomas and sarcomas of other organs (excluding GIST) have an estimated annual incidence of 4-5 per 100 000.<sup>8</sup> Rectal sarcomas are very rare since gastrointestinal sarcomas represent 2.6% of all sarcomas and, amongst these, only 15% are colorectal.<sup>69</sup> There are numerous histologic subtypes as they are classified according to the cells of origin of the tissue. In the rectum, the most frequent type is leiomyosarcoma.<sup>69</sup> The histologic grade of malignancy (G1, G2 or G3) is determined by 3 parameters: differentiation, tumor necrosis, and the number of mitoses.<sup>8,70</sup>

There is no clear etiology for these tumors, but an increased risk for the appearance of sarcomas after ionizing radiation has already been identified. They generally appear 7-10 years after radiotherapy.<sup>71</sup> Leiomyosarcomas and angiosarcomas have been detected after pelvic radiotherapy.<sup>72-75</sup> Furthermore, Kaposi's sarcoma has been associated with AIDS.<sup>76</sup>

Leiomyosarcomas have a different origin than GIST: they derive from the cells of the muscularis mucosae or the

muscular propria.<sup>36,47</sup> Immunohistochemistry studies show their positivity to smooth-muscle actin and desmin and negativity to CD117 and CD34, which differentiates them from GIST.<sup>47,70</sup> They frequently present as polypoid lesions measuring between 2 and 5 cm<sup>47</sup> (Fig. 4). They are usually well-differentiated tumors with high mitotic activity, but it seems that their prognosis can be better than GIST with a similar number of mitosis.<sup>47</sup>

The histologic grade, size, and invasion of neighboring organs determine the prognosis.<sup>69,70</sup>

Surgical resection with free margins is the treatment of choice.<sup>69</sup> Lymph node metastases are uncommon.<sup>8</sup> It is not clear whether local resection is sufficient for small low-grade tumors.<sup>69</sup> The indication for anterior resection or abdominoperineal resection is done according to the size and location of the tumor. Radiotherapy can have results similar to those of the treatment of sarcomas of the extremities and it is recommended in high-grade tumors and those larger than 5 cm.<sup>77</sup>

Recurrences can present as liver, lung or local pelvic metastases. Depending on their characteristics, treatment may include surgical resection, ablation, radiotherapy or chemotherapy.<sup>8</sup> As there is no specific marker, follow-up should be done with imaging tests.<sup>8</sup>

### Lymphomas

Gastrointestinal lymphomas are rare, but the digestive tract is the most frequent non-lymph node location of non-Hodgkin lymphomas (NHL). Colorectal involvement is rarer than gastric or small bowel locations. This lymphoma is considered primary when there is no systemic involvement, meaning that there are no peripheral lymphadenopathies, no mediastinal lymph node involvement, normal peripheral blood and bone marrow biopsy studies, lymphadenopathies located only in the proximity of the lesion, and no involvement of the liver or spleen.<sup>78,79</sup>

Secondary rectal lymphoma is a generalized process with rectal involvement due to lymph node metastasis. The

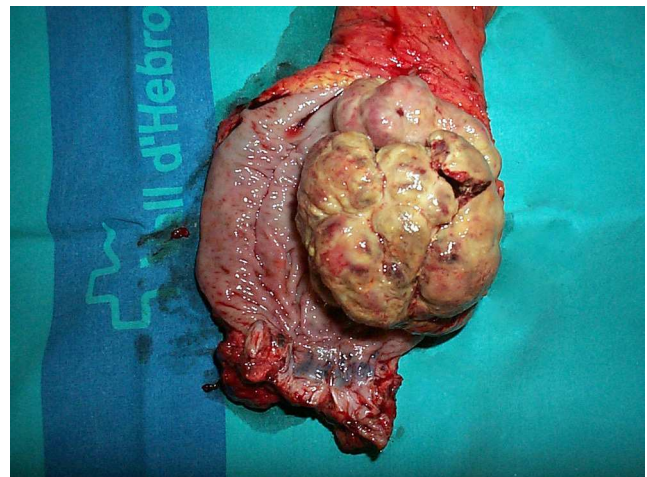


Fig. 4 – Rectal sarcoma.

differentiation between primary and secondary lymphoma is important because treatment and prognosis are different for each. The treatment of secondary lymphoma is chemotherapy and five-year survival is 15%.<sup>1</sup>

In the rectum, all histological lymphoma subtypes may be present, but the majority of primary lymphomas are B-cell NHL,<sup>79-81</sup> with their different variations: large B-cell, mantle-cell, follicular, Burkitt, and mucosa-associated lymphoid tissue (MALT).<sup>78,82,83</sup> The proportion of these different subtypes varies according to geographical region.<sup>79</sup> T-cell NHL are more frequent in Asia than in Western countries.<sup>79,80</sup>

Different factors have been involved in the genesis of gastrointestinal lymphomas; these are generally associated with immunosuppression, such as HIV infection, inflammatory bowel disease, organ transplantation or treatment with corticosteroids.<sup>79,80</sup> They have also been related with infectious agents, such as *Helicobacter pylori* and others.<sup>80</sup>

Mean age at diagnosis is 55.<sup>78,79</sup> The most frequent symptoms are abdominal pain, weight loss, change in bowel habits, and rectal bleeding.<sup>79,81</sup>

Although in the colon it presents as a polypoid lesion (possibly ulcerated), stenosing mass, segmental polyposis, or nodularity of the mucosa,<sup>79,80,83</sup> the most typical rectal presentation is a homogenous mass (due to the concentric wall thickening) with luminal stenosis.<sup>39,84</sup> Suspicion of lymphoma is due the existence of large, numerous lymphadenopathies.<sup>79</sup> Ultrasound biopsy with immunohistochemistry provides the diagnosis, although in many cases precise preoperative diagnosis can be difficult.<sup>81,85-87</sup>

Due to the small number of patients and the various histological subtypes, there is no standardized treatment for colorectal lymphomas.<sup>79,88</sup> A combination of surgery and chemotherapy can be used, reserving radiotherapy for certain cases.<sup>82,83</sup>

Oncologic surgical resection is the most common treatment for localized lymphomas<sup>78,79,81-83</sup> as it offers the possibility of a cure without adjuvant treatment and prevents complications such as bleeding, obstruction or perforation.<sup>82,85</sup>

Chemotherapy as an initial treatment is usually reserved for patients with locally advanced tumors<sup>81</sup> or disseminated disease.<sup>83</sup> Adjuvant chemotherapy after surgery is recommended in aggressive lymphomas or advanced stages.<sup>79,85</sup> The most widely used chemotherapy regime is CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone).<sup>78,82,83,85,89</sup> Results improve when an anti-CD 20 monoclonal antibody, rituximab, is added to this classic protocol (R-CHOP).<sup>79</sup>

Adjuvant radiotherapy could play a role in locoregional control after incomplete resection<sup>82,83</sup> or in cases of chemoresistant tumors.<sup>79</sup>

Rare rectal MALT lymphomas have been treated in many different ways. In some *H. pylori*-positive MALT, antibiotic therapy has been used successfully alone<sup>90,91</sup>; in other cases, radiotherapy, chemotherapy or surgery has been used.<sup>92</sup>

Five-year survival of colorectal lymphomas is between 25% and 57%, which is worse than gastric and small intestine lymphomas.<sup>82</sup>

## Squamous-Cell Carcinoma

Squamous-cell carcinoma is an uncommon tumor that is usually found in the esophagus and anus. Rectal involvement is very rare. In many cases, supposed rectal squamous-cell carcinomas are, in reality, an extension of an anal carcinoma.<sup>93</sup> Occasionally, they have a mixed histologic pattern and are called adenosquamous carcinoma.<sup>94</sup>

Mean age is 57 years and this pathology is somewhat more frequent in women than in men.<sup>93,95</sup> There are no clear risk factors, but there has been an association with inflammatory diseases of the rectum, human papilloma virus (HPV), and colorectal adenocarcinoma.<sup>95</sup>

Symptoms are similar to those of rectal adenocarcinoma, and the most frequent is rectal bleeding.<sup>93,95</sup> Endoscopic findings can be varied, from a polypoid formation up to an ulcerative and stenosing tumor<sup>95</sup>; biopsy provides the diagnosis. Occasionally, there can be difficulties in distinguishing it from a poorly differentiated tumor, but immunohistochemistry can define the lesion.<sup>95</sup> The most useful cytokeratins are CAM 5.2, AE1/AE3, and 34B12.<sup>95</sup>

For staging, MRI (Fig. 5), CT and endorectal ultrasound are used. Squamous-cell carcinoma antigen is a tumor marker that is high in some patients. It is not used for diagnosis but can be used for monitoring response or progression.<sup>95,96</sup>

Traditionally, the usual treatment has been surgery, followed by adjuvant radiotherapy or chemotherapy in some cases.<sup>97,98</sup> In the last decade, given the good results of chemoradiotherapy in squamous-cell carcinoma of the anus, this traditional approach has been questioned<sup>99</sup> and, even though a standard treatment has not been established,<sup>93</sup> there has been a tendency to modify this approach, making chemotherapy the initial treatment for squamous-cell carcinoma of the rectum, and reserving surgery for persistent tumors after treatment.<sup>93,96,100,101</sup> The regimes used are the same that have been shown to be effective in squamous carcinoma of the anus.<sup>95</sup> Treatment entails a combination of mitomycin-C with 5-fluorouracil and radiotherapy at a minimum dose of 45-50 Gy.<sup>102-104</sup> The response to chemoradiotherapy is assessed 6-8 weeks after the end of treatment using rectoscopy with biopsy, MRI or PET.<sup>93,99-101</sup> If there is complete clinical and radiological response, periodical follow-up is performed; cases of tumor persistence should be



Fig. 5 – Squamous carcinoma of the rectum.

re-evaluated after 4–6 weeks, as recommended in anal cancer.<sup>104</sup> Rescue surgery may be necessary, which entails anterior resection or amputation, depending on the tumor and patient characteristics.<sup>97</sup>

There are few published series in which the initial treatment was chemoradiotherapy and they include few cases, but between 66% and 100% showed complete response and did not require later surgery.<sup>93,96,99–101</sup> After complete response, clinical follow-up should include rectal biopsies and radiological studies, which become progressively spaced out over time.<sup>99</sup>

Five-year survival is 50% in stage II and drops to 33% when there is lymph node involvement.<sup>95</sup>

## Conclusions

The rarity of these tumors and their heterogenous origin, treatment, and prognosis mean that physicians may have difficulties in the management of these patients. A multidisciplinary approach including pathologists, radiologists, oncologists, radiotherapists, and surgeons is recommended.

## Conflict of Interest

The authors declare having no conflict of interests.

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