Bull Cancer 2015; □□: □□□
en ligne sur / *on line on*
www.em-consulte.com/revue/bulcan
www.sciencedirect.com

Primary signet ring cell carcinoma of the colon and rectum

Samia Arifi [1,2], Omar Elmesbahi [1], Afaf Amarti Riffi [2,3,4]

Received 14 April 2015
Accepted 11 July 2015
Available online:

1. Hassan II university Hospital, Sidi Mohamed ben Abdullah University, School of medicine, Medical oncology department, Fez, Morocco
2. Hassan II university hospital, Mohamed ben Abdullah University, School of medicine, Laboratory of cancer biology, Fez, Morocco
3. Hassan II university Hospital, Mohamed ben Abdullah University, School of medicine, Pathology department, Fez, Morocco
4. Laboratory of pathology Al Azhar, Fez, Morocco

Correspondence:
Arifi Samia, Hassan II university hospital, Sidi Mohamed Ben Abdullah University, The School of medicine, Medical Oncology Department, Fez 30000, Morocco.
drsarifi@yahoo.fr, samia.arifi1@usmba.ac.ma

Carcinome colorectal primitif à cellules en bague à chaton

Keywords
Colorectal cancer
Signet ring cell
Molecular biology
Pathology
Treatment

Summary

Colorectal primary signet ring cell carcinoma (SRCC) is a rare entity accounting for nearly 1% of all colorectal carcinomas. It is an independent prognostic factor associated with less favorable outcome. This aggressiveness is mainly due to the intrinsic biology of these tumors. Here is an overview of the literature related to clinicopathological features, molecular biology, and management of SRCC of the colon and the rectum.

Introduction

Colorectal signet ring cell carcinoma (SRCC) was first described by Laufman and Saphir in 1951 [1]. It is a rare histological colorectal cancer subtype defined by the WHO classification of tumors as a variant of colorectal adenocarcinoma with > 50% of tumour cells with prominent intracytoplasmic mucin [2]. These tumors are characterized by distinct clinical presentation, and different outcome [3]. SRCC of the colon and the rectum have been associated with poor prognosis compared with common colorectal adenocarcinomas [3]. They have been introduced by the 7th edition of the AJCC cancer staging manual as an independent prognostic factor associated with less favorable outcome [4]. Despite the current progress in the management of colorectal cancer, SRCC still has poor outcome. This aggressiveness is mainly due to the intrinsic biology of these tumors [3]. Several studies have investigated molecular patterns of this histological subtype in order to determine new biomarkers, and new tumor-related prognostic factors for stratification for new therapeutic approaches to improve colorectal SRCC-patient's survival.

The aim of the current manuscript is to present an overview of the literature related to SRCC of the colon and rectum.

http://dx.doi.org/10.1016/j.bulcan.2015.07.005

Epidemiologic features

Colorectal SRCC is an extremely rare subtype among all colorectal cancer. The reported frequency varies from 0.3 to 4.6% of all colorectal carcinomas with slight differences between western countries, Asia and Africa (*figure 1*) [3,5–12]. The highest incidence of SRCC of the colon and rectum is reported in countries with low overall prevalence of colorectal cancer, such as Tanzania [10]. However, these data should be interpreted carefully because the majority of epidemiological data on SRCC of the colon and rectum are based on single institution studies [5,6,10], rarely from large population-based studies of colorectal cancer histology [11,12]. The mean age at diagnosis of colorectal SRCC reported in published series ranges from 48 to 70 years old [7,9]. This large difference in age among series is likely due to the bias associated with single institution studies including small number of patients. However, all studies have shown that SRCC of the large bowel significantly occurs in younger individuals as compared to other colorectal carcinomas [9,11,13]. Incidence rates for colonic and rectal SRCC differ by race/ethnicity. Lower percentages were found in African Americans and Hispanic populations than in Caucasians [11,12]. With regard to gender, similar incidence rates for SRCC were found among males and females [9,11], however SRCC of the rectum was more frequently diagnosed in men [13]. SRCC are largely located within the right colon [12,13], and rectum location represents about 20% [13]. SRCC are usually diagnosed at advanced stages as opposed to non-SRCC of the colon and the rectum [3,12]. A large cohort from US found that 80% of colorectal SRCC were diagnosed at stage III and IV versus 50% in non-SRCC ($P < 0.01$) [13]. This finding is consistent with the other published data, including cohort from Europe, and Asia [3,6]. SRCC of the large bowel are more likely to have transmural extension and lymph node involvement [3,12]. Distant metastases at presentation are found in about 22 to 40% of SRCC of the colon and rectum [3,9,12]. This neoplasm, preferentially, metastasizes to peritoneal surfaces and is more likely to involve ovaries and distant lymph node [7,14,15]. A percentage of 51.2% and 43.9% for peritoneal dissemination and distant lymph node were respectively reported by Hugen et al. The proportion of patients with dissemination to the peritoneum and distant lymph node was statistically different as compared to non-SRCC [15]. Furthermore, SRCC patients presented more frequently with more than one metastatic site with the involvement of rare metastatic sites, such as heart, bone, pancreas, leptomeningeal structure, and skin in some cases [15,16]. These findings confirm a distinct tumour spread of colorectal SRCC and may have significant implications for the treatment and follow-up approaches.

Colorectal SRCC is independently associated with higher risk of death [4]. The median overall survival was 18.6 months in Ramya et al. study including 206 patients with colonic SRCC [12]. The stage specific 5-year survivals decreased with increasing stage with a 5-year survival exceeding 50% for early stages (I–II) versus less than 5% for stage IV colorectal SRCC (*table I*). Although the identification of several environmental factors, inherited syndromes, and genetic susceptibility as significant aetiological factors in the development of colorectal adenocarcinomas, no specific risk factors related to colorectal SRCC development have been determined [2]. Large population-based studies are needed to identify epidemiological associations between the occurrence of SRCC subtype and environmental and/or genetic factors, so that we could be able to take preventive measures to reduce the incidence of this aggressive neoplasm and its mortality. There is emerging evidence for an increased risk of colon cancer with signet ring cell features in some hereditary diffuse gastric cancer (HDGC) families [17]. It is therefore advised by the consensus guidelines to consider colonoscopic screening in *CDH1* family members with documented cases of colon cancer in mutation carriers [18]. However, at this time, there is limited data to support this measure as an

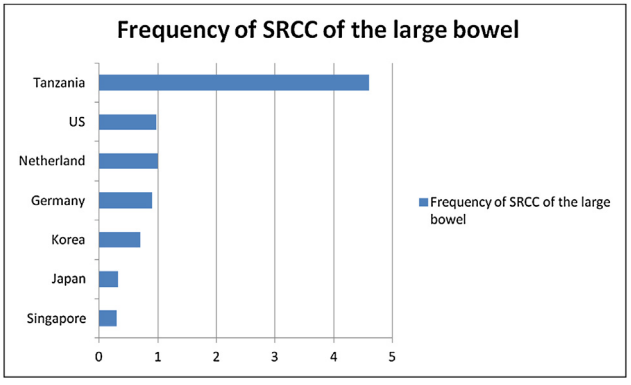

FIGURE 1

Differences in the incidence rates of colorectal cancer SRCC with regard to countries