RESEARCH COMMUNICATION

Pediatric Rhabdomyosarcomas in Tunisia

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Abstract

Introduction: Rhabdomyosarcoma is the most common soft tissue sarcoma in the first two decades of life. Since there is a paucity of reports on the pattern of its occurrence in Tunisia, we here analysed the epidemiological pattern, clinical features, and pathology. Design: We retrospectively studied 30 consecutive cases of histologically proven rhabdomyosarcoma in children aged 0-15 years extracted from the database of the Cancer Registry of the Center of Tunisia for the period 1993-2007. Results: Rhabdomyosarcomas represented 53.6% of soft tissue sarcomas and 3.8% of all children cancer cases registered during this period. The male/female ratio was 2.7 with a mean age at diagnosis of 5.9 years. The embryonal subtype was the most frequent (60%) and the two most common sites of disease were the head and neck (50%) and genito-urinary tract(23.3%). Chemotherapy was used in 90% of patients; 43.3% of patients had radical surgery and 26.7% of patients received radiation therapy. Conclusion: The epidemiology, pathology and clinical features of rhabdomyosarcoma in Tunisian children are close to those reported from other countries.

Keywords: Children - rhabdomyosarcoma - epidemiology - Tunisia

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Introduction

Rhabdomyosarcoma is the most common pediatric soft tissue sarcoma in patients younger than 20 years old, with a peak incidence in very young children (Boue et al., 2000). In Europe, the age-standardised incidence rate (ASR) was 5.4 per million children of 0-14 years of age (Pastore et al., 2006). After neuroblastoma and Wilms'tumor, rhabdomyosarcoma is the third most common neoplasm among the extra-cranial solid tumors of childhood and the tumor is more common in males (Gurney et al., 1999; Parham and Ellison, 2006).

Rhabdomyosarcoma is a highly malignant childhood cancer thought to arise from striated muscle progenitor cells and it may arise almost anywhere in the body; nevertheless, certain distinctive clusters of features emerge regarding age at diagnosis, site of primary tumor, and histology (Parham and Ellison, 2006; Wexler et al., 2006). The head and neck localizations are most common in children younger than 8 years of age. However, extremity tumors are seen more commonly in adolescents and are more frequently of the alveolar tumors (Parham and Ellison, 2006; Pastore et al., 2006; Wexler et al., 2006; Hessissen et al., 2010).

Data on pediatric rhabdomyosarcomas from Tunisia were sparse. In the current study, we present for the first time, the epidemiological pattern, clinical features, histology, and the outcome of rhabdomyosarcoma based on the data of the Cancer Registry of the Center of Tunisia during the period 1993-2007.

Materials and Methods

This retrospective study included all histologically proven cases of rhabdomyosarcoma in patients younger than 15 years diagnosed from January 1993 to December 2007 at the Pathology Department of the Farhet Hached University Hospital of Sousse and registered in the Cancer Registry of the Center of Tunisia, Sousse, Tunisia.

The region of the Center of Tunisia includes six provinces: Sousse, Monastir, Mahdia, Kasserine, Sidi Bouzid and Kairouan covering a total surface of 28 426 km^2, which has a population of 2 760 900 in 2004 (Curado et al., 2007; Missaoui et al., 2010). The life expectancy at birth is 71.9 years for males and 76.1 years for females (The National Institute of Statistics in Tunisia). The total expenditure on health per capita is $488 (World Health Statistics, 2008).

The population-based cancer registry of the Center of Tunisia was established in 1987 under the auspices of the International Agency of Research on Cancer (IARC), Lyon, France and located in the Pathology Department of the Farhet Hached University Hospital, Sousse, Tunisia. The cancer registry has provided important information on cancer patterns over the previous years (Parkin et al., 2003; Curado et al., 2007; Missaoui et al., 2010).

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In the current study, we reviewed the medical records for data on age, sex, antecedents, origin, delay to diagnosis, signs and symptoms, paraclinical data at time of diagnosis, and follow-up. All cases had a histological confirmation of rhabdomyosarcoma and were classified as botryoid, alveolar, embryonal or undifferentiated subtypes. The site of primary tumor was classified into five groups: head and neck nonorbital, orbital, genito-urinary tract, extremities, and other localizations. Patients were divided into four groups I through IV according to the post-surgical clinical group system employed in the Intergroup Rhabdomyosarcoma Studies (IRSG) (Maurer et al., 1988). Treatment included surgery, radiation therapy, and chemotherapy.

Results

Thirty patients with newly diagnosed rhabdomyosarcoma were included in our study, and comprised 53.6% of soft tissue sarcomas and 3.8% of all pediatric cancers registered during the study period (1993-2007). The median follow-up time was 14.8 months (range, 25 days to 18 months). The median age at diagnosis was 5.9 years (range, 5 months to 15 years). Nineteen of the rhabdomyosarcoma cases were 7 years of age or younger and eight patients had 2 years of age or less. The male to female (M/F) ratio was 2.7.

Among the 30 patients included, 17 had no medical insurance. The median time from the first symptoms to diagnosis was 5.3 months (range, 15 days to 60 months). Most of the patients were diagnosed between 1 and 4 months and 85.2% of cases had 6 months of delay or less. The main symptoms in 16 cases were pain, redness, or swelling of soft tissues (facial, pelvic and extremity masses) followed by ophthalmic signs (exophthalmia and proptosis) in 6 cases, genitourinary tract symptoms in 4 patients (testicular masses and urinary obstruction), oropharyngeal symptoms in 3 cases and then abdominal signs.

Histology was embryonal in 18 patients (60%), alveolar in 4 cases, and unclassified in 8 cases. For the embryonal subtype the most frequent primary sites was genito-urinary (7 cases) with an M/F ratio of 3.5 and a median age of 5 years. The alveolar subtype had a median age of 5 years with an M/F ratio of 1.0. The unclassified rhabdomyosarcoma was frequent in head and neck tumors with an M/F ratio of 3.0 and a median age of 8.5 years.

The primary site of disease was head and neck in 15 cases (50%) and genito-urinary in 7 cases (23.3%). In head and neck tumors, the primary site was non-orbital in 10 cases and 5 had an orbital head and neck primary site. Extremities and others localizations were involved in 4 cases, respectively. Regarding the Intergroup Rhabdomyosarcoma Studies (IRSG) staging, 3 patients were Group I, 13 Group II, 8 Group III, and 6 had metastatic disease (Group IV). The most common sites of metastasis were regional lymph nodes followed by the lung.

Most patients received chemotherapy (90%); 3 also received radiation therapy, 7 radical surgery, and 5 both methods of local control. Of the 13 radical surgical patients (43.3%), 8 had surgery after chemotherapy, 4 underwent surgery prior to initiation of chemotherapy, and one patient had surgery alone. Radiation therapy was the only local treatment after chemotherapy in three patients with head and neck localizations (amygdale and nasopharyngeal). Twelve patients had chemotherapy alone. Two patients received no treatment.

During the follow-up, 22 abandoned treatment and no additional information on their outcome is available. Among the remaining patients, only patient is alive, 2 had relapses, and 5 patients died.

Discussion

In the Center of Tunisia, rhabdomyosarcoma represented 3.8% of all cases of pediatric cancer and the most frequent childhood soft tissue sarcomas registered in the Cancer Registry during the study period. It was more common in males and almost two third of patients were diagnosed before 7 years of age. Our results are close to that reported previously (Gurney et al., 1999; Boue et al., 2000; Parham and Ellison, 2006; Wexler et al., 2006). In Europe and based on the Automated Childhood Cancer Information System (ACCIS), rhabdomyosarcomas corresponded to 50% of all childhood soft tissue sarcomas with an M/F ratio of 1.4 (Pastore et al., 2006).

Nevertheless, there is a paucity of reports on the pattern of its occurrence in African countries. In Morocco, Hessissen et al., reported 100 new cases of rhabdomyosarcoma followed at the Pediatric Oncology Unit of the Children's Hospital of Rabat during a 10-year period (1995-2004) (Hessissen et al., 2010). The M//F ratio was 2.0 and the median age was 5 years (range, 6 months to 15 years) (Hessissen et al., 2010). In Egypt, Abd El-Aal et al., reported 55 new cases of rhabdomyosarcoma treated at the pediatric unit clinic of Kasr El-Aini Center of Radiation Oncology (Abd El-Aal et al., 2006). Males comprised 63.6% of the patients and the median age was 6 years (range, 1-9 years) (Abd El-Aal et al., 2006). In another report of 190 Egyptian children with rhabdomyosarcoma treated at the National Cancer Institute of Cairo University, the M/F ratio was 1.5 (Shouman et al., 2005). The median age at diagnosis was 6 years and 60% were younger than 10 years (Shouman et al., 2005). The Ibadan Cancer Registry of Nigeria reported 91 children with rhabdomyosarcoma followed at the University College Hospital Ibadan in Nigeria between 1984 and 2003 (Brown and Oluwasola, 2006). The M/F ratio was 1.5 and the mean age at diagnosis was 6.2 years (Brown and Oluwasola, 2006).

Histologically, the embryonal subtype was the most frequent (60%) in the Center of Tunisia similar to the rate reported from Cairo (Shouman et al., 2005). The embryonal subtype was also the most frequent rhabdomyosarcoma in Morocco (73%), in Egypt (87.3%) and in Nigeria (Abd El-Aal et al., 2006; Brown and Oluwasola, 2006; Hessissen et al., 2010). In the population-based study carried out in Europe for the period 1978-1997 by Pastore et al., 71.9% of rhabdomyosarcoma cases were of embryonal subtype (Pastore et al., 2006).

Head and neck localization was the most common

site of disease (50%) followed by the genito-urinary tract. Our results were similar to that observed in Europe and Morocco (Pastore et al., 2006; Hessissen et al., 2010). Compared to previous reports, we found a high rate of head and neck localization (Maurer et al., 1988; Koscielniak et al., 1992; Maurer et al., 1993; Stevens et al., 2005). Extremities and others localizations were less frequent. In Egypt, the site of the primary tumor was found to be highest in the head and neck (36.4%) followed by abdominal sites (23.6%) excluding the genito-urinary system (Abd El-Aal et al., 2006). However, at the National Cancer Institute, Cairo University, the most common primary sites were head and neck, trunk, and extremities (Shouman et al., 2005). Among Nigerian children, the majority of tumors were in the head and neck region (Brown and Oluwasola, 2006). In European children, the most common site of occurrence was head and neck, which, if orbit is included, was almost twice as common as any other group of sites (Pastore et al., 2006).

According to the IRSG, more than 50% pf our patients presented with clinical Groups I and II disease. However, in Cairo, the Clinical Group III was the most frequent presentation (67%) (Shouman et al., 2005). In Rabat, most of patients (64%) presented with clinical Groups III and IV disease (Hessissen et al., 2010), similar to the rate reported by the IRS I, II, and III studies (Maurer et al., 1988; Maurer et al., 1993; Crist et al., 1995).

The three currently recognized modalities of treating children with sarcomas are surgical removal, radiation therapy for control of residual bulk or microscopic residual tumor after surgery, and systemic chemotherapy (Wexler et al., 2006). Most of our patients abandoned treatment. Interestingly, Hessissen et al., reported that 89% of abandonment occurred during chemotherapy and that abandonment and relapse were the major causes of treatment failure among Moroccan patients (Hessissen et al., 2010).

In conclusion, epidemiology, pathology and clinical features of rhabdomyosarcoma in Tunisian children are close to that reported from others countries. The outcome of rhabdomyosarcoma can be improved using a total care strategy, including the use of locally adapted protocols, access to essential chemotherapy drugs, and socio-economic, educational and psychological support to reduce abandonment.

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