Clinico-Epidemiological Study of Kaposi Sarcoma At Kasr El-Einy Center Of Clinical Oncology And Nuclear Medicine (NEMROCK)

Thesis

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Abstract

Purpose: The aim of this retrospective analysis was descriptive clinico-epidemiological survey of Kaposi sarcoma (KS) cases that presented to NEMRCK between 2000 and 2011. **Materials and methods**: A review of medical records of all patients with proven KS who were referred to to NEMRCK during study period. **Results**: KS incidence rate was 0.14% at NEMROCK during 2006 and 2011. The median age of all cases at presentation time was 61 years. The age of patients ranged from 33 to 76 years old. Male to female ratio was 7:1. The classical type (CKS) was diagnosed in 81.2 % of patients, 12.5% of patients were diagnosed as AIDS-KS type with mean age 36.5 years and 6.3% of patients were immunosupprtion-related type, post renal transplantion. The radiotherapy was used to treat 62.5% of Patients. **Conclusions**: KS is a rare neoplasm at NEMROCK. CKS is the most common type with male predominance. Presence of AIDS-KS type with disappearance of African type compared with the study in 1997 cancer. Registration and proper documentation of data are important to accurate epidemiological information in retrospective study.

Key words: Kaposi sarcoma, classical Kaposi sarcoma, epidemic Kaposi sarcoma

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Abbreviations

AIDS	Acquired Immune Deficiency Syndrome
ACTG	AIDS Clinical Trials Study Group
AKS	African Kaposi Sarcoma
CKS	Classical Kaposi Sarcoma
DNX	Liposomal Daunorubicin
EKS	Epidemic Kaposi Sarcoma
HAART	Highly Active Antiretroviral Therapy
HHV-8	Human Herpes Virus-8
HIV	Human Immunodeficiency Virus
IFN-α	Interferon alpha
IKS	Iatrogenic Kaposi Sarcoma
IRIS	Immune Reconstitution Inflammatory Syndrome
KS	Kaposi Sarcoma
KSHV	Kaposi Sarcoma–associated Herpes Virus
NEMROCK	Kasr El-Einy Center of Clinical Oncology and Nuclear Medicine
NRTI	Nucleoside Reverse Transcriptase Inhibitors
PLD	Pegylated Liposomal Doxorubicin

Introduction

Kaposi Sarcoma (KS) is a multifocal angioproliferative disorder of vascular endothelium, primarily affecting mucocutaneous tissues with the potential to involve viscera (Lynen et al., 2005). Previously a rare disease, it is now a global health care and clinical problem because of its association with the human immunodeficiency virus (HIV) pandemic and other immunosuppressed states (Pyakurel et al., 2007).

KS was first identified in 1872 by Moritz Kaposi, a Hungarian dermatologist who described it as an idiopathic multiple pigmented sarcoma of the skin. This classical form of KS (CKS) was further described as a rare, indolent tumor mostly developing in the extremities of elderly males patients (all HIV negative) of southern European and Middle Eastern origin. In the 1950s, a more aggressive form of KS, was identified in parts of sub-Saharan Africa, it has existed for many decades, long preceding HIV (known as 'endemic or African' (AKS). Unlike CKS, endemic KS also occurs in children, where they often present with lymphadenopathy, rather than skin lesions (Boshoff et al., 2002). Shortly thereafter, an 'iatrogenic' form of KS (IKS) was diagnosed in immunosuppressed organ-transplant patients, the first case of post-kidney transplantation KS was reported in 1969 (Einollahi , 2007). A fourth form of KS, 'epidemic' KS (EKS), was identified in the 1980s, initially in homosexual men with acquired immune deficiency syndrome (AIDS) (Bartolo and Cesarman, 2004).

At NEMROCK, a retrospective study of 31 KS patients attended to NEMROCK during the period (1986-1995) showed that the incidence of KS was 0.16% of all malignant cases presenting to NEMROCK during the same period (Haggag et al., 1997).

In spite of the clear clinical differences, the histopathology of the various KS forms is essentially the same, with characteristic changes related to stage in the development of the KS tumor (Kaaya et al., 1992). Since the discovery of Kaposi sarcoma–associated herpesvirus (KSHV), in 1994, substantial evidence has been accumulated that implicates it as an essential factor in the pathogenesis of all forms of KS (Gaidano et al., 1999).

In the absence of therapy, the clinical course of KS varies from indolent lesions seen in the classic variant to rapidly progressive and fatal lesions of epidemic KS. The spectrum of therapeutic strategies is broad and selection of appropriate intervention mandates a thorough understanding of disease spread and the patient's symptoms, as well as risks and benefits of therapy (Martellotta et al., 2009).

Aim of work

The aims of this study were:

- Review of recent literature about different types of Kaposi sarcoma and changes in the last years regarding epidemiology, pathology, clinically and treatment modalities.

- A retrospective study of clinical features and epidemiology of all Kaposi Sarcoma cases that presented to NEMROCK since January 2000 till September 2011.

Epidemiology

Classical Kaposi sarcoma

Classic KS is also known as chronic, European, or sporadic KS. It is an uncommon disease among middle-aged and elderly men of Mediterranean or Jewish lineage. KS incidence in the Mediterraneans had been up to tenfold higher than in the rest of Europe and the USA, with a particularly high incidence in Italy, Greece, Turkey, and Israel (Grulich et al., 1992). In southern Italy, the incidence in men has been estimated at 3.01/100,000 which is about 2–3 times higher than in the USA (Grabar et al., 2008) and 10–20 times higher than in England (Iscovich et al., 2000). The prevalence of KS among Egyptian general population ranged from 0.00001 to 0.00007 (Said et al., 1990).

CKS mainly affects males over 60 years old, with a male to female ratio 10:1 or 15:1. The higher incidence rate of CKS among men compared with women suggests that gender is a risk for KS (Lorenzo, 2008). A study by Brenner found that Immunosuppression and advanced age are strongly associated with a poorer prognosis among Classic KS patients (Brenner et al., 2002). A direct correlation between HHV8 prevalence and classic KS incidence has been documented. A variety of unusual factors have also been identified as increasing the risk of the development of KS: reduced frequency of bathing, asthma, and the presence of symptomatic cutaneous eczematous states (Terhorst et al., 2010). A study by Goedert et al. (2002) focused on the risk factors for CKS. The authors found that cigarette smoking was associated with a statistical significantly reduced risk of KS where the risk for CKS was approximately fourfold lower in cigarette smokers.

AIDS-Associated Kaposi sarcoma

The AIDS epidemic has altered KS epidemiology worldwide (Schwartz et al., 2008). Before the acquired immunodeficiency syndrome epidemic, Kaposi's sarcoma was rare in the United States, occurring mainly in elderly men from Italy and Eastern Europe and Sporadic reports of KS following organ transplantation appeared. Among AIDS patients, KS is the most common cancer. The risk of development of KS for an HIV-infected patient in the pre-HAART era was estimated to be greater1000 times than the risk in the HIV-uninfected population (Dal et al., 2001).

With the onset of the AIDS epidemic in the United States in 1981, KS Incidence increased sharply (Jaffe et al., 1983). In the late 1980s, well before the discovery of KSHV and even before the advent of effective antiretroviral therapies, KS incidence in homosexual men with AIDS began to decline (Biggar, 2001). Several factors may have contributed to this decline. During the 1980s, American homosexual men responded to the AIDS epidemic by reducing the number of unprotected sex acts with new partners. This change may have restricted not only the dissemination of HIV but also that of KSHV (O'Brien et al., 1999). Although the incidence of Kaposi's sarcoma in American men with AIDS decreased from 40 percent in 1981 to less than 20 percent in 1992, it remains the most common AIDS-associated cancer in the United States (Biggar and Rabkin, 1996).

During the 1990s, the dynamics of the AIDS epidemic changed. KS Incidence decline sharply. A decline in new HIV infection reduced KS frequency in AIDS patients in the mid-1990s to about 15–25% (Renwick et al., 1998). Also, the incidence has been declining with the

use of highly active antiretroviral therapy (HAART) for HIV disease resulted in a substantial improvement in host immunity, resulting in reduced risk of developing KS (Schwartz, 1996). Still, approximately 15% of AIDS patients develop KS (SEER). In the beginning of the AIDS epidemic, about 15–25% of all HIV-infected homosexual men suffered from KS, in the era of HAART, the incidence among HIV-positive homosexual men is only 5–7%. HAART use may reduce excess risk of KS (Terhorst et al., 2010).

The incidence of KS varies among groups of patients with AIDS. The AIDS-associated KS almost exclusively afflicts homosexual or bisexual males (>95% of all AIDS related KS. Moreover, the risk of KS among homosexual men with HIV infection increased with reported number of sexual partners and with sexual contact with individuals with KS (Beral et al., 1990). Taken together, these observations suggested that, in addition to HIV, there was a second sexually transmissible causative agent for KS. In 1994, this agent was discovered to be a novel KSHV (Chang et al, 1994). By contrast, patients who acquire HIV infection through nonsexual blood-borne exposure (from intravenous drug use or transfusion of blood or blood products) are at lower risk for KSHV infection and for the development of KS. Among persons who are seropositive for KSHV and HIV, the sequence of exposure is an important risk factor for the development of KS. When KSHV seroconversion follows HIV seroconversion, the risk of developing KS is higher (Jacobson et al., 2000).

African (Endemic) Kaposi sarcoma

African KS was well described before appearance of HIV-AIDS. Before the human immunodeficiency virus (HIV) epidemic, Kaposi's sarcoma showed a greater geographic variation in incidence than almost

any other cancer. It was as common in parts of sub-Saharan Africa, such as Uganda and eastern Zaire, as colon cancer is in Europe and the United States, representing up to 9% of all cancers in men (Cook-Mozaffari et al, 1998). In eastern and southern Africa, Kaposi's sarcoma makes up 25 to 50 percent of soft-tissue sarcomas in children and 2 to 10 percent of all cancers in children (Athale et al., 1995).

An explosion in the incidence of the disease have seen in parts of Africa with a high prevalence of HIV and where Kaposi's sarcoma was relatively common even before the era of AIDS. The incidence of Kaposi's sarcoma has increased about 20-fold in Uganda (Wabinga et al., 1993) and in Zimbabwe (Bassett et al., 1995). Kaposi sarcoma has become the most prevalent form of cancer in men and the second in incidence among women (Parkin et al., 2003). In a South African study, the relative risk of Kaposi's sarcoma in HIV-infected individuals, compared with HIV uninfected individuals was 62 (Newton et al. ,1991). The rare wearing of shoes is associated with an increase of endemic Kaposi sarcoma (Ziegler et al., 2003).

Immunosuppression-Associated,Transplantation-Associated, Kaposi's Sarcoma, or Iatrogenic Kaposi Sarcoma

Another group susceptible to develop KS are patients receiving immunosuppressive medication, particularly (but not exclusively) following organ transplantation. The incidence of KS in transplant recipients is 500 times greater than that in the general population. KS occurs in approximately 2.5% of all transplant recipients (Lebbé et al., 2008). The long-term use of immunosuppressive agents for prevention of allograft rejection increases the risk of malignancy approximately 100 times as high as that in the general population (Einollahi et al., 2001). KS risk peaked in the 0- to 2-year period after transplantation and decreased