Medullary Carcinoma of the Colon :A case report

ABSTRACT :

Medullary adenocarcinoma (MC) is a variant of colonic cancer,it has morphological similarity to poorly differentiated adenocarcinomas.

MC has been categorized as a rare variant of colorectal adenocarcinoma of sheets of malignant cells with vesicular nuclei, prominent nucleoli, and abundant eosinophilic cytoplasm. MC is a Colorectal Carcinome subtype that is most commonly seen in older females and is mostly localized in the right colon. However, there are rare cases in which it is localized in the left colon or the rectum. the mean age of MC patients 69.3± 12.5 The tumors tended to present with a larger size.

The differential diagnosis of MC includes poorly differentiated colorectal adenocarcinoma, neuroendocrine carcinoma and "lymphoepithelioma-like carcinoma. The distinction between medullary carcinoma of the colon and these other malignancies is made via microscopy and special staining for markers.

MC appears to be a distinctive clinicopathologic entity, with good prognosis and should be distinguished from other more aggressive, non-glandular tumors of the colon.

Due to the rarity of the tumor, optimal treatment strategies including specific chemotherapy regimens have not been determined.

Though rare,the medullary Carcinoma of the Colon deserve special interest due to the broad spectrum of differential diagnosis; their clinical course; their favorable prognosis.

We report the case of a patient operated on for medullary carcinoma of the right colon in the Department of Digestive Cancer Surgery and Liver Transplantation of Ibn Rochd University Hospital.

Keywords : Medullary adenocarcinoma, colon, good prognostic, surgery

INTRODUCTION :

Medullary adenocarcinoma (MC) of the large intestine, also termed large cell carcinoma, is a variant of colonic cancer that has been recognized as a separate entity only during the last decade. [1]

It is a new histological subtype, a predominantly solid tumor with little-to-no glandular differentiation [2]. MC has morphological similarity to poorly differentiated adenocarcinomas, it has a relatively better prognosis and their recurrence and metastasis are quite rare [3,4]. It is a rare entity, accounting for less than 0.1% of colonic adenocarcinoma that poses a diagnostic challenge for the practicing pathologist [5].

There are few reports in the literature, but it has been shown that MC is frequerently located at the proximal parts of the colon,it also has a female tendency according to the literature. Inrecent years, the incidence of MC has increased due to increased incidence of colon cancer and improved histopathological investigation methods [6]

CASE PRESENTATION :

The patient was 60 years old, with no previous pathological history, presented on June 1, 2020 with a subocclusive syndrome consisting of cessation of matter without cessation of gas associated with vomiting evolving for 5 days, without externalized digestive hemorrhages.At the examination in admission, the patient was conscious,stable on the haemodynamic and respiratory level, with normo-coloured conjunctiva, the abdominal examination showed a collapsed abdomen with a slight generalized abdominal sensitivity. the abdominal CT scan showed an ileocolic invagination with circumferential thickening of the transverse colon and the ascending colon (Fig . 1). the surgical exploration objectified the presence of a tumour of the right colon extended from the cecum to the right colonic angle without peritoneal effusion nor hepatic metastasis nor peritoneal carcinosis nodule, the operation consisted of an ileo-haemicolectomy with terminal ileo-colic anastomosis (Fig. 2). The postoperative follow-up unremarkable, the patient leaved hospital 5 days after. The anatomical and pathological examination showed a morphological and immunohistochemical aspect of a CK7+,CK20- phenotype compatible with invasive medullary carcinoma of the colon, and the proximal and distal resection limits on the specimen are healthy, absence of lymph node metastasis 0N/61N (Fig. 3 and 4).

the patient did not receive postoperative chemotherapy.

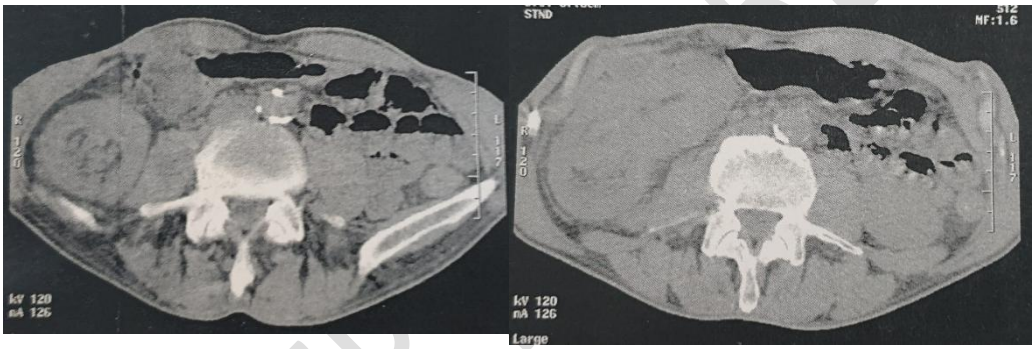

Fig. 1 : the abdominal CT scan showed an ileocolic invagination with circumferential thickening of the the ascending colon and transverse colon.

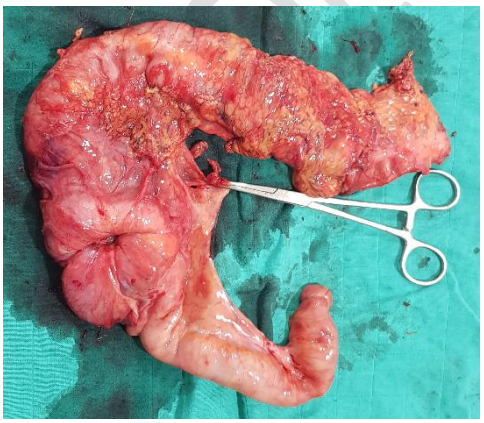

Fig. 2 : ileo hemicolectomy taking a tumor of the right colon extended from the cecum to the right colonic angle .

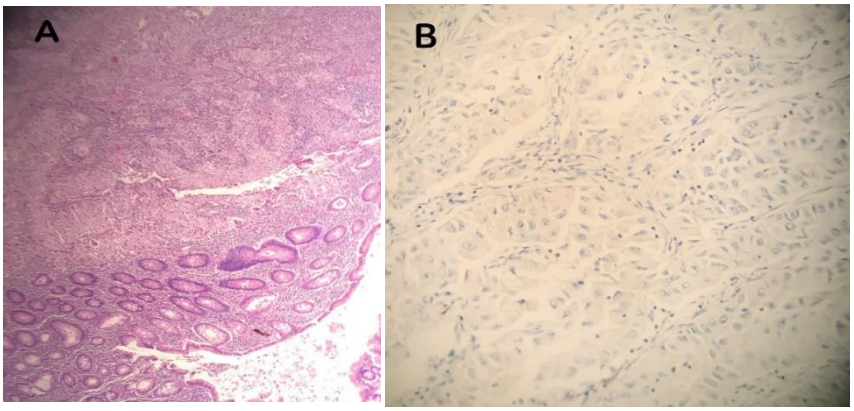

Fig. 3 : A: Carcinomatous proliferation arranged in solid masses and clusters of syncytial appearance with a lymphoid stroma (Haemathein-Eosin at low magnification). B: Absence of cytokeratin 20 expression.

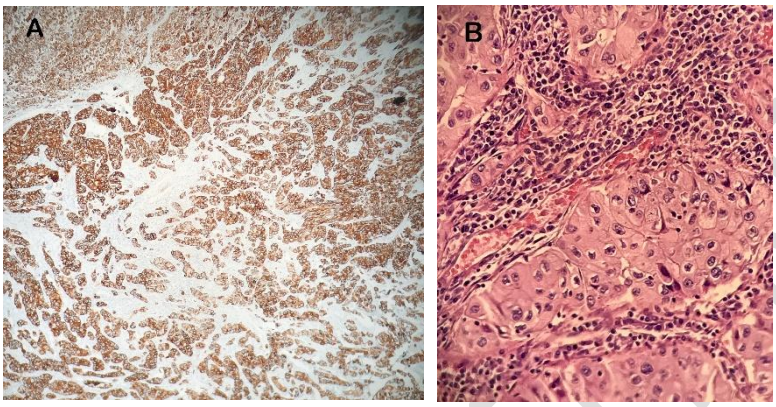

Fig. 4 : A: Diffuse expression of cytokeratin 7. B: Large tumour cells with irregular and sometimes polylobed nuclei within abundant cytoplasm, sometimes clarified and sometimes eosinophilic (Haematin-eosin at high magnification).

DISCUSSION :

MC has been categorized as a rare variant of colorectal adenocarcinoma composed of sheets of malignant cells with vesicular nuclei, prominent nucleoli, and abundant eosinophilic cytoplasm [6]. The cells are arranged in nests, cords, and sheets and may widely infiltrate the intestinal wall; geographic necrosis and perineural and angiolymphatic invasion are common. Intense intratumoral or peritumoral lymphocytic infiltrates, lymphocytic infiltrates at the advancing tumor margin and conspicuous “Crohn’s-like” lymphoid reactions are common [7]. Positivity with neuroendocrine immunohistochemical markers is found in approximately one third ofcases. Thrinavukarasu et al. reported that MC is seen in only 5–8/10,000 patients with colon cancer [8]

Medullary carcinoma of the colon is a relatively recent addition to the histological types of colorectal carcinomas and has been dealt with in only a handful of studies that have primarily dealt with its pathological aspects [9]. As early as 1977, Gibbs reported a small series of undifferentiated adenocarcinomas with a tendency to grow to larger sizes before producing symptoms but had a favorable prognosis [10] . In 1997, Ruschoff et al. reported a series of poorly differentiated non-glandular colorectal adenocarcinomas, most of which exhibited an expansive growth pattern and significant peritumoral lymphoid infiltrate, resembling solid or medullary carcinomas of the stomach [11].

MC is a CRC subtype that is most commonly seen in older females and is mostly localized in the right colon. However, there are rare cases in which it is localized in the left colon or the rectum [8, 12, 13]. Thirunavukarasu et al. [8] indicated that the mean age of MC patients 69.3± 12.5 and the female-to-male ratio is 2.12:. Knox et al. [13] found the mean age to be 76.8, and the female-to-male ratio to be 3.33:1. In study of Serkan et al [14] , the femaleto-male ratio was 3.33:1 and 84.5% of the tumors were localized in the right colon . However, the mean age is 59± 18, which is comparatively young. These studies indicated that 86% of the tumors were localized in the right colon [8, 12,13,14]. tumors tended to present with a larger size. Median tumor size was 7 cm in the Thirunavukarasu et al. study [8].

The diagnosis of medullary carcinoma of the colon includes the clinical features of a colonic tumour, imaging or visualisation by endoscopy, an elevation of tumour markers, and histological confirmation of the diagnosis [2].

The differential diagnosis of MC includes poorly differentiated colorectal adenocarcinoma, neuroendocrine carcinoma and “lymphoepithelioma-like carcinoma [7]. The distinction between medullary carcinoma of the colon and these other malignancies is made via microscopy and special staining for markers.[15]

Despite their similar histology to neuroendocrine tumors, medullary carcinomas of the colon maintain some intestinal differentiation, frequently staining positive for Mucin1, cell surface associated (MUC1), Mucin2, oligomeric mucus gel- forming (MUC2), and transcription termination factor 2 (TTF2). Medullary carcinoma of the colon can be differentiated from poorly differentiated and undifferentiated colon adenocarcinoma by microsatellite instability, with loss of staining for MLH1 and intestinal transcription factor CDX2. There is also a strongly positive calretinin staining compared to other poorly differentiated colonic adenocarcinomas. In one study, it was also noted that there was more commonly a lack of stabilization of the p53 protein, and microsatellite instability (MSI) was almost completely limited to poorly differentiated adenocarcinoma of the medullary type.[15]

Although most published series claimed that medullary carcinoma has better prognosis, the definition and identification of MC are not very clearly stated. However, the better prognosis of microsatellite instability (MSI) carcinomas is very debatable; there are many studies demonstrating that MSI have at least similar clinical behavior compared with microsatellite-stable (MSS) carcinomas, and the clinical benefit has been observed only in stage II tumors [16–17]. This heterogeneity of clinical behavior could be explained by the multitude of molecular heterogeneity underlying MSI tumors, because they also harbor BRAF mutations and KRAS mutations. We believe that MSI does not have strong prognostic significance, and our data confirm this affirmation. We consider that histologic grade could have the most prognosis significance because by definition all MCs are grade 3 or 4 carcinomas, and possibly this could explain their worse prognosis in our study. Another interesting finding is the fact that high lymphovascular invasion did not correlate with the N stage; we do not have a good explanation for that. Tumor burden could explain some of these findings; however, tumor size has not been demonstrated to be a poor prognostic factor [9].

Treatment strategies in medullary carcinoma versus high-grade adenocarcinomas have not been compared to date. In the study by Thirunavukarasu et al., all patients with medullary carcinoma had undergone surgery [8]. In Jessurun et al., all 11 patients studied in the case series had undergone right hemicolectomy or total colectomy [18]. for our patient had undergone an ileo-haemicolectomy with terminal ileo-colic anastomosis.

Due to the rarity of the tumor, optimal treatment strategies including specific chemotherapy regimens have not been determined.[15]

CONCLUSION :

Though rare,the medullary Carcinoma of the Colon deserve special interest due to the broad spectrum of differential diagnosis; their clinical course; their favorable prognosis; and the unique molecular changes. MC appears to be a distinctive clinicopathologic entity, with good prognosis and should be distinguished from other more aggressive, non-glandular tumors of the colon.

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