

Pure Micropapillary Rectal Carcinoma with CK7 and CK20 Coexpression and Loss of CDX2 Reactivity

Carcinoma Micropapilar Rectal Puro con Coexpresión
de CK7 y CK20 y Pérdida de Reactividad CDX2

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LINO-SILVA, L. S. Pure micropapillary rectal carcinoma with CK7 and CK20 coexpression and loss of CDX2 reactivity. *Int. J. Morphol.*, 30(1):25-29, 2012.

SUMMARY: The micropapillary carcinoma is regarded as an aggressive variant of adenocarcinoma in any location. Histologically is characterized by papillary cell clusters surrounded by clear spaces. The reported proportion of micropapillary carcinoma component to the entire tumor ranged from 5 to 80% and no pure cases has been reported. There are near of 130 cases reported to date in colorectum. We experienced a patient with a pure micropapillary carcinoma showing coexpression of CK7, CK20, and absence of CDX2, which had an aggressive neoplasm with extense perineural, vascular and lymphatic invasion also extensive nodal metastasis. The presence of a micropapillary carcinoma in the colorectum seemed to be closely related with nodal metastasis, similar to the case for micropapillary carcinomas in other organs. Therefore, if a micropapillary component is identified in a tumor, particularly in a biopsy specimen, even if the pre-operative diagnosis is a pedunculated early colorectal cancer, should be carefully consider the extent of surgical resection due to the high potential for nodal metastasis.

KEY WORDS: Micropapillary carcinoma; Adenocarcinoma; CK7; CK20; CDX2; Colorectal cancer.

INTRODUCTION

The micropapillary carcinoma is regarded as an aggressive variant of adenocarcinoma in any location described, namely bladder, lung, pancreas, salivary glands and recently colon, rectum and stomach (Verdú *et al.*, 2011; Amin *et al.*, 2002; Amin *et al.*, 1994; Nassar, 2004; Nassar *et al.*, 2001; Paterakos *et al.*, 1999; Siriaunkgul & Tavassoli, 1993; Zekioglu *et al.*, 2004). Histologically is characterized by papillary cell clusters surrounded by clear spaces. The reported proportion of micropapillary carcinoma component to the entire tumor ranged from 5 to 80% and no pure cases has been reported. In gastrointestinal tract the most reported location is the sigmoid and rectum (Haupt *et al.*, 2007; Kim *et al.*, 2006; Kuroda *et al.*, 2007; Sakamoto *et al.*, 2005; Wen *et al.*, 2008; Xu *et al.*, 2009). In total, are near of 130 cases reported to date in colorectum.

This variant had consistently showed that independently of their location is associated with lymphovascular invasion, lymph node metastasis and aggressive clinical behavior.

We present, to knowledge, the first case of pure micropapillary carcinoma, which also shows CK7 and CD20 coexpression and loss of CDX2 reactivity.

CASE REPORT

A 61-year-old Mexican men with cystoprostatectomy 2 years ago by a invasive High grade urothelial papillary carcinoma T1 N0 M0 (TNM staging system 7th edition) presented with an abdominal pseudo-occlusion syndrome for 1 month and was admitted in the Emergency Department of Mexico's National Cancer Institute and subsequently underwent a rectal low anterior resection. His clinical course was uneventful 1 month after the surgery.

The surgically resected specimen was processed accord to established protocols, in brief, the assessment is performed by direct visual inspection of the fresh specimen, and then the mesorectal fat is inked about its circumferential resection margin including all non-peritonealised bare areas anteriorly and posteriorly. The rectum is opened anteriorly, apart from the segment 2 cm above and 2 cm below the tumor, where the specimen is left intact. Then the specimen is pinned on a corkboard to prevent shrinkage artifact and place a gauze in the lumen, the specimen fixes in 10% formalin by 48 hours. Passed this time, the unopened portion is then sliced into thin transverse sections (3-5 mm in thickness). All off cross-sectional rings should be laid out to

further assess the quality of the mesorectum and the relationship of tumor of the margin and the tumor was full submitted in cassettes and further are embedded in paraffin. Sections in 3 micrometers thick were stained with hematoxylin and eosin. After deparaffinization, antigen retrieval was performed using a Ventana automated immunostainer (Tucson, AZ) with mild CC1 reagent. Tissue sections were incubated with the antibodies; this was followed by washing and detection with the i-View DAB kit from Ventana. Antibodies employed in the present study

are summarized in Table I and described below: CK 20 (Dako, Carpintera, California, clone 20.8 dilution 1:100), MUC-1 (Novocastra, Newcastle, England, clone Ma695, dilution 1:100), CKAE/1AE3 (Dako, Carpintera, California, clone AE1/AE3 dilution 1:200), CK7 (Dako, Carpintera California, Clone OV-TL 12/30, dilution 1:160), EMA (Dako, Carpintera California, clone E29, dilution 1:100), CDX2 (Abcam, Cambridge, England, Clone AMT28, dilution 1:50) and Uroplakin III (Research Diagnostics, Inc, Flanders, New Jersey, clone AU-1, dilution 1:100).

Table I. Summary of antibodies performed.

Antibody	Laboratory	Clone	Dilution
CK 20	Dako, Carpintera CA	20.8	1:100
MUC-1	Novocastra, Newcastle, UK	Ma695	1:100
CKAE/1AE3	Dako, Carpintera CA	AE1/AE3	1:200
CK7	Dako, Carpintera CA	OV-TL 12/30	1:160
EMA	Dako, Carpintera CA	E29	1:100
CDX2	Abcam, Cambridge, UK	AMT28	1:50
Uroplakin III	Research Diagnostics, Inc, Flanders, NJ	AU-1	1:100

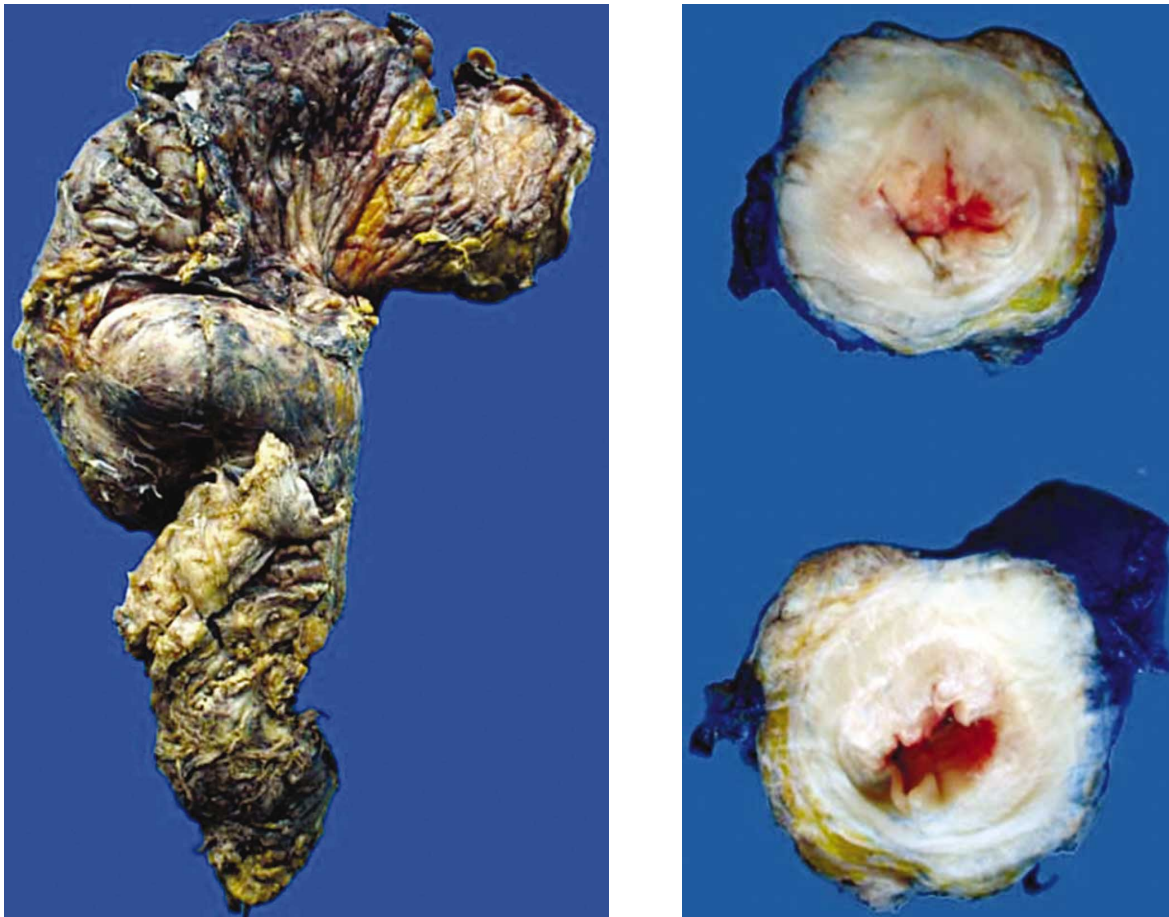


Fig. 1. The rectal specimen shows incomplete mesorectal excision (left) and a exophytic and ulcerant neoplasms infiltrating the whole rectal wall (right).

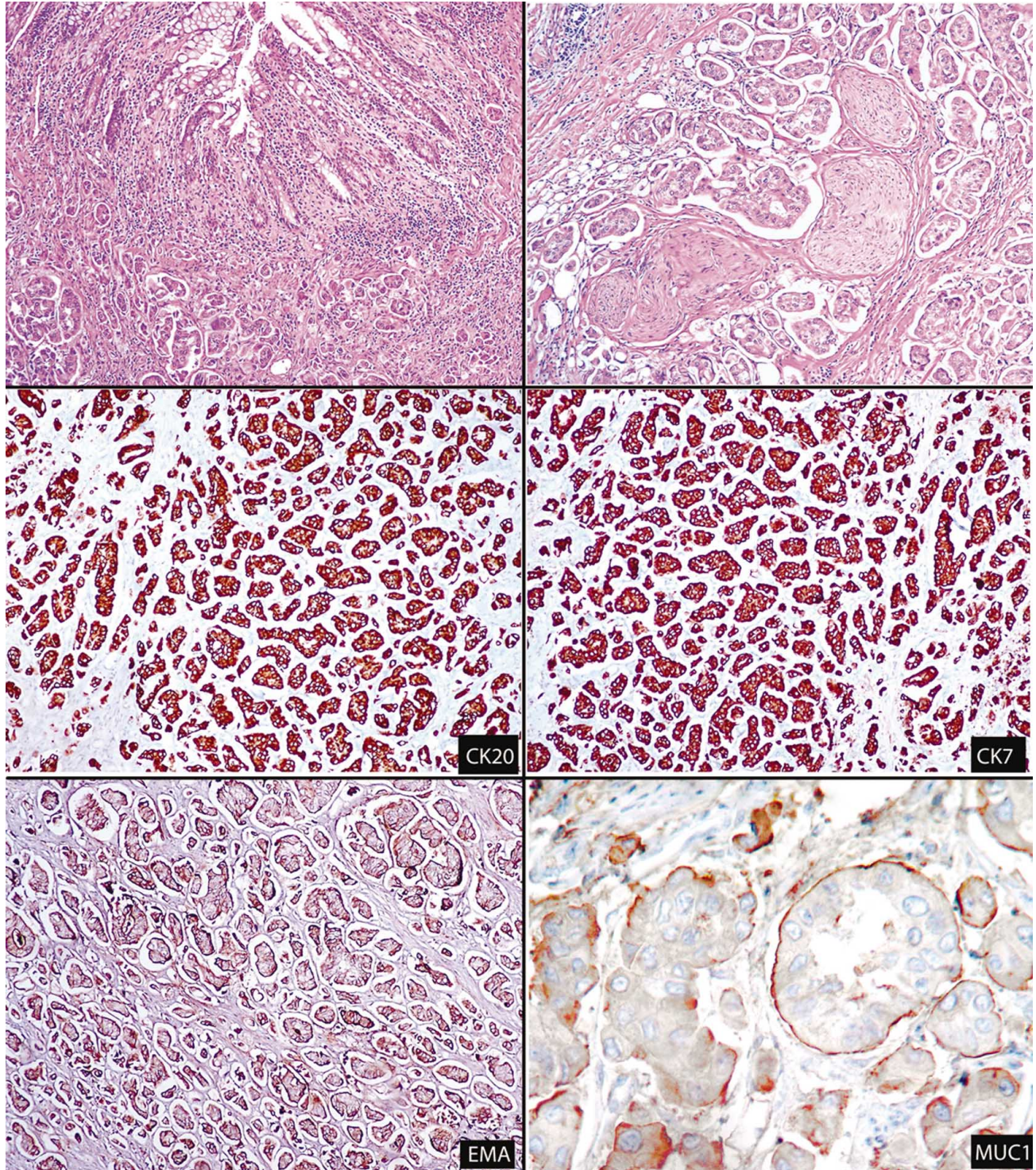


Fig. 2. There is a malignant gland-forming neoplasia diffusely infiltrating the submucosa. In the top of the image are the normal colonic mucosa (A). The classic pattern of infiltration of micropapillary carcinoma consists in nests and glandular structures with focal papillary projections without fibrovascular cores lying within clear stromal spaces reminiscent of vascular lumens (B). The neoplastic cells are positive to CK 20 (C), CK7 (D), EMA (E) and MUC-1 (F); the last two shows the classic “reverse polarity pattern”.

Pathological findings. Macroscopically, the tumor was intraluminal, localized in the rectum over the anterior

peritoneal reflexion a 6 cm of the nearest margin (distal). The neoplasms was a exophitic and infiltrant bulky mass,

which measured --6.0 x 5.0 x 4.0 cm, was observed in the rectum (Fig. 1). Microscopically, there is a neoplastic proliferation of atypical glandular cells disposed in nests and glandular structures with focal papillary projections without fibrovascular cores lying within clear stromal spaces reminiscent of vascular lumens (Fig. 2A,B). There was a very focal natural transition between conventional tubular carcinoma in small focus and micropapillary carcinoma (>95 % of the total tumor area). In depth, the tumor invaded into the subserosal layer. Marked infiltration into lymphatic vessels and veins was observed, also perineural invasion, neoplastic cells in distal and circumferential margin and metastasis in 21 of 22 regional lymph nodes were present.

The neoplasm react immunohistochemically with CK20 (Fig.2C), CK7 (Fig.2D) and for MUC1 (Fig.2E) and EMA (Fig.2F) in the characteristic “inside-out” pattern.

DISCUSSION

Recently, micropapillary carcinoma has been reported in various anatomic sites. Except for the ovary, micropapillary carcinoma arising in many organs seems to pursue an aggressive clinical course because of frequent invasion into lymphatic spaces, metastasis into lymph nodes, or systemic metastasis (Verdú *et al.*; Amin *et al.*, 2002; Amin *et al.*, 1994; Nassar; Nassar *et al.*; Paterakos *et al.*; Siriaunkgul & Tavassoli; Zekioglu *et al.*; Haupt *et al.*; Kim *et al.*; Kuroda *et al.*; Sakamoto *et al.*; Wen *et al.*; Xu *et al.*). Micropapillary carcinoma of the colon macroscopically seems to be indistinguishable from conventional adenocarcinoma.

Microscopically, micropapillary carcinoma in the present case was not associated with conventional adenocarcinoma, contrary to all previous reports were the micropapillary component form part of a combined tumor, and is the less predominant component of such neoplasms. In the most large series recently published by Verdú *et al.*, from

a total of 379 cases finds 60 that have at least a 5% of micropapillary carcinoma, it corresponds to 5-80% of tumor, generally less of 30%, and no found a pure example. These results are very similar to those obtained by Horuda *et al.* and Kim *et al.* In other report by Sonoo *et al.* (2009) presents a case of micropapillary carcinoma originated in a pedunculated polyp, and this pattern comprised 80% of the tumor and the remaining 20% was moderately differentiated tubular adenocarcinoma.

Thus, pure micropapillary carcinoma is extremely rare in any location. Our case represents the first pure micropapillary carcinoma reported to date in all colon and rectum.

Immunohistochemical study surprised us because CK7 expression, but there are studies that shows CK7 expression in poorly differentiated colorectal carcinomas in near of 10% of cases (Saad *et al.*, 2009; Hernandez *et al.*, 2005). Additionally, there are cases of absence of expression of cdx2 in colorectal carcinoma in up 29% of cases (Choi *et al.*, 2006; Baba *et al.*, 2009). At last, not exist to date a good designed study that explores the immunohistochemical panel to define the primary site of metastatic micropapillary carcinomas, only are one study exploring this issue (Lotan *et al.*, 2009). Thus, the clinical and pathological data of our case are supportive of rectal origin.

In conclusion, we experienced a patient with a pure micropapillary carcinoma showing coexpression of CK7, CK20, and absence of CDX2, which had an aggressive neoplasm with extense perineural, vascular and lymphatic invasion also extensive nodal metastasis. The presence of a micropapillary carcinoma in the colorectum seemed to be closely related with nodal metastasis, similar to the case for micropapillary carcinomas in other organs. Therefore, if a micropapillary component is identified in a tumor, particularly in a biopsy specimen, even if the pre-operative diagnosis is a pedunculated early colorectal cancer, should be carefully consider the extent of surgical resection due to the high potential for nodal metastasis.

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RESUMEN: El carcinoma micropapilar es considerado como una variante agresiva del cáncer en cualquier localización. Histológicamente se caracteriza por grupos de células papilares rodeada de espacios libres. Se informó que la proporción del componente carcinoma micropapilar en la totalidad de un tumor varió entre 5% a 80% y no se han reportado casos puros. Existen cerca de 130 casos reportados hasta la fecha en colon y recto. Se describe el caso de un paciente con un carcinoma micropapilar puro que muestra coexpresión de CK7, CK20, y la ausencia de CDX2, que tenía un tumor agresivo con extensa invasión perineural, vascular y linfática además de metástasis nodular extensa. La presencia de un carcinoma micropapilar en la región colorrectal parece estar estrechamente relacionada con metástasis nodular, similar al caso del carcinomas micropapilar en otros órganos. Por lo tanto, si un componente micropapilar se identifica en un tumor, sobre todo en una muestra de biopsia, incluso si el diagnóstico pre-operatorio es un cáncer colorrectal temprano pediculado, se debe considerar cuidadosamente la extensión de la resección quirúrgica debido a la alta probabilidad de metástasis nodular.

PALABRAS CLAVE: Carcinoma micropapilar; Adenocarcinoma; CK7; CK20; CDX2; Cáncer colorrectal.

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Received: 03-06-2011
Accepted: 22-10-2011