Changing Trends in HIV AIDS Kaposi’s Sarcoma

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Introduction

- Commonest cancer in men and second commonest in women
- The incidence of KS in Africa has increased with the exponential spread of HIV and poor HAART coverage
- In KZN, incidence increased 30 fold
  - 19.7/100 00 in men
  - 11.5/100 00 in women

Wabinga et al Br J Cancer 2000
Mosam et al IJSA 2009
<table>
<thead>
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<th>Site</th>
<th>ALL n</th>
<th>% Total</th>
<th>Rank</th>
<th>Age 18-49 n</th>
<th>% Total</th>
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<td>11</td>
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<td>14</td>
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<td>Stomach</td>
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<td>1.4</td>
<td>15</td>
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<td>14</td>
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<td>Melanoma**</td>
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<td>33</td>
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<td>15</td>
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<td>Other</td>
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<td>8.9</td>
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<td>287</td>
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<td>TOTAL</td>
<td>8955</td>
<td>100</td>
<td>NA</td>
<td>3045</td>
<td>100</td>
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Distribution of Cancers
KZN
Jan 2001 to June 2004
All vs 18-49 yrs

Unpublished data
Global HHV 8 Seroprevalence

Chatlynne LG, Semin Cancer Biol 1999 (3) : 175 - 178
HHV8 in Africa

- Different assays used by different studies
- No clear evidence of geographic difference
- Common in Uganda & Cameroon pre HIV era
- Botswana and Gambia KS was rare before onset of HIV

*Dedicoat M. Br J Cancer. 2003;88,1-3.*
Age-dependent increase in hhv8 prevalence in children under age 10
Increases from early childhood reaching near adult prevalence before puberty
The inferred mode of transmission is ongoing horizontal transmission in childhood

Mayama 1998
HHV8 Seroprevalence in Children
SA and Uganda

South Africa p=0.96
Uganda p<0.001

Dollard Int J Cancer 2010 Nov 15;127(10):2395-401
HHV8 Seroprevalence
Children vs Adult caregivers

Trend test, p<0.001

Dollard Int J Cancer 2010 Nov 15;127(10):2395-401
Age Standardised Incidence of KS

ASIR / 100 000
1983 - 0.52
2003 - 14.76

HIV seroprevalence
1989 - 1.6%
2006 - 39%

Mosam et al. IJSA 2009 Aug;20(8):553-6
KS Age Specific Incidence
Pre-AIDS vs AIDS Epidemic

Figure 2. Age Specific Incidence per 100 000

Peak Incidence

Pre-HIV era
(1983-1989)
55-60 yrs

HIV eras
fourth and fifth decades of life

Mosam et al. IJSA 2009 Aug;20(8):553-6
Cutaneous Features

- Asymptomatic pink to purple or brown
- Patches, papules, plaques, nodules or tumours
- Round, oval, elongated, fusiform
- Undiagnosed or overlooked
Early lesions
Sites
Advanced Lesions
Mucosal Involvement

- Oral cavity in 20% at diagnosis
- Tongue, hard & soft palate
- Associated with GIT KS
Lymphatic Involvement

- Lymphadenopathy
- Lymphoedema
- Woody hard induration
- Non-pitting oedema
Visceral Involvement: GIT

- >50% clinically
- 80% at autopsy
- May be asymptomatic
- Symptoms: Abd pain, bloody stools, LOW
Pulmonary

- 30% clinically
- 50% at autopsy
- Symptoms: dyspnoea, cough, effusions
- Survival poor
KS mimickers

Patch stage

- Bruises
- Purpura
- Haemangioma
- Naevi
Papules/ Plaques

- Discoid Lupus
- Lichen planus
- Keloids
- Chromomycosis
Nodules

- Pyogenic granuloma
- Bacillary angiomatosis
- Deep fungal
- Erythema nodosum
Diagnosis

Biopsy: Skin, endoscopic or transbronchial

- Proliferation of abnormal vascular spaces, lymphoplasmacytic infiltrates
- Endothelial cells contain HHV 8
- Spindle cells predominate
Investigations

- CD4 and HIV-1 viral load
- CXR
- Stool occult blood
- Sputa MCS and AFB
- If GIT symptoms, endoscopy
- If abnormal CXR or symptoms, bronchoscopy
## Staging Classification- “TIS”

<table>
<thead>
<tr>
<th></th>
<th>Good Risk (All)</th>
<th>Poor Risk (Any)</th>
</tr>
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<tbody>
<tr>
<td><strong>T</strong></td>
<td><strong>(Tumor)</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>T0: 27 mo survival Skin, minimal oral mucosa, lymph node only</td>
<td>T1: 15 month survival Edema or ulceration Extensive oral mucosa Visceral KS</td>
</tr>
<tr>
<td><strong>I</strong></td>
<td><strong>(Immune System)</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>I0: 40 month survival CD4&gt;150</td>
<td>I1: 13 month survival CD4&lt;150</td>
</tr>
<tr>
<td><strong>S</strong></td>
<td><strong>(Systemic Illness)</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>S0: 22 month survival No OI’s or thrush No B symptoms Karnofosky &gt;70%</td>
<td>S1: 16 month survival Hx of OI’s or thrush B symptoms present Karnofosky&lt;70%</td>
</tr>
</tbody>
</table>

*Krown, SE, Metroka C, Wernz, JC J Clin Oncol 1989; 7:120*
Efficacy of HAART

• All patients with HIV-KS should receive HAART

• HAART has been associated with:
  – Decrease in new KS lesions
  – Regression in size of existing KS lesions
  – Improved survival

• Mechanism:
  – Likely immune reconstitution
  – Antiangiogenic properties of PIs

• May be associated with immune reconstitution inflammatory syndrome
HAART in AIDS-KS

• Response rates:
  – Up to 79% reported response rate for HAART alone
  – Can take up to a year
  – SA cohort, 39% response T1 disease

• Response most likely if:
  – T0 tumor
  – ART naïve
  – CD4 increase >150 cells/mm$^3$

Mosam JAIDS June 2012
Treatment

• Major goals
  – Symptom palliation
  – Prevention of disease progression
  – Tumor shrinkage
Indications for Systemic therapy

• Widespread skin involvement (>25 lesions)

• Extensive cutaneous KS unresponsive to local treatment

• Extensive oedema

• Symptomatic visceral involvement

• IRIS
KS IRIS

- Worsening of existing KS or development of new lesions on HAART in 12 weeks
- Associated with rapid decline in HIV VL and increase in CD4
- Pulmonary involvement fatal
- CXT
- British cohort of 150 KS  6.6% developed IRIS KS
- Higher CD4, KS oedema, PI + NNRTI regimen
- SA cohort 112  21%

*Bower J Clin Oncol 2005 Aug 1;23(22):5224-8
Mosam JAIDS 2012 Jun 1;60(2):150-7.*
Multinational Cohort  HIV KS

- 3 SSA sites 1 UK
- Prevalence KS IRIS 13 %
- 2.5 X >er risk in African cohorts
- Baseline KS IRIS predictors:
  - Advanced T1 disease
  - ART alone as KS therapy
  - HIV-1 RNA VL > 5 log_{10} copies/ml

Letang CROI 2011
Corticosteroids and KS

- Corticosteroids have been associated with the induction or exacerbation of KS in HIV patients
- Generally, should be avoided
- Use only in:
  - acute respiratory distress syndrome accompanying HIV-related opportunistic pulmonary infection
  - tuberculosis meningitis or pericarditis
  - immune thrombocytopenic purpura, if necessary
KS in Africa

- suboptimal HAART availability
- co-infections
- late presentation
- poor follow-up
- increased disease burden
- shortcomings of appropriate oncological services

Stein et al Acta Oncologica 1996
Cancer In Africa

• HAART provision cost effective intervention in decreasing the burden of HIV cancers
• especially KS
• potential for dramatic improvements in overall survival and quality of life for patients with HIV KS
• cancer control programmes in Africa are sparse
• provision of RXT, CXT & palliative care is inadequate

Sitas et al Lancet Oncol 2008
Hypothesis

Rollout of HAART led to changes in the management of HIV KS in KZN
Objectives

To assess temporal trends over 12 years 1995-2006 at Addington Hospital

- Demography
- HIV serostatus
- Provision of HAART
- Provision of KS specific Rx: CXT/ RXT
- Outcomes of patients with HIV KS in KZN
Method

- Anonymised record review
  - 95 - 97 no HAART
  - 98 - 00 no HAART

Growing AIDS epidemic
- 01 - 03 limited HAART
- 04 - 06 early HAART availability

Mature AIDS epidemic
- Demographics
- HIV status
- CD4 count
- HAART regimen
- Site of KS
- Extent of disease
- Therapy prescribed
- Outcome of KS
Results

n=701

3 children (3, 14 & 17 yrs)
3 non Black Africans
F: M ratio = 1:1.1
## Characteristics

<table>
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<tr>
<th></th>
<th>95-97</th>
<th>98-00</th>
<th>01-03</th>
<th>04-06</th>
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<tr>
<td><strong>Number of Patients</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>76</td>
<td>81</td>
<td>165</td>
<td>379</td>
</tr>
<tr>
<td>Men</td>
<td>35</td>
<td>54</td>
<td>99</td>
<td>148</td>
</tr>
<tr>
<td>Women</td>
<td>40</td>
<td>27</td>
<td>66</td>
<td>231</td>
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<tr>
<td><strong>Mean Age (Range)</strong></td>
<td>36 (19-78)</td>
<td>38 (21-79)</td>
<td>36 (17-76)</td>
<td>35 (3-76)</td>
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<tr>
<td><strong>Disseminated Disease</strong></td>
<td>47%</td>
<td>28%</td>
<td>37%</td>
<td>50%</td>
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<tr>
<td><strong>Documented HIV +</strong></td>
<td>65%</td>
<td>62%</td>
<td>86%</td>
<td>92%</td>
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<tr>
<td><strong>CD4 Counts Available</strong></td>
<td>0%</td>
<td>0%</td>
<td>28%</td>
<td>80%</td>
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<tr>
<td><strong>Proportion CD4&lt;200</strong></td>
<td>NA</td>
<td>NA</td>
<td>57%</td>
<td>54%</td>
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<td><strong>HAART</strong></td>
<td>0%</td>
<td>0%</td>
<td>9.3%</td>
<td>44%</td>
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Documented HIV Status of Patients with KS

1995-1997
- HIV + 65%
- UK 20%

1998-2000
- HIV + 62%
- UK 19%

2001-2003
- HIV + 86%
- UK 13%

2004-2006
- HIV + 92%
- UK 5.3%

Legend:
- unknown
- seropositive
- seronegative
KS Specific Therapy Provided

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<tr>
<th>Year</th>
<th>CXT</th>
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<td>1995-1997</td>
<td>23%</td>
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<td>2001-2003</td>
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<td>1998-2000</td>
<td>5%</td>
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<td>2004-2006</td>
<td>38%</td>
<td>56%</td>
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<tr>
<td>Category</td>
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<td>Palliative Care – Observation (%)</td>
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<td>ARVs (95-06)</td>
<td>182</td>
<td>25.6</td>
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Outcomes by HAART use

- HAART was associated with significantly higher CXT administration
  - 56% vs 17%  \( p < 0.001 \)

- HAART associated with fewer patients receiving palliative care
  - 36% vs 75%  \( p < 0.001 \)

Mosam Int J STD 2011; 22: 671-673
Outcomes by HAART use

- 38% of patients not on HAART missed planned therapies
- vs 13% of those receiving HAART
- HAART was associated with significantly fewer lost to follow up (p< 0.001)
Outcomes by HAART Use

No HAART
- 14% improved
- 79% lost

HAART
- 48% improved
- 38% lost

Legend:
- Blue: lost to follow-up
- Red: clinically improved
- Dark Green: clinically stable
- Orange: clinically worse
- Gray: dead
HAART in Hand in 2011

- Changes in KS presentation in KZN
- Addington Hospital in 2011
- 198 charts reviewed
- 194 HIV KS, 4 HIV –ve
- 100 % documented HIV (92% in 2006)
- 88.6% on HAART at first presentation to oncology (44% in 2006)

Naidoo L MMed UKZN
HAART in Hand

- 58% presented within 3 months of histological diagnosis
- Mean CD4 266 cells/mm$^3$ (218 in 2006)
- 94% Poor Risk Disease
- Rural patients 3X more likely than urban patients to be on HAART
- Age > 30 yrs 3 X more likely than those < 30 of being on HAART

Naidoo L Mmed UKZN
Conclusion

• HIV KS important HIV surveillance tool in KZN
• HAART is associated with improved diagnostic evaluation, better follow-up, and increased chemotherapy use
• continued access to HAART and
• better access to CXT
• critical for the optimal management of HIV KS

Mosam Int J STD 2011; 22: 671-673