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LEVEL: 400

COURSE CODE: ANA 404 (HISTOPATHOLOGY)

TOPIC:

1. Write on cancers epidemiology in Africa generally and Nigeria in particular.
2. Critically examine the involvement of angiogenic genes in the development and progression of osteosarcomas.

LECTURER: MR EDEM EDEM

QUESTION 1

Cancer is an increasing problem in Africa because of aging and growth of the population as well as increased prevalence of risk factors associated with economic transition (including smoking, alcohol, obesity, physical inactivity, and reproductive behaviors), and of certain infectious agents of importance in cancer etiology. According to United Nations population estimates (Forman D et al, 2013), the population of Africa between 2010 and 2030 is projected to increase by 60% overall (from 1.03 billion to 1.63 billion) and by 90% for those 60 and older (from 55 million to 103 million), the age at which cancer most frequently occurs (Forman D et al, 2013).

Despite this growing burden, cancer continues to receive a relatively low public health priority in Africa, largely because of limited resources and other pressing public health problems, including communicable diseases such as Acquired Immune Deficiency Syndrome (AIDS)/Human Immunodeficiency Virus (HIV) infection, malaria, and tuberculosis. Another factor may be a general lack of awareness among policy makers, the general public, and international private or public health agencies, concerning the magnitude of the current and future cancer burden on the continent and its economic impact (Forman D et al, 2013).

**The major cancers**

*Breast cancer.*

Breast cancer is the most commonly diagnosed cancer in Africa, and in Sub-Saharan Africa, and is also the leading cause of death from cancer (63,100 deaths in 2012) (Chu KC et al, 2012). breast cancer is the most commonly diagnosed cancer in women in all of North Africa, and has also become the leading cancer in women in many Sub-Saharan countries. However, the geographic pattern does not closely follow the conventional regions (Chu KC et al, 2012). Apart from the island populations of Mauritius and Reunion, the highest rates are seen in Egypt, Algeria, Nigeria, and Republic of South Africa. Although the reasons for the increasing importance of breast cancer must be speculative, they most likely include increases in the prevalence of risk factors such as early menarche, late child bearing, having fewer children, obesity, and increased awareness and detection, which are associated with urbanization and economic development(Chu KC et al, 2012).

*Cervical cancer.*

Cervical cancer is the second most frequently diagnosed cancer in Africa (99,000 cases) and Sub-Saharan Africa (93,200, 25.2% of cancers in women) in 2012, but is much rarer in North Africa (only 5800 cases, 5.1% of cancers in women). in East Africa, with cumulative risk in Malawi, Zimbabwe, and Mozambique in excess of 6%, whereas in some countries of North Africa (Egypt, Sudan and Tunisia) the cumulative risk is below 1%. These high rates reflect a high prevalence of the causative virus, HPV (Denny L et al, 2006) as well as a lack of screening services for the prevention and early detection of the disease (Denny L et al, 2006). It is noteworthy that before the introduction and wide dissemination of Pap testing in the 1960s in the United States, the incidence of cervical cancer (cumulative risk, 0–74) in ten selected metropolitan areas in 1947–48 [3.1% in whites and 6.7% in non-whites (Denny L et al, 2006)was of the same order of magnitude as the highest rates found in Eastern Africa today. There is little evidence for any decline in incidence in recent years; incidence rates in both Kampala and Harare show persistent increases in incidence. (Denny L et al, 2006)

*Prostate cancer.*

With almost 60,000 new cases estimated in 2012, cancer of the prostate is the most frequently diagnosed cancer in men, although in North Africa, it lies in fourth position (after lung, liver, and bladder). It is the third most common neoplasm overall (after breast and cervix), both in Africa as a whole and in Sub-Saharan Africa. In the latter region, the risk of developing prostate cancer before age 75 (3.4%, affecting almost 1 in 30 men) is in fact not dissimilar to the equivalent risks for breast (3.5%) and cervical cancer (3.8%) among women. .(de Sanjose S, et al, 2007)

*Liver cancer.*

Given the poor prognosis of liver cancer, the number of new cases (58,500) and deaths (56,000) estimated in 2012 are rather similar, and in terms of both indicators, liver cancer (predominantly hepatocellular carcinoma) ranks as the fourth most frequent cancer on the African continent and in Sub-Saharan Africa, accounting for about 7% of the total cancer burden.(de Sanjose S, et al, 2007). Rates are 2-fold greater in North Africa than in Sub-Saharan Africa largely because of the very high incidence rates in Egypt and indeed liver cancer rates tends to be low elsewhere in the region; compare, for example, the cumulative incidence in Morocco (0.2%), Algeria (0.2%), and neighboring Libya (0.7%) among men with those estimated for Egypt (4.6%). The incidence and mortality rates are also elevated elsewhere, particularly in Western Africa, where liver cancer is the most common malignancy of men in 12 countries with a cumulative risk ranging from 1% to 3% in 2012. .(de Sanjose S, et al, 2007)

*Lung cancer.*

About 30,300 new lung cancer cases and 27,000 deaths were estimated to have occurred in 2012 in Africa, with men accounting for over 70% of the total cases and deaths. .(de Sanjose S, et al, 2007) There is over a 30-fold difference in incidence and mortality rates between countries in both males and females, with the lowest rates found in the Western Africa and Middle Africa and the highest rates in Southern and Northern Africa. Notably, lung cancer is the most commonly diagnosed cancer among males in most countries in Northern Africa, including Tunisia, Libya, Morocco, and Algeria.(de Sanjose S, et al, 2007)

QUESTION 2

Osteosarcoma is the most common type of primary bone cancer, and this cancer is a malignant tumor arising from mesenchymal tissues. Osteosarcoma mostly occurs in the long bones of the body, such as distal and proximal tibia and proximal humerus.( Kramárová E et al, 1996) This cancer often affects children, adolescents and young adults between 10 and 25 years of age, and often occurs in males than in females.( Mirabello L et al, 2009) Osteosarcoma is a kind of disease which is caused by complex, multistep, and multifactorial process. The exact etiology of osteosarcoma is not well understood, and previous studies have shown that many environmental and genetic factors are involved. It is well known that certain bone diseases and inherited cancer syndromes play an important role in the development of osteosarcoma.( Klein MJ et al, 2006)

It is well known that vascular endothelial growth factors (VEGF), a potent angiogenic growth factor, plays an important role in altering proliferation to inflammatory and ischemic processes. (Shibuya M, Claesson-Welsh, 2006) The human VEGF is located at 6p21.1, and it is highly polymorphic in the promoter 5’untranslated region (5’-UTR) and 3’UTR. It is reported that single nucleotide polymorphisms (SNPs) in VEGF could regulate the expression of this gene through altering initiation of transcription and internal initiation of translation. (Shibuya M, Claesson-Welsh, 2006)

Expression of VEGF has been used as a more objective means of evaluating the prognostic importance of angiogenesis in osteosarcoma. VEGF is a key tumor-derived angiogenic factor that has multiple functions, including stimulation of angiogenesis, vasculogenesis, inflammation, and vascular permeability, which

constitutes the most important signaling pathways in tumor angiogenesis. There are a number of different VEGF molecules (VEGFA through VEGFE) that bind to VEGF receptors (VEGFR1-3). VEGFA binds to VEGFR2 and initiates a number of divergent signaling pathways

(Shibuya M, Claesson-Welsh, 2006). Among the proteins that are upregulated upon VEGF activation are the matrix metalloproteinase (MMP) and plasmin proteases ( Carmeliet P, 2005), which act on the vascular network by breaking down the extracellular matrix (ECM) and allow for tumor cell invasion, as well as the migration of the precursor cells that give rise to vascular structures: pericytes and endothelial cells. Additionally, VEGF signaling also induces the expression of the anti-apoptotic factors Bcl-2 and survivin, as well as the ERK/NF-kB and PI3K pathways (Steeg, 2006). These effectors promote tumor cell proliferation and survival. Angiogenesis‐related factors other than VEGF have also been evaluated as possible markers of prognosis in osteosarcoma.

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