ORIGINAL CONTRIBUTION

Endoscopic Ultrasound-Guided Fine Needle Aspiration Is Highly Accurate for the Diagnosis of Perirectal Recurrence of Colorectal Cancer

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BACKGROUND: Endoscopic ultrasound-guided fine needle aspiration is highly accurate for the diagnosis of malignancies surrounding the gastrointestinal tract. There is a lack of information on the usefulness of this technique in the diagnosis of colorectal cancer recurrence.

OBJECTIVE: The purpose of this work was to investigate the performance characteristics of endoscopic ultrasound-guided fine needle aspiration for the cytologic diagnosis of perirectal recurrence of colorectal cancer.

DESIGN: This was a retrospective study on the clinical and radiologic suspicion of perirectal recurrence of colorectal cancer.

SETTINGS: The study was conducted at 4 tertiary hospitals.

PATIENTS: Consecutive patients with suspicion of perirectal recurrence of colorectal cancer undergoing endoscopic ultrasound-guided fine needle aspiration between 2000 and 2013 were included in this study.

INTERVENTIONS: The study intervention was endoscopic ultrasound-guided fine needle aspiration.

MAIN OUTCOME MEASURES: Endoscopic ultrasound-guided fine needle aspiration performance characteristics and outcome (malignant or benign) were analyzed. The gold standard was cytologic results if malignancy or follow-up if benignity.

RESULTS: A total of 58 patients were included (32 men; mean age, 64.2 ± 10.0 years [range, 44–88 years]). The location of the initial neoplasm was the rectum for 42 patients and the colon for 16 patients. Endoscopic ultrasound findings included a mass in the anastomosis (n = 8), perirectal fat (n = 23), lymph nodes (n = 20), or asymmetric thickness of the rectal wall (n = 6). Cytology showed malignancy in 38 patients (67%), benign features in 17 (30%), and was not evaluable in 2. Mean follow-up to confirm a benign outcome was 51.3 ± 30.3 months (range, 5.2–180.0 months). Final outcome was recurrence in 40 patients (69%) and benignity in 18 patients (31%). Performance characteristics of endoscopic ultrasound-guided fine needle aspiration were sensitivity (97%), specificity (100%), positive predictive value (100%), negative predictive value (94%), and accuracy (98%). In the intention to diagnose analysis, the corresponding values were 95%, 100%, 100%, 90%, and 96%.

LIMITATIONS: This was a retrospective series with a limited number of patients.

CONCLUSIONS: Endoscopic ultrasound-guided fine needle aspiration is a highly accurate tool for the cytologic diagnosis of perirectal recurrence in patients with previous colorectal cancer.

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Survival of patients with colorectal cancer (CRC) recurrence depends on the possibility of applying curative surgery. Therefore, early diagnosis results in a better prognosis.[1,2]

In most cases, the workup of a CRC recurrence includes an abdominal CT scan or MRI and positron emission tomography scan. However, inflammatory changes around the anastomosis may mimic recurrence and turn out positive in the positron emission tomography scan.[3] On the other hand, regional lymph nodes may appear as a response to inflammation, and morphologic characteristics obtained by CT, MRI, or endoscopic ultrasound (EUS) usually are not able to rule out metastases or recurrence. Therefore, cytologic confirmation is crucial to rule out malignancy and make a decision on management.

EUS fine needle aspiration (FNA) is highly accurate for diagnosing gastrointestinal and surrounding tissue, including mediastinal, celiac, perigastric, and perirectal lymph nodes, as well as pancreatic tumors. Overall, the accuracy of EUS FNA in these indications is between 85% and 97%.[4–7]

Recurrences of CRC arise from residual tumor cells in the perirectal fat or lymph nodes missed at surgery. As a consequence, they are usually found in the anastomosis or in the surrounding tissue and can be easily targeted by EUS FNA.

Although used in clinical practice, data on the accuracy of EUS FNA for the cytologic diagnosis of CRC recurrence is scarce. Our hypothesis is that EUS FNA is highly accurate in this setting. Therefore, the aim of the present study was to assess the performance characteristics of EUS FNA for the diagnosis of perirectal recurrence of CRC.

PATIENTS AND METHODS

This retrospective study was conducted in 4 tertiary hospitals in Spain following the Standards for the Reporting of Diagnostic Accuracy Studies statement for reporting studies of diagnostic accuracy.[8] It was approved by institutional ethics committee of all of the participant centers.

Study Population

The study was performed between January 2000 and December 2012. To avoid selection bias, data from all of the patients with radiologic suspicion of perirectal CRC recurrence in whom lower EUS FNA was performed were retrieved from the database of EUS procedures in each hospital. All of the patients included underwent surgery for CRC as part of the initial treatment of the disease and were routinely followed at the outpatient clinic of different hospitals.

Methods

EUS was performed first with a 360° radial echoendoscope (GF-UM160 or GF-UE160, Olympus America Inc, Melville, NY), and for EUS FNA, a linear array echoendoscope was used (GF-UC140P or GF-UCT140, Olympus America Inc). Briefly, patients were lying in a left lateral position, and the balloon at the tip of the instrument was filled with deaerated water to improve visualization. Water was also instilled into the rectum to assist acoustic coupling if necessary. The procedure was carried out under conscious sedation.

The transducer was placed at the upper third of the rectum to explore the fat around the iliac vessels and then gradually pulled back to the anus to rule out the presence of lymph nodes. The anastomotic area and rectal wall were also systematically explored for possible masses consistent with recurrence.

The criterion standard used was cytologic results when malignant cells were present and follow-up in case of benign or inconclusive cytology. The presence of inflammatory cells, fibrosis, or purulent material was considered as a benign cytology. The primary outcome of the present study was accuracy and diagnostic yield of EUS FNA for pelvic CRC recurrence.

Statistical Analysis

Continuous variables are expressed as mean ± SD. Sensitivity, specificity, positive and negative predictive values, and accuracy of EUS FNA in the diagnosis of CRC recurrence with their 95% CIs were calculated by using the standard formulas. All of the calculations were done with SPSS statistical software (SPSS Inc, Chicago, IL).

RESULTS

During the study period, 58 patients with a history of CRC underwent EUS and EUS FNA for the suspicion of recurrence. Thirty-two patients were men, with a mean age of 64.2 ± 10.2 years (range, 44.0–88.0 years). Among them, 42 had a history of rectal cancer, and the remaining 16 had a history of colon cancer. Forty-two patients underwent neoadjuvant and/or adjuvant therapy. Mean and median time to recurrence were 25.0 ± 26.4 months and 16.0 months (range, 1.2–120.0 months). The suspicion of recurrence was established by CT for most patients (n = 44). Characteristics of the patients are shown in Table 1.

Final diagnosis was established on the basis of EUS FNA–obtained cytology in case of malignancy (n = 38) or extended clinical and imaging follow-up in case of benign or inconclusive cytology (n = 20), as detailed in the study flowchart (Fig. 1). Mean ± SD and median lengths of follow-up in the latter group were 51.3 ± 30.3 months (range, 5.2–180.0 months) and 29.3 months.

Recurrences were localized in the pelvic region, and the most frequent was a mass unrelated to the anastomosis or lymph nodes in the perirectal fat (n = 43; Figs. 2 and 3). In 1 patient the lesion seen in CT was not found

Table 1. Characteristics of the patients with suspicion of pelvic CRC recurrence

Variable	*n*	*%*
Location of initial CRC		
Rectum	42	72
Sigmoid colon	10	17
Ascending colon	5	9
Transverse colon	1	2
Oncologic treatment		
Neoadjuvancy	22	37
Adjuvancy	15	25
Both	5	9
None	16	28
Imaging technique with suspicion of recurrence		
CT	44	75
PET	9	16
MRI	5	9
Radiologic findings suspicious of recurrence		
Pelvic mass	24	41
Local lymph nodes	17	29
Anastomotic mass	13	22
Rectal wall thickening	4	7
Final outcome		
Recurrence	40	69
No recurrence	18	31

CRC = colorectal cancer; PET = positron emission tomography.

in EUS, and FNA was not performed. EUS findings are detailed in Table 2.

Cytology disclosed tumor recurrence in 38 patients (65%) and inflammatory or benign cells in 17 (32%) and was considered inadequate for diagnosis in the remaining 2 patients (3%). Final outcome was tumor recurrence in 40 patients (69%) and no recurrence in 18 patients (31%). The only false-negative result occurred in a patient with a rectal wall thickening, and the diagnosis of recurrence was made by laparoscopy. The patient in whom no lesion was seen at EUS was diagnosed with recurrence based on the increasing size of the initial lesions a few months later.

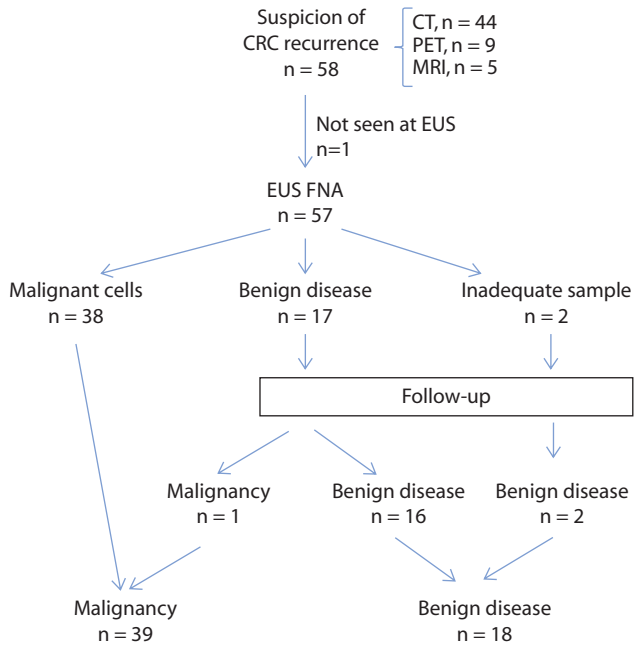

Figure 1. Study flowchart. CRC = colorectal cancer; PET = positron emission tomography; EUS FNA = endoscopic ultrasound fine needle aspiration.

Performance characteristics of EUS FNA in the cytologic diagnosis of CRC recurrence were as follows: sensitivity, 97% (95% CI, 86%–100%); specificity, 100%; positive predictive value, 100%; negative predictive value, 94% (95% CI, 71%–100%); and accuracy, 98% (95% CI, 89%–100%). When taking into account the patients in whom the sample was not adequate or the lesion was not seen at EUS (n = 3; intention-to-diagnose analysis), the corresponding values were 95% (95% CI, 82.6%–99.5%), 100%, 100%, 90% (95% CI, 68.7%–98.4%), and 96% (95% CI, 87.6%–99.7%). The concordance between EUS FNA–obtained cytology and final outcome is shown in Table 3.

DISCUSSION

Our study demonstrates that EUS FNA is an excellent tool to confirm or exclude malignancy in patients with colorectal anastomosis for CRC in whom perirectal recurrence of the disease is suspected by means of radiologic techniques. Until now, there were scarce data on the usefulness of EUS FNA in this setting. Most of the available information in this field stemmed from case reports or small series of patients.[6] The number of patients included in the present study is, to our knowledge, the largest in the literature, and, although it does not incorporate the whole group of patients followed after CRC excision, we included consecutive patients with a suspicion of pelvic recurrence who were amenable to a lower EUS exploration. These patients constitute a homogeneous subgroup frequently seen in clinical practice. Moreover, the participation of 4 different centers widens the applicability of the results and indirectly validates our findings.

The gold standard is always a problem when patients under study have oncologic diseases that are managed with treatments other than surgery, because the resected specimen is not available, and this was the case for most patients from our series. EUS FNA–obtained cytology has shown an excellent positive predictive value in previous studies[9] and is considered an alternative for reporting the true positive results, as supported in the literature with high-quality publications.[10,11] On the other hand, follow-up is a well-recognized reference test if it is long enough. In our study, in all but 3 patients with benign cytology, the time to follow-up was >1 year, which we consider

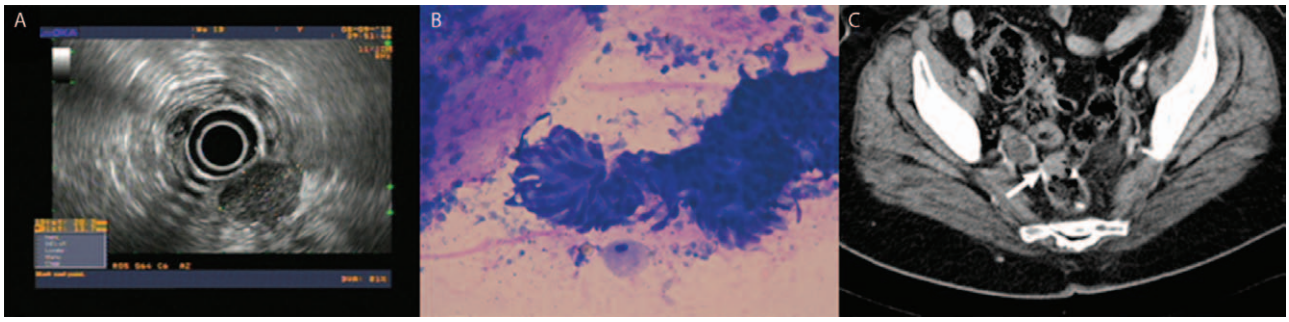

Figure 2. Rectal cancer recurrence adjacent to the anastomosis. A, Endoscopic ultrasound (EUS) image showing a hypoechogenic, 20-mm lesion in the perirectal fat, consistent with colorectal cancer (CRC) recurrence. B, Stain on the EUS fine-needle aspiration smear showing elongated nuclei, palisade cell distribution, and necrotic background. C, Axial CT that shows a nodular lesion corresponding with recurrence at the site of the rectal suture.

time enough to observe tumor growth in case of false-negative FNA.

A limitation of our study is its retrospective approach. This influences the way in which follow-up was done, but because we recruited patients once a perirectal CRC recurrence was suspected by radiology, the retrospective nature of the study is not an important limitation in this case. Moreover, local recurrence rates in rectal cancer have dropped drastically after the introduction of preoperative radiotherapy and improved surgical techniques, such as total mesorectal excision (dissection of the rectum and all of the mesenteric lymph nodes within the mesorectal envelope). Therefore, the low incidence of recurrence of CRC makes a prospective study unrealistic. A second limitation could be that all of the patients included had lesions amenable to EUS FNA. Most pelvic recurrences of CRC are found in the colorectal anastomosis or in the surrounding fat and are easily targeted by EUS FNA. However, in case of an unusual pelvic recurrence located far from the rectal wall (ie, external iliac node), other methods of sampling should be used.

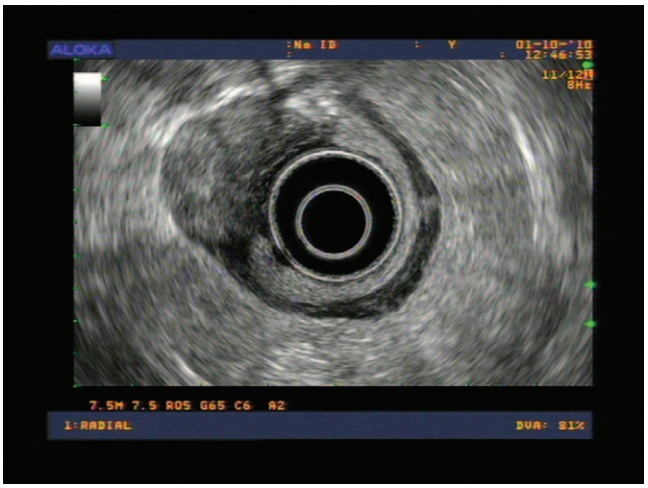

Figure 3. Endoscopic ultrasound (EUS) image of an anastomotic recurrence that infiltrates all of the layers of the rectal wall.

Different authors have investigated the diagnostic yield of EUS FNA in perirectal lesions. Glesson et al[12] demonstrated that EUS-guided sampling is helpful in the diagnosis of local recurrence of pelvic urologic malignancies. The same authors demonstrated the usefulness of EUS FNA to confirm nodal metastases in patients treated with local excision for early rectal cancer,[13] as well as to assess extramesenteric lymph node status as staging of rectal cancer.[14] Another recently published study aimed at assessing the use of EUS FNA in the diagnosis of pelvic diseases: 5 patients with CRC recurrence were included, and cytology confirmed the diagnosis in all but 1 of them.[6] Boo et al[15] performed EUS FNA or EUS-Trucut biopsy in 4 patients with perirectal lesions and were able to obtain cytology or tissue for diagnosis in all of them. Finally, Maleki et al[16] described the usefulness of EUS FNA in the diagnosis of perirectal lesions. In this series, only 9 patients with a history of CRC were included, and in all of them the cytology confirmed the recurrence of the tumor. Although the results of our study are consistent with those in the literature, our findings are novel because this study is the first and largest to focus on a homogeneous population with a long follow-up.

Table 2. EUS findings and cytologic results

Variable	*n*	*%*
Needles		
22G	44	77
25G	11	19
19G	2	3
Location of recurrences		
Pelvic mass	23	40
Local lymph nodes	20	34
Anastomotic mass	8	14
Rectal wall thickening	6	10
None	1	2
Cytology		
Malignancy	38	67
Benignity	17	30
Inadequate sample	2	3

EUS = endoscopic ultrasound.

Table 3. Concordance between EUS FNA–obtained cytology and final outcome in 55 patients

	Final outcome	
EUS FNA	Malignant	Benign
Malignancy	38	0
Benignity	1	16

Excluding the 2 patients with inadequate sample and the patient in which the lesion was not sampled because it was not seen during endoscopic ultrasonography.
EUS FNA = endoscopic ultrasound-guided fine needle aspiration.

CONCLUSION

The present study demonstrates that EUS FNA is an excellent tool, either to confirm or rule out malignancy in patients with previous CRC in whom perirectal recurrence of the disease is suspected by means of radiologic techniques. Because of its high diagnostic yield and safety, it should be performed as soon as possible when it is suspected in these patients. The usefulness of EUS FNA when a CRC recurrence in other locations is suspected should be evaluated in future investigations.

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