RESEARCH COMMUNICATION

Clinicopathological Patterns of Colorectal Cancer in Tunisia

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Abstract

Introduction: Colorectal cancer is the third most commonly diagnosed cancer worldwide. Design: In order to review the clinical and pathological features of colorectal cancer in Tunisia, a retrospective study was carried out on 1,443 cancer cases diagnosed in the Pathology Department, Farhet Hached University Hospital of Sousse, for a 15-year period (1993-2007). Results: The median age was 61 years. Adenocarcinoma was the most frequent (90.9%) with moderately differentiated tumors accounting for 76.7% of cases. Only eighty patients were identified as being in early stages (0 and A) and 85.8% in advanced stages (B-D). Over time, we observed a significant decrease of stage B (p=0.02) and a significant increase of stage D (p=0.002). The tumor size was larger than 5 cm in 67.5% of cases. Conclusion: The large proportion of patients presented at advanced stages, compared to only 5.5% of patients at early stages, emphasizes the need to plan and develop a screening program for the early detection of this cancer and its precursor lesions in Tunisia.

Keywords: Colorectal cancer - clinicopathological study - screening program - Tunisia

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Introduction

Colorectal cancer is the third most common cancer worldwide (Parkin et al., 2003; Parkin, 2004). The incidence of colorectal cancer varies widely with higher incidence in North America, Australia, and northern and western Europe (Ferlay et al., 2010). Developing countries have lower rates, particularly Africa and Asia (Ferlay et al., 2010). In Tunisia, cancer of the colon and rectum was ranked fourth in males with an age-standardized incidence rate (ASR) of 10.7 per 100,000, but third among women with an ASR of 9.4 per 100,000 (Missaoui et al., 2010). Colorectal cancer is one of the cancers that can be prevented by secondary prevention. The precursor of advanced colorectal cancer is either an adenomatous polyp or a flat neoplastic lesion. The majority of cancers arising in the colon and rectum are adenocarcinomas that account for more than 90% of all large bowel tumors. Colorectal cancer fulfils the conditions required for mass screening since it represents a major cause of morbidity and mortality in industrialized countries and can be cured by the detection at earlier stage and even prevented by the removal of adenomas.

The purpose of this study is to report for the first time the clinical and pathological features of all colorectal cancer cases diagnosed in the Center of Tunisia during the span of time between 1993 and 2007, based on the database of the population-based Cancer Registry of the Center of Tunisia.

Materials and Methods

We carried out a retrospective study of 1,443 cases of colorectal cancer diagnosed in the Pathology Department of the Farhet Hached University Hospital, Sousse and registered in the Cancer Register of the Center of Tunisia during 15-year period time (January 1993-December 2007). The study was approved by the Human Ethics Committee at the Farhet Hached University Hospital of Sousse, and it conformed to the provisions of the Declaration of Helsinki.

Among three Cancer Registries in Tunisia, only the Cancer Registry of the central region was judged to be of sufficient quality for its data to appear in *Cancer Incidence in Five Continents (CI5) Vol. IX* (Curado et al., 2007). The cancer registry of the Center of Tunisia has provided important information on cancer patterns over previous years (Parkin et al., 2003; Curado et al., 2007; Missaoui et al., 2010). The cancer registry includes six provinces (Sousse, Monastir, Mahdia, Kasserine, Sidi Bouzid and Kairouan) covering a total surface of 28 426 km^2.

The International Classification of Diseases, 10th revision (ICD-10) was used for cancer classification in the Cancer Registry of the Center of Tunisia (Percy et al., 1992). The inclusion criteria were a cancer of the colon, rectum and anus (C18, C19-20, C21) (Percy et al., 1992) diagnosed between 1st January 1993 and 31st December 2007 (recurrences and metastases of an anterior diagnosed cancer were not recorded) and the residence place at the

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diagnosis time in the Center of Tunisia. For each patient, we reviewed the medical records for data on age, sex, antecedents, delay to diagnosis, signs and symptoms, paraclinical data at time of diagnosis, histopathology, tumor grade and stage, treatment, and follow-up. SPSS, version 17 (SPSS Inc., Chicago, IL) was used for statistical analysis and probability values of 0.05 or less were considered statistically significant.

Results

A total of 1443 new cases of colorectal cancer were registered over the 15-year period (1993-2007). Non invasive colorectal cancer was diagnosed in 23 cases. There were 781 males (54.1%) and 662 females (45.9%). The median age at diagnosis was 61 years with a mean age of 58.8 years (ranged from 9 to 94 years). There was no significant change in median age over time (p=0.44). In the current study, 29.3% of our patients are of 50 years of age or younger. Among our patients, 0.8% was diagnosed under age 20; 11.2% between 20 and 34; 12.1% between 35 and 44; 20.2% between 45 and 54; 24.3% between 55 and 64; 21.2% between 65 and 74; 13.1% between 75 and 84; and 2.1% 85+ years of age.

The predominant presenting symptoms were abdominal pain (72%), bleeding by rectum (68%), weight loss (59%), constipation (54%), melena (19%), and fever and anemia (11%). Symptoms were present for 6.6 months in average (0-120 months). In the majority of cases, the diagnosis was based mainly on primitive histology (98.3%). Forty-seven patients had a family history of colorectal cancer. One hundred fifty-six more patients have a history of inflammatory bowel disease (ulcerative colitis).

The tumor was located in the colon in 714 patients (49.5%), in the rectum (34.7%), in the sigmoid (8%), and in the anus (3.5%). Left-sided lesions constituted 67.7% of all tumors. The tumor size was lower than 2 cm for only 84 cases (5.8%). It was higher than 2 cm in 1302 cases and higher than 5 cm in 67.5% of cases. The most represented histological type was adenocarcinoma (90.9%) followed by carcinoma (5.5%) (Table 1).

Histologically, 76.7% of colorectal cancer were moderately differentiated (962 cases), followed by well-differentiated tumors (15.9%) and poorly differentiated tumors (6.8%). During the study period, no significant change of tumor grade was observed (p > 0.05). According to Duke's system classification, only eighty patients (6.1%) were identified as being in early stages (stage 0 and A) and 1238 patients (93.9%) were presented in advanced stages: stage B in 38.6% (509 cases), stage C in 32.8% (433 cases), and stage D in 22.4% (296 cases). One hundred twenty-five cases were identified as not being assessable. During the study period, no significant change was observed for early stages (p=1.0 and 0.76) as well as stage C (p=0.45). While, significant decrease was observed for stage B tumors over time (p=0.02). A significant increase was observed among the most advanced stage (p=0.002).

Among our patients, 82% received a surgical treatment (1183 cases). For 672 patients (56.8%), adjuvant treatment (radiation therapy and/or chemotherapy) had been indicated. Among these patients, 70 cases were handled by chemotherapy associated to radiation therapy; 464 cases received chemotherapy and 138 patients received radiation therapy. Surgery was the only treatment for 511 patients. An exclusive chemotherapy has been indicated for 39 patients. Radiation therapy was the only local treatment after chemotherapy for 11 patients. An exclusive

Table 1. Clinicopathological Features of Colorectal Cancer in Central Tunisia, 1993-2007

	Cases number (%)
Tumor size	
≤ 2 cm	84 (6.1%)
3-4 cm	366 (26.4%)
≥ 5	936 (67.5%)
Histological Type	
Adenocarcinomas	1312 (90.9%)
Adenocarcinomas	1096 (83.5%)
Mucinous adenocarcinomas	123 (9.4%)
Adenocarcinomas, intestinal type	79 (6%)
Other types	14 (1.1%)
Carcinoma	80 (5.6%)
Other tumors	51 (3.5%)
Tumor grade	
Well-differentiated	200 (15.9%)
Moderately differentiated	962 (76.6%)
Poorly differentiated	85 (6.7%)
Undifferentiated	7 (0.5%)
Tumor Stage	
0	15 (1.2%)
1	65 (5.2%)
2	509 (38.6%)
3	433 (32.8%)
4	296 (22.4%)

Table 2. Comparison of Colorectal Cancer Patients Under and Above 50 Years

	< 50 years	≥ 50 years
Cases number	423 (29.2%)	1020 (70.8%)
Males	208 (26.7%)	573 (73.3%)
Females	215 (32.5%)	447 (67.5%)
Tumor size		
≤ 2 cm	15 (17.9%)	69 (82.1%)
3 - 4 cm	118 (32.3%)	248 (67.7%)
≥ 5 cm	175 (18.7%)	761 (81.3%)
Site of primary tumor		
Colon	219 (28.2%)	557 (71.8%)
Sigmoid	34 (29.3%)	82 (70.7%)
Rectum	157 (31.3%)	344 (68.7%)
Anus	13 (26%)	37 (74%)
Histological type		
Adenocarcinomas	349 (26.6%)	963 (73.4%)
Carcinomas	13 (16.3%)	67 (83.7%)
Other tumors	25 (49%)	26 (51%)
Histological grade		
Well-differentiated	59 (29.5%)	141 (70.5%)
Moderately differentiated	258 (26.8%)	704 (73.2%)
Poorly differentiated	25 (29.2%)	60 (70.8%)
Undifferentiated	1 (14.3%)	6 (85.7%)
Tumor stage		
0	7 (46.7%)	8 (53.3%)
1	15 (25.1%)	50 (76.9%)
2	141 (27.7%)	368 (72.3%)
3	132 (30.5%)	301 (69.5%)
4	96 (32.5%)	200 (67.5%)

radiation therapy has been indicated for only 42 patients. Unfortunately, 250 patients had received no treatment.

When we compared patients who were above 50 years of age to those of who were under 50 years of age, we found no significant difference between the two groups of patients in terms of sex, site of primary tumor, stage of the tumor at diagnosis, histological grading, and tumor size ($p > 0.05$) (Table 2).

Discussion

Colorectal cancer is the fourth most common cancer in men and the third most common cancer in women worldwide (Parkin et al., 2005). Risk factors for colorectal cancer include obesity, a diet low in fruits and vegetables, physical inactivity, and smoking (Giovannucci et al., 2002; Giovannucci et al., 2006; Botteri et al., 2008), and as such it was once a disease primarily observed in longstanding developed nations whose populations typically exhibit these factors (Popkin et al., 2004). Significant international variations in the distribution of colorectal cancer have been observed (Parkin, 2004; Kuriki and Tajima, 2006; Center et al., 2009; Center et al., 2009). In the United States and based on cases diagnosed in 2003-2007 from 17 Surveillance, Epidemiology and End Results (SEER) geographic areas, the ASR was 47.9 per 100,000 men and women per year (Altekruse et al., 2010). Nevertheless, incidence rates are decreasing among both American males and females (Meissner et al., 2006; Center et al., 2009; Center et al., 2009). In economically transitioning countries such as the Czech Republic and Slovakia, incidence rates increased continuously during the last years (Center et al., 2009; Center et al., 2009). There was more significant increase in colorectal cancer incidence rates in men compared with women and this could reflect the slower adoption of certain risk behaviors associated with colorectal cancer such as: smoking, heavy alcohol consumption and obesity (Popkin, 2004; Knai et al., 2007; Baillie et al., 2008; Center et al., 2009; Center et al., 2009). Targeted prevention and early detection programs could reverse the trend of colorectal cancer incidence rates (Benson et al., 2008). In the United States, colonoscopy has been the most prevalent of all colorectal cancer screening tests (Meissner et al., 2006), contributing to the marked decline in incidence rates of this cancer (Espey et al., 2007; Jemal et al., 2008; Levin et al., 2008; Center et al., 2009; Center et al., 2009). However, in Tunisia, there is still no screening program for the colorectal cancer which could explain the increasing trends described recently (Missaoui et al., 2010).

In the Center of Tunisia, the median age of patients with colorectal cancer was higher than the rate described in other Arab countries such as Saudi Arabia (Aljebreen, 2007). However, the median age described here was younger than the age described in most developed countries (Koo et al., 2008; Altekruse et al., 2010). In the United States, from 2003-2007, the median age at diagnosis was 70 years (Altekruse et al., 2010). The likelihood of colorectal cancer diagnosis increases progressively from age 40, rising sharply after age 50 (Ries et al., 2008). The incidence rate is more than 50 times higher in persons aged 60 to 79 years than in those younger than 40 years (Ries et al., 2008; American Cancer Society, 2009). More than 90% of colorectal cancer cases occur in people aged 50 or older (National Institutes of Health, 2006; Ries et al., 2008). Nevertheless, colorectal cancer appears to be increasing among younger persons (O'Connell et al., 2003; 2004). In the United States, colorectal cancer is now one of the 10 most commonly diagnosed cancers among men and women aged 20 to 49 years (Fairley et al., 2006). In our study, more than 29% of our patients are of 50 years of age or younger. Data from Saudi Arabia showed that more than 37% of patients were 50 years of age or younger (Mansoor et al., 2002; Aljebreen, 2007). These findings suggest a possible hidden familial risk for colorectal cancer and justify the need for a mass screening program for colorectal cancer, preferably for individuals aged 40 years and above.

Seventy-six percent of tumors were moderately differentiated which is relatively higher than previous findings (Ries et al., 2000; Mansoor et al., 2002; Aljebreen, 2007). According to Duke's classification, more than one half of our patients were diagnosed at advanced stages (C or D) with increasing rates of stage D tumors over time. Moreover, the tumor size remains higher than 5 cm in 67.5% of colorectal cancer cases diagnosed during the 15-year period. This can be attributed mainly to the absence of specific screening measures for colorectal cancer among Tunisian population.

In the current study, we did not find any differences in either the clinical or the pathological features among patients who were above 50 years of age and those who were under 50 years of age as reported by Aljebreen (Aljebreen, 2007). While, Al-Jaberi et al. (Al-Jaberi et al., 1997) reported that 68% of their patients who were younger than 40 years already had an advanced stage of colorectal cancer compared to only 40% of those who were above 40 years of age (Al-Jaberi et al., 1997).

In conclusion, we found that Tunisian patients present with colorectal cancer at a more advanced stage of the disease at younger ages compared to developed countries. The large proportion of patients presented in stages B to D and the significant increase of the most advanced stage emphasize the need to plan and develop a screening program for the early detection of this cancer and its precursor lesions in Tunisia.

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