RESEARCH COMMUNICATION

Cervix Cancer in Tunisia: Clinical and Pathological Study

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Abstract

Introduction: Uterine cervix cancer is the second most commonly diagnosed cancer among women worldwide. Design: In order to review the clinical and pathological features of cervix cancer in the center of Tunisia, a retrospective study was carried out on 410 cancer cases diagnosed in the Pathology Department, Farhet Hached University Hospital, Sousse, Tunisia (1993-2006). Results: The mean age was 52.1 years. Of the 410 patients, 90.5% had squamous cell carcinoma and 7.3% had adenocarcinoma. One hundred thirty-eight patients were identified as being in early stages (0 and I) (33.6%) and 58.2% in advanced stages (II-IV). Therapy consisted mainly in combination of radiotherapy and surgery in early stages (28.8%), and radiotherapy alone or associated with the chemotherapy in advanced stage (29.7%). Surgery was the only treatment in 29.5% of cases. Conclusion: A relatively large proportion of patients presented in stages II to IV, compared to only 36% with early stages, emphasizing the need to reinforce the early detection of this cancer and its precursor lesions in the center of Tunisia.

Key Words: Uterine cervix - cancer - clinicopathological study - Tunisia

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Introduction

Uterine cervix cancer is the second most commonly diagnosed cancer among women worldwide (Parkin et al., 2005). Marked differences in the relative frequency of cervix cancer are observed throughout the world because of the differences in the availability of screening programs and risk factors. Most cases occur in developing countries where cervix cancer accounts for 15% of female cancers (Parkin et al., 2005). In these countries, organized screening programs of the uterine cervix cancer were absent or limited making it the leading cancer affecting women (Dargent, 1999; Sankaranarayanan et al., 2001). However, this cancer accounts for only 3.6% of new cancers in developed countries where well-developed screening programs had led to an important decline of cervix cancer incidence and mortality rates during 40 last years (Parkin et al., 2005; Arbyn et al., 2007). Despite advances in the detection and management, cervical cancer continues to be a significant health problem on a world-wide scale. In the center of Tunisia, invasive uterine cervix cancer represented the fourth cancer among women with a world age-standardized incidence rate of 7.1 per 100,000 women (North and South, 2007).

The majority of these tumors are squamous cell carcinomas (SCC), whereas adenocarcinomas are relatively rare (Vizcaino et al., 1998; Gien et al., 2010). Although the incidence of squamous cell carcinomas has decreased during the last decade (Parkin et al., 2005; Arbyn et al., 2007), adenocarcinomas are diagnosed more frequently (Vizcaino et al., 1998; Sasieni and Adams, 2001; Gien et al., 2010). Numerous epidemiologic and molecular studies have demonstrated that high-risk types of human papillomavirus (HPV) are the agents of the majority cases of invasive SCC and endocervical carcinomas and their precursor lesions (zur Hausen, 2002; Castellsagué et al., 2006).

In order to show how risk factors of disease interfere and to set rational priority of healthcare activities, we analyzed the clinical and pathological features of the uterine cervix cancer in the center of Tunisia during 14-year period (1993-2006). Data were provided by the Cancer Registry of the Center of Tunisia.

Materials and Methods

We carried out a retrospective study of 410 cases of uterine cervix 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 14-year period time (January 1993 – December 2006). 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 (North and South, 2007). The cancer registry of the central region of Tunisia

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includes six provinces: Sousse, Monastir, Mahdia, Kasserine, Sidi Bouzid and Kairouan, covering a total surface of 28 426 km2.

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 uterine cervix (C53) (Percy et al., 1992) diagnosed between January 1993 and December 2006 (recurrences and metastases of an anterior diagnosed cancer were not recorded) and the residence place at the diagnosis time in the center region of Tunisia. For each patient, we analyzed the clinical and pathological data.

Results

Between January 1993 and December 2006, 410 new cervix cancer cases were diagnosed in the Pathology Department, of the Farhet Hached University Hospital of Sousse and registered in the Cancer Registry of the center of Tunisia, with an average of 29 new registrations per year. Two hundred forty-six cases (60%) were coming from the region of Sousse. The age range was 23–85 years, with a median age of 52.1 years. 33.4% of patients were aged 40-49 years; only 2.7% (11 cases) were aged 20-30 years.

The predominant presenting symptoms were abnormal vaginal bleeding (93.4%), malodorous discharge (38%) and pelvic pain (31%). Symptoms were present for 6.9 months in average (0-60 months). In the majority of cases, the diagnosis was based on primitive histology (94.6%); it was based on cytology in only 22 cases (5.4%).

The tumor size was lower than 2 cm for 15 cases and higher to 2 cm in 80 cases. The most represented histological type was squamous cell carcinoma (SCC) (90.5%) followed by adenocarcinomas (7.3%) (Table 1). Among SCC cases, 12.9% were keratinized tumors (48 cases). Six cervix cancers were associated to rare histological variants. The majority of adenocarcinomas were of the endocervical type (77.8%) constituted by glandular formations in the scalloped, irregular outlines which opposes to the rather regular aspect of glands normal endocervicales (Table 1).

Histologically, 61% of cervix cancer were intermediate-differentiated (250 cases), followed by poorly-differentiated tumors (23.5%) and undifferentiated tumors (2%). Only 13.6% of cervix cancers were well-differentiated (56 cases). According to FIGO classification, one hundred thirty-eight patients (33.6%) were identified as being in early stages (stage 0 and I) and 240 patients (58.5%) were presented in advanced stages: stage II in 26.1% (107 cases), stage III in 25.4% (104 cases), and stage IV only in 7.1% (29 cases). Forty-two cases (10.2%) were identified as not being assessable. Stage 0 cancers were treated mainly by surgery (86.1%). The surgical treatment is also indicated for 94% of patients presented in stage I (62 cases); followed by radiotherapy for 18 patients (29%) and chemotherapy for only patient. The patients with stage II tumors were treated by an exclusive radiotherapy (41 cases) or associated to chemotherapy (6 cases). The surgery was practiced for 39 patients (36.4%), followed by a postoperative radiotherapy (30 patients) and by an association of radiotherapy and chemotherapy (2 patients). An exclusive chemotherapy was indicated for a single patient.

Table 1. Morphological Aspects of Uterine Cervix Cancers in the Center of Tunisia

Histopathological type	Number of Cases
Carcinomas	371 (90.5%)
Squamous cell carcinoma	320 (86.2%)
Keratinizing squamous cell carcinoma	48 (12.9%)
Large cell non keratinizing carcinoma	3 (0.8%)
Transitional cell carcinoma	1 (0.2%)
Papillary transitional cell carcinoma	1 (0.2%)
Mucoepidermoid carcinoma	1 (0.2%)
Adenocarcinomas	30 (7.3%)
Adenocarcinoma endocervical	21 (77.8%)
Mucinous adenocarcinoma	4 (14.8%)
Clear cell adenocarcinoma	1 (3.7%)
Papillary serous cystadenocarcinoma	1 (3.7%)
Other tumors	9 (2.2%)

An exclusive radiotherapy is indicated for 49 patients with stage III cervix cancer (47.1%). It was associated to chemotherapy for 8 patients. A surgery was practiced for 25 stage III cancers (24%); followed by a postoperative treatment for 22 patients including radiotherapy (18 cases), chemotherapy (one case) or an association of radiotherapy and chemotherapy (3 cases). The patients with stage IV cancer were essentially handled by an exclusive radiotherapy (55.2%); an exclusive chemotherapy, a surgery and an association of chemotherapy and radiotherapy are respectively indicated for two patients.

Discussion

This study investigated clinical and pathological features of invasive uterine cervix cancer in the center of Tunisia, diagnosed in the Pathology Department of Farhet Hached University Hospital, Sousse (1993-2006). According to the Cancer Registry of the center of Tunisia, cervix cancer took the fourth rank among cancer in women with a world age-standardized incidence rate of 7.1 per 100,000 women (North and South, 2007). Cervix cancer constitutes a real problem of public health in Tunisia because only 17.5% of cases (72/410) were diagnosed at preinvasive stage (stage 0). Considering the incidence, the feasibility and the profitability of the screening programs, the uterine cervix cancer occupies the first row, with the cancer of the breast, in the scale of the priorities of the Ministry of Public Health in Tunisia. National strategy of cancers screening has been already fixed in 1998, and a screening program by cervico-vaginal smears practice was set up by the National Office of the Family and the Population. Cytological screening programs have been practiced in fourteen governorates (among twenty-four in Tunisia). Other possible reason for the low incidence of cervical cancer reported in the center of Tunisia, compared to other African countries, could be attributable to the monogamy and the advanced age of first sexual contact (Maalej et al., 2004). Thus, in the center of Tunisia, only 2.7% of patients were aged 20-30 years. Number of sexual partners, age at first sexual intercourse

and age at first pregnancy are important factors of carcinogenesis in cervix cancer since the relative risk is multiplied by at least 3 for women who have more than four partners compared to women with only one partner (Koss et al., 1998; Maalej et al., 2004).

In the center of Tunisia, the mean age of patients with cervix cancer was 52.1 years close to the average age described since 1984 in the north of Tunisian (51.3 years) (Ben Youssef et al., 1987) and the mean age reported in 1994 among global Tunisian population (Maalej et al., 2004). In Morocco, another North African country, the mean age is equal to 44.8 years (Setouani et al., 1987). Elsewhere in Africa, the mean age was lower: 35 years in Dakar 16 and 48 years in Burkina Faso (Lankoande et al., 1998) and Madagascar (Pignon et al., 1993).

Our pathological data joined those already described with the large predominance of squamous cell carcinoma (Vizcaino et al., 1998; Gien et al., 2010); the adenocarcinomas represented only 7.3% of all cervix cancers in the center of Tunisia. In Iran, of the total number of pathologic specimens, squamous cell carcinoma was reported in 88% and adenocarcinoma in 11% of the specimens (Haghdel et al., 1999). Over the past 40 years, multiple reports have documented the increase in relative distribution of adenocarcinoma compared to SCC in developed countries (Eifel et al., 1995; Smith et al., 2000; Wang et al., 2004). In the United States, from 1973 to 1977, the proportions of SCC and adenocarcinoma were 88% and 12%, respectively; however, from 1993 to 1996, the proportions were 76% and 24% (Smith et al., 2000). In our study, clinical data show evidence that the advanced stages of cervix cancer are decreasing (58.5%), but they are still predominant. The rate of advanced stages was 73% in 1974 (Ben Youssef et al., 1987) and 63% in 1994 (Maalej et al., 2004). Similarly, in the Cancer Institute of Dakar the diagnosis of advanced stages has decreased from 77% to 68% (Dem et al., 2008). Only 33.6% of patients with cervix cancer were presented at early stages in the center of Tunisia. However, early stages were estimated to 88.3% in The Netherlands (1989–1994) and 58.9% in Italy (1986–1994) (Parkin et al., 1997). In countries with organized screening programs such as Canada and Scandinavian countries, the lowest incidence of cervical cancer is observed with higher level of early stages (Colman et al., 1993). In North America, roughly 60% of patients are diagnosed at stage I, 25% at stage II, 10% at stage III, and 5% at stage IV (Waggoner, 2003). In many less developed countries, most cervical cancers are diagnosed in the third or fourth stage.

Treatment choices for cervical cancer are based on the stage of the disease, but primarily involve surgery, radiotherapy and chemotherapy (Waggoner, 2003; Allen and Narayan, 2005; Moore, 2006; Hughes, 2009). The surgery is essentially practiced for the patient having in situ or localized tumors (stage 0 and I). The surgery is complemented essentially by radiotherapy for patients with stage I cancer. The radiotherapy remains the best treatment for the advanced stages. For stage II tumors, the treatment is surgical followed by the radiotherapy or then based on the radiotherapy exclusive or associated with the chemotherapy. For the advanced stages (III and IV), the radiotherapy exclusive or associated with the chemotherapy was the most indicated.

In conclusion, squamous cell carcinomas were the predominant histological type among cervix cancer in the center of Tunisia. The relatively large proportion of patients presented in stages II to IV, compared to only 33.6% of patients at early stages, emphasizes the need to reinforce the early detection of this cancer and its precursor lesions despite the relatively low incidence rate of the cervix cancer in the center of Tunisia.

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