

MODULE 5

MALIGNANCIES ASSOCIATED WITH IMMUNOSUPPRESSION

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Learning Objectives

When you have completed this module you should:

- Understand the magnitude of the problem of HIV related malignancies
 - Know the common types of cancers associated with HIV
 - Know some special considerations and implications in the management of the persons with HIV related malignancies
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General points on HIV related malignancies

- 40% of all pts with aids, during the course of illness develop malignancy.
- This can be primary cause of death although not always.
- Malignancies associated with HIV cause a lot of morbidity.
- Improved survival is seen with use of ART.
- There is also a reduced incidence of KS and NHL in communities where ART extensively used.
- The use of ART increases efficacy of other treatments also in KS and NHL.
- More side effects are seen from other conventional therapies compared to HIV negative individuals with the same disease on the same treatments.
- Co-morbidity from other HIV related disorders could be a relative contraindication to some treatments.
- Treatment to address the immunosuppression problem should always be given together with specific treatment for the malignancy.

5.1 KAPOSI'S SARCOMA

Epidemiology

Kaposi's sarcoma occurs more in males than females. This difference is less in HIV related KS (epidemic) than KS occurring in the absence of HIV infection (endemic). KS is the most common cancer in Zimbabwe.

The age distribution closely follows that of HIV infection. There are also no racial or ethnic differences as those seen in the endemic forms.

There is however a geographic variation in incidence which is determined by the geographic distribution of high-risk sexual behavior, endemic forms and use of ART.

Etiology

KS is caused by the KSHV (KS-associated herpes virus) or HHV8 (human herpes virus type 8) This virus is found in >90% of AIDS-KS tumors but is also found in the other forms of KS as well. The virus induces KS in susceptible individuals such as those infected with the HIV virus. Females may have a hormonal protection against the oncogenic effects of the virus but this is not proven.

Signs and symptoms

The lesions range from innocent looking on the skin to symptom producing life-threatening visceral lesions. The skin lesions range from flat to nodular, and pink to very dark. There is dermal and lymphatic infiltration, which causes gross swelling and non-pitting oedema particularly of the limbs.

Different sites of disease will present with different signs and symptoms. Common sites of involvement are the limbs especially the feet, mouth, other head and neck sites, gastrointestinal and pulmonary involvement.

Diagnosis

Usually this is relatively easy if based on clinical grounds as the lesions are quite typical in appearance. A histological biopsy is mandatory to confirm the diagnosis except in situations where this cannot be done for some reason or the treatment would be unreasonably delayed. Common biopsy sites are the easily accessible skin lesions, lymph nodes and in cases of visceral disease only through bronchoscopic or endoscopic biopsy.

A plain chest X ray is not very useful in the diagnosis of pulmonary KS. The finds cannot be easily distinguished from conditions such as **PTB or PCP pneumonia**.

Treatment

The first thing is to assess for a need to treat the actual lesions. If there is only one small lesion that has been completely excised, there might be no need treat immediately. The patient would however need close follow-up.

Treatment has to address the problem of immunosuppression and nearly all patients with KS qualify to receive ART. Regression of the KS can be seen with ART alone.

If there is no response or partial response to ART, then other treatments should be

considered.

KS is both radiosensitive and chemosensitive. Rapidly progressive disease responds well to these treatments.

Radiotherapy treats the lesions locally. Treatments can however be extensive such as treating the upper or lower hemibody. Radiotherapy is well tolerated.

Chemotherapy employs the use of systemic drugs given mainly intravenously, to kill the cancer cells. Various drugs are used for this and they include bleomycin, vincristine, adriamycin, etoposide, paclitaxel and liposomal anthracyclines.

Other treatments include intra-lesional injections of chemotherapy, topical gels, alpha interferon and anti herpetic therapy.

Non-Hodgkin's lymphoma (NHL)

In the presence of HIV infection the lymphomas mostly present at a higher stage. They also tend to be high grade, B-cell lymphomas mostly. Burkitt's lymphoma belongs to this group. CNS lymphomas are seen more frequently in this group.

Epidemiology

NHL occurs more in men than women. The age distribution follows that of the distribution of HIV infection. No geographic differences are seen in the occurrence of NHL.

Etiology

It is thought that these lymphomas arise as a result of continued B-cell proliferation stimulus from the viral infection. The EBV virus is also found in the cells of these tumours as well as the HHV8 virus in body cavity-based lymphoma.

Signs and symptoms

The presentation is usually that of swollen lymph glands mainly in the neck and groin. Extra-nodal disease has a variable presentation depending on the involved site. Head and neck sites may present with respiratory obstruction. Primary CNS lymphomas usually present with signs of raised intra-cranial pressure, Primary effusion lymphomas may present with signs of an effusion/ascites. B symptoms i.e. fever, night sweats, weight loss and pruritus are seen more with HIV related NHL.

Diagnosis

A histological diagnosis is mandatory. This is usually achieved from a lymph node or involved organ biopsy.

Following this, complete staging is necessary and involves among other tests, CT scanning of neck, chest abdomen and pelvis.

Treatment

The mainstay of treatment is chemotherapy combined with ART. The two can be used simultaneously.

Chemotherapy entails the use of various combinations of drugs. Doses may have to be reduced to decrease the toxicity of these treatments in the presence of HIV infection. There are number of combinations used e.g. CHOP, m-BACOD, EPOCH.

Side effects include nausea, vomiting and lowered white cell counts (neutropenia).

Neutropenia can be limited where growth factor support is used.

Radiotherapy can be given as cranial or cranio-spinal prophylaxis in some high grade NHLs.

It is also used to treat primary brain lymphomas. Radiotherapy is also very useful in palliating large fungating offensive and obstructive masses.

Cervical cancer

This is the most common cancer in women here in Zimbabwe. Cervical cancer is also very common in other countries in the developing world.

Cervical intraepithelial neoplasia (CIN) is the precursor lesion to invasive cancer. In both cases there is an association with HIV infection but more so with CIN.

Epidemiology

HIV positive women have 10 times the risk of abnormal PAP smear. More cervical dysplasia is seen as the CD4 counts decline. An association between this malignancy and HIV infection is seen more in younger women below the age of 50 years. The majority of women below 30years with cervical cancer are HIV positive.

Etiology

Prior infection with the HPV virus is necessary for the development of cervical cancer. The common subtypes of the HPV virus that are responsible are types 16, 18, 31, 33 and 35.

Compromised immune defenses in the presence of oncogenic viruses results in the malignant transformation.

All other factors previously known to predispose to cancer of the cervix, in common with HIV infection, have to do with sexual practices i.e. multiple sexual partners, previous STIs, early age at first intercourse etc.

Smoking is also an etiologic factor.

Signs and symptoms

CIN is not symptomatic and is an incidental finding at screening. Invasive lesions are symptomatic and can present with post coital bleeding, dyspareunia, irregular or postmenopausal bleeding, foul vaginal discharge, lower back and abdominal pain.

Screening and diagnosis

HIV positive women should be screened every 6-12 months. If CIN is detected, screening

should be done more frequently.

A positive screening test (pap or HPV screening) should always be followed by a colposcopy and biopsy. If invasive cancer is detected full staging must be performed.

Treatment

Treatment for CIN lesions includes superficial ablative therapies, loop electro-surgical excision procedure (LEEP), cone biopsy and hysterectomy. Early lesions are usually treated with ablative therapy such as cryosurgery and diathermy.

For invasive lesions, the treatment varies according to the stage and ranges from radical hysterectomy alone to various **combinations of this with chemotherapy and radiation.**

Radiotherapy can be used alone to palliate certain symptoms.

ART should be incorporated into the management.

Other tumors

Other tumors known to have an increased incidence in persons with HIV but not necessarily considered part of the AIDS epidemic are:

- Anal carcinoma
- Conjunctival squamous cell carcinoma
- Pediatric leiomyosarcoma
- Hodgkin's disease

Important Points to Remember

- HIV related malignancies are the most common in Zimbabwe
- They can occur in individuals without HIV infection.
- In the presence of HIV infection, these cancers are much more difficult to manage.
- Other viruses are implicated in the etiology of these cancers.
- The most important management strategy is to include ART.
- Other treatment options vary according to the type of tumor and the stage of the disease.
- Screening for cancer is possible in cervical cancer.
- Management of these cancers is generally best left to a tertiary institution

Activity 5.2

This is a group exercise

Discuss the statement: *Cervical cancer (carcinoma of the uterine cervix) is a sexually transmitted disease.*

There will be a discussion when this exercise has been completed

Important points to remember

- A number of cancers are associated with HIV infection and immune suppression
- Many of these cancers have a viral aetiology
- With the advent of the pandemic of HIV infection the commonest cancer in men and women in Zimbabwe is Kaposi's sarcoma
- A strong association has been found between Kaposi's sarcoma and the human herpes virus type 8 (HHV8)
- Cervical cancer is commonly found in women in Zimbabwe and the incidence has increased with the spread of the HIV epidemic
- A strong association exists between cervical cancer and the human papilloma virus (HPV)
- Lymphomas including primary intracranial lymphoma, non-Hodgkins lymphoma and Burkitt-type lymphoma occur more commonly in HIV infected individuals
- Other cancers that occur more frequently in persons with HIV infection include squamous cell cancer of the genital tract and conjunctiva