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Aids-related kaposi's sarcoma in a four year old child: the challenge of a missed opportunity

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Abstract: *Background:* AIDS-related Kaposi's sarcoma (KS) is an AIDS-defining illness and is now increasingly recognized in children infected with HIV. Many of these cases are missed due to low index of suspicion. Vertical transmission of HIV is the commonest route of transmission in children and this is preventable by early maternal antenatal diagnosis, early commencement of HAART by the mother and adoption of the safest possible mode of delivery. The index case did not benefit from these services, making her acquire HIV and then develop AIDS-defining illness (KS) at a tender age of 4 years.

Aim and objective: The study is aimed at emphasizing the need for all pregnant women to have antenatal screening as soon as pregnancy is confirmed so as to prevent vertical transmission of HIV to the unborn child. It is also aimed at creating awareness in clinical practice so as to increase index of suspicion among clinicians when evaluating chronically ill children.

Case Description: GG was a 4year old girl who presented at 108 Nigerian Air force Hospital, Abuja with non-itchy skin rashes of two weeks duration, generalized body swelling, cough and haematochezia of one week duration, and fever of four days duration. She was a paternal orphan having lost her father a year prior to presentation to Acquired immunodeficiency syndrome (AIDS)-related illness. Her

mother also tested positive to Human Immunodeficiency virus (HIV) and has been on highly active anti-retroviral therapy (HAART) for a year. Physical examination revealed moderate pallor, bilateral pitting pedal oedema, and matted non-tender peripheral lymphadenopathy. There were papular and nodular skin lesions with a reddish solid lesion on the hard palate. She tested positive to HIV. Abdominal ultrasound scan revealed moderate hepatomegaly with ascites, while chest x-ray showed bilateral interstitial pneumonitis, right hilar lymphadenopathy, right pulmonary nodule and ipsilateral pleural effusion. Excisional biopsy of one of the skin nodules confirmed the diagnosis of Kaposi's sarcoma. She was commenced on HAART and antibiotics, with a unit of blood transfused. Her condition deteriorated, which necessitated referral to university of Abuja Teaching Hospital where she eventually died after a day of admission.

Conclusion: Paediatric AIDS-related KS is becoming increasingly common in Nigeria and as such, high index of suspicion is required while evaluating pediatric patients. This, coupled with early commencement of HAART is required to avert the pitfalls observed in this case; bearing in mind that childhood AIDS-related KS is lethal.

Keywords: Generalized lymphadenopathy; Kaposi's sarcoma; Missed opportunity; Paediatric AIDS; Skin rashes

Introduction

A Vienna-based Hungarian dermatologist, Moritz

Kaposi, first described Kaposi's sarcoma (KS) in 1872 as a rare multifocal angioproliferative tumour involving blood and lymphatic vessels.¹ In 1981, first case of

AIDS-associated Kaposi's sarcoma was reported by Friedman-Kien et al² This aggressive form of Kaposi's sarcoma is the most frequent cancers in patients with HIV infection.³ HIV-related KS was 20,000 times more prevalent when compared with uninfected population before the advent of highly active anti-retroviral therapy (HAART).⁴

It is a well known fact that Human immunodeficiency virus (HIV) infection predisposes to several opportunistic infections and neoplasms, such as KS and non-Hodgkins Lymphoma (NHL).⁵ While KS is the most common neoplasm seen in HIV-infected adults, it is rare in childhood AIDS in western countries.⁶ It is an AIDS-defining disease in 0.5% of children in Europe, compared with 0.9% in the United States.⁷ This observation is however different in Africa as KS is increasingly being recognized among infected children in many African countries.⁸

Different types of KS have been documented. These are epidemic (AIDS-related) KS, classic (Mediterranean) KS, endemic (African) KS and iatrogenic (transplanted-related) KS. The AIDS-related KS is the commonest. It is note-worthy that all varieties of KS are associated with Herpes virus, and irrespective of the types, KS presents similarly but have differences in clinical aggressions, prognosis and treatment.⁹ AIDS-associated KS typically presents with cutaneous lesions that begins as one or several red to purple-red macules, rapidly progressing to papules, and plaques, with a predilection for head, back, neck, limbs, trunk and mucous membranes. Lesions could also be found in the stomach and intestines, lymphnodes and the lungs.⁹ Mouth is involved in about 30% of cases and is the initial site in 15% of AIDS-related KS.¹⁰ In the mouth, the hard palate is most frequently affected, then the gums.¹⁰

KS is not curable, but often treatable. In KS-associated with immune deficiency, treating the cause of the immune system dysfunction can impair or abolish the progression of KS. Radiation therapy or cryosurgery, and chemotherapy combined with HAARTS are found useful in its treatment.^{11,12} Despite strict adherence to the outlined treatment protocol, the fatality associated with AIDS-related KS in children is high. Progression of disease is rapid, with high mortality in the initial hospitalization.¹³

This case is presented to create awareness among clinicians and other health workers, on AIDS-related Kaposi's sarcoma in paediatric age group so as to avert the observed missed opportunity in the nearest future. It emphasizes the need for early antenatal diagnosis and commencement of active management of an infected mother so as to prevent mother to child transmission of HIV.

Case presentation

GG was a four year old girl who presented to our health facility (108 Nigerian Air force Hospital, Abuja) with generalized body swelling of one week duration with associated body rashes noted at about two weeks prior to

onset of the body swellings. The body swellings were first noted in the lower limbs and thereafter on the face. There was no diminution in urine volume and the body swelling did not regress with ambulation. The body rashes were discoid, hyperpigmented skin lesions found all over the body but more on the extremities. There was no associated itching and no antecedent history of drug use, insect bite or allergy prior to onset of the rashes. There was however an associated one week history of cough and passage of bloody stools. There was no history of bleeding from any other site and no history of abdominal pains or swellings. At the time of presentation, there was a four day history of fever for which patient was commenced on paracetamol.

No medical or unorthodox intervention had been sought at the time of presentation. The mother had routine antenatal care at a local primary health facility and had spontaneous vaginal delivery. There had been no history of hospital admissions, blood transfusions or scarifications in the past. Haemoglobin genotype was unknown but there was no history suggestive of sickle cell disease. Her immunization status was up to date according to the National Programme on Immunization (NPI) Schedule. She was exclusively breastfed up to six months with complementary feeds introduced thereafter and breastfed for up to a year. Her milestones were within normal limits when compared with her sibling and peers. She was the second of her parents' two children in a monogamous family setting of low social class, and a paternal orphan having lost her father a year prior to presentation to AIDS related illness. The mother was screened for HIV at the same time and found to be reactive and subsequently commenced on HAARTS.

On examination, she was a pre-school age child not in any painful distress, afebrile, acyanosed, anicteric, but moderately pale and she had bilateral pitting pedal oedema up to the middle of the thigh. There was significant matted non-tender peripherallymphadenopathy (supraclavicular, axillary and inguinal groups). There were also multiple, brownish-black lesions noted at the extremities and all over the body with those on the limbs being nodular (figure 1). She was 16kg which was 89% of expected. Mid-upper Arm Circumference was 13.5cm and Occipito-frontal Circumference was 48cm. She was not dyspnoeic and had good air entry bilaterally. Also, she had normal volume regular pulse with a blood pressure of 90/50mmHg and an apex beat located at the 5th left intercostal space mid clavicular line. Examination of the digestive system however revealed a reddish lesion involving the hard palate. The abdomen was protuberant with a reducible umbilical hernia, the liver was 6cm enlarged below the right costal margin, smooth surfaced and non tender. There was no other palpable intra-abdominal organ and no demonstrable ascites clinically. The child's retroviral screening using rapid antibody testing was positive. Full blood Count showed a Packed Cell Volume of 20%, with normal white cell and platelet counts but with the white cells having a relative neutrophilia for age. The liver function test showed severe hypoproteinemia and hypoalbuminemia. Urinalysis,

urine microscopy and renal function tests were within normal limits. Patient had an excision biopsy of a skin nodule with histology result showing a tumour containing proliferating spindle cells arranged in bundles, separated by sinusoidal spaces. Focal areas of old haemorrhage with haemosiderin pigments were also present. Chest X-Ray done at presentation showed non-homogeneous opacities with background nodularity and streakiness at the upper and mid zones bilaterally, more marked on the left. The right hilum was full and lobulated with convex outer margin, connoting hilar lymphadenopathy (figure 2). The recesses, heart and bony thorax were initially unremarkable. At the interval of two weeks however, she had a repeat chest x-ray done in view of repeated non-abating cough and severe respiratory distress. Findings at this time showed right pleural effusion and a rounded nodular opacity of soft tissue density at the right mid zone, in addition to the earlier findings (figure 3). Simultaneously, an abdominal ultrasound scan was done as a result of gradual abdominal distension despite good bowel habit. This revealed moderate hepatomegaly with a scites (figure 4). The remaining abdominal viscera were preserved, and no abdominal lymphadenopathy was observed sonographically.

In view of the aforementioned clinical, radiological and laboratory findings, a diagnosis of AIDS-related Kaposi Sarcoma was made which was confirmed histologically. She was commenced on Highly Active Anti Retroviral Therapy (HAART), antibiotics and transfused once on account of severe anaemia. She was then referred to University of Abuja Teaching hospital when her condition deteriorated, and she subsequently died after a day of admission.

Fig 1: Clinical photograph of the child showing generalized oedema with hyperpigmented nodular skin lesions on the limbs, chest, abdomen and ear lobes.



Fig 2: Chest X-Ray showing non-homogenous opacities with background nodularity and streakiness in the upper and middle zones of both lungs, more marked on the left. The right hilum is full and lobulated with convex outer margin, connoting lymphadenopathy.



Fig 3: Chest X-Ray of the same patient at two weeks interval showing right pleural effusion with a rounded nodular opacity of soft tissue density in the right middle zone, in addition to fig.2 findings.



Fig 4: Abdominal ultrasonogram at the level of the psoas muscles showing 'echo-free' extra-luminal fluid collection (ascites) at the right iliac fossa.



Discussion

Human immunodeficiency virus (HIV) infection results ultimately into Acquired Immunodeficiency syndrome (AIDS) if not managed early and appropriately. The main modes of transmission is via sexual intercourse, vertical transmission from mother to child, blood and blood products transfusion, and sharing of needles or sharp objects, particularly among intravenous drug abusers (IDA).¹⁴ Vertical transmission was the most likely mode of transmission in the index case.

Patients could be asymptomatic at the beginning (group A), but later develop symptoms but do not have AIDS-defining condition. This group is termed group B (AIDS-related complex-ARC) based on Centre for Disease control (CDC) classification. Group C in this category includes patients who have AIDS-defining illness, which is the group the index patient belonged to. At this point, opportunistic infections and secondary neoplasm such as KS, NHL and other neoplasm set in.^{14,15}

KS is the most common non-infectious AIDS-defining diagnosis in HIV disease.¹⁵ It is relatively rare among children compared to adults. In the developing countries however, frequent lesions of KS have been reported among children in central and southern Africa, and this had been attributed to the endemic presence of Human Herpes virus type 8 (HHV8).¹⁶ There is evidence from epidemiologic, serologic, and molecular studies that KS is associated with this virus. The disease starts as a reactive polyclonal angioproliferative response to the virus, in which polyclonal cells change to oligoclonal cell populations that expand and undergo malignant transformation.¹⁷ There are very few reported cases of HIV-related KS among children in Nigeria¹⁸, and the index case happened to be the first in our institution which has a dedicated HIV treatment centre.

This histological proven case of KS in a 4 year old child in Abuja, Nigeria further adds to the existing literature showing the increasing trend of AIDS-associated KS in developing countries. This is still relatively rare hence; high index of suspicion is required when evaluating a chronically sick child, so as to avert further diagnostic pitfalls observed in the index case.

The mother had antenatal care at a primary health centre in Abuja, but she was not screened of HIV as the facility for the test was not available at the health centre. She was therefore not diagnosed antenatally and not commenced on HAARTS until when the husband was diagnosed a year prior to the presentation of the child to our hospital. This further confirms the poor accessibility of

Nigerians to quality health care delivery. This needs to be worked upon so as to avert this scenario in the near future.

Between 1981 and 1990 in Zaria, Nigeria, four children with KS were histologically diagnosed, and none of them was HIV positive.¹⁸ In another report from the same institution between 1991 and 1995,⁸ two of the four cases of childhood KS were HIV positive, and two were also noted in Maiduguri within the same period.^[19] One would expect this to decrease significantly with the advent of widely available HAART in Nigeria, particularly in Abuja, the Federal Capital Territory. Diagnostic flaws were however noted in the index case. Her parents were not diagnosed in good time so, the child did not benefit from the widely available prevention of mother to child transmission (PMTCT) of HIV. Her father died a year prior to her presentation as a result of AIDS-defining illness. It was at that point that the mother was screened and diagnosed of HIV infection. The index case was three years old then, and the attending physician did not deem it necessary to screen her, more so that she was the last child. If peradventure she was diagnosed earlier, she wouldn't have developed AIDS-defining KS as she would have commenced HAART. It was only at the time of recent and only presentation at our health facility that her status was known. We considered this a missed opportunity.

KS lesions are nodules that may be red, brown, purple or even black depending on the patient's skin colour. The lesions are usually non-itchy and papular, and the commonly affected areas are the lower limbs, face, mouth, and genitalia. The index case had her lesions at the aforementioned sites, which arouse the suspicion of the attending paediatrician, making him to screen her the first day she presented to him. She also had a reddish nodular mass on the hard palate, which is the commonest site of oral KS lesions.^{11,19,20} In addition, the index patient presented with heamatochezia, hepatomegaly and ascites. The heamatochezia could be due to deposition of KS lesions on the stomach and/or intestines. This gastrointestinal tract lesion and hepatic enlargement are indicative of visceral involvement which connotes severity of the disease with attendant high fatality rate.²⁰ Also, interstitial pneumonitis and pulmonary AIDS-associated KS were parts of this patient's presentation, and both connote severe disease.²⁰ This could explain why the patient could not survive despite prompt intervention at our level.

As earlier noted, KS is not curable but treatable. AIDS-associated KS usually shrinks upon commencement of HAART. Patients with a few local lesions may be treated with radiotherapy and cryosurgery, but chemotherapy with HAART is more effective in those with widespread disease. Also, affection of internal organs as in the index case could be treated with Interferon Alpha, Liposomal anthracyclines or paclitaxel.^{10,11,12} These drugs are not readily available in Nigeria and when available, they are not affordable. It is therefore recommended that PEPFAR and other donor agencies include them as part of the drugs for paediatric AIDS patients, especially those that have already developed AIDS-related Kaposi's sarcoma. Our patient could not survive after commencing HAART due to overwhelming pulmonary and other systemic afflictions. She therefore did not benefit from other outlined regimen. Early presentation could have averted this. This was first hampered by inability to diagnose the mother antenatally due to poor facilities at the primary health centre she attended. Antenatal HIV screening should be enforced and facilities for such made available at all levels of antenatal care, primary, secondary or tertiary health centre. Local, State and Federal Governments should increase allocation for Primary Health Care services as it is the most accessible health facility for over 70% of Nigerians. The staffers of such institutions should be better trained and retrained on all aspects of care of HIV patients. A vibrant system for home visits and home-based care is also advocated as that will go a long way to avert the observed missed opportunity.

Conclusion

Paediatric AIDS-related KS is becoming increasingly common in Nigeria and as such, physicians are admonished to have high index of suspicion while evaluating pediatric patients. This coupled with early commencement of HAART is required to avert the pitfalls observed in this case; bearing in mind that childhood AIDS-related KS is lethal.

Conflict of Interest: None

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