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optimising care 2021

Optimising the care of people living with HIV: An update on management of comorbidities to improve patient health

HIV and Cancer: A review in 2021

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Australian cancer database – need links to AHOD

HIV status – positive negative unknown - not collected

Why?

Need to link ACD and AHOD to get some information

Overseas data in particular US and UK data provide information from a bigger database

History – a brief review

- Kaposi's Sarcoma (KS) noted to be excessively common in MSM 12/1981 – anecdote created a question which became a reality
- Previously KS was an "endemic" disease in certain Mediterranean and Ashkenazi Populations
- Hence the new "epidemic" form of the disease
- Excess of high-grade Non-Hodgkin's Lymphoma (NHL) in MSM

AIDS defining cancers (ADC)
Non-AIDS defining cancer (NADC)

ADC – KS, high grade NHL, cervical carcinoma

- Non- ADC – include anal cancer (AC) , Hodgkin's Lymphoma (HL), hepatocellular carcinoma (HCC) , lung cancer
- Many have an "infection mediated" causation or association

Infection Mediated Cancers - definition

- Known infectious **cause** eg KS and HHV8, HPV and cervical carcinoma and anal carcinoma
- Probably **associated** eg NHL and EBV

cART or HAART era – 1996 until now

- KS and NHL dramatically down
- HL probably stable
- Anal cancer and lung cancer slowly rising. They are continuing to rise. Probably due to aging and other risks as well as HIV infection

What we understand from epidemiology

- NADC – no **general** established link with cART as a cause
- Infection related NADC – established link with immune-deficiency. Eg; Anal cancer, Hepatocellular cancer
- Increasing CD4 count established link with reduced incidence of ADC (Thanykou Andrew Grulich and AHOD– old data 2013)

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Infection Related (IR)

- EBV – HL, NHL
- HPV – cervix, anus, oral cavity, vagina, penis (SCC esopghagus)
- HHV8 – KS
- Hep B and C – HCC
- Helicobacter – stomach
- Schistosoma – bladder (leukaemia)

Non-infection Related (NIR)

- Lung cancer – independently linked to HIV, lower CD4 and MSM (who smoke twice as much 42% vs 23%)

- American SEER data – risk for colorectal same and breast, prostate may be reduced

General Overview HIV Cancer 1 of 3

- Australia is small
- Reviewing other data bases important – unfortunately only developed countries do data well
- Eg Swiss Cohort, Asian HIV ODB, Chelsea and Westminster ODB
- cART protects against ADC but less so NADC
- cART probably allows aging and so NADC time to develop
- ADC and NADC are both strongly associated with immune deficiency

General Overview HIV Cancer 2 of 3

- Pattern of malignancy has changed with time
- Since cART 1996 lower rates ADC
- ADC: US 2006-2010 – Shiels and Engels 2017
- KS (800x) – MSM only due to sexual co-infection with HHV8
- NHL(10x)
- CC (4x)

General Overview HIV Cancer 3 of 3

- NADC 2006-2010
- Anal cancer (32x)
- Liver cancer (2x)
- Lung cancer (2x) – high incidence smoking confounds
- HD (10x)

Cancer Burden in PLWHIV

- cART era – US 242,000 in 1996 to 516,000 in 2013 and so on
- Cancer risk increases with age
- Mainly NADC
- Increasing cancer burden overall
- Issues: smoking, HPV vaccination, HCV and HBV Rx
- PAP screen: start earlier

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HIV Cancer: to follow – not exhaustive

- ADC – KS, NHL, CC
- NADC – anal, HCC, lung
- NADC and immunosuppression

KS 1

- Presentation – skin and systemic
- Severe widespread disease is less prevalent since cART in1996
- Prolonged untreated (sustained immune depletion) HIV can present with KS anywhere – systemic disease is usually associated with bad skin disease
- Severe disease is now rare
- Less extensive disease is now common in my practice

KS 2

HHV8 mediated
Vertically transmitted in some populations
Sexually co-transmitted with HIV in MSM
Can test serum HHV8 - PCR, antibodies and viral load
HHV8 is always present on IHC histopathologically
Please always to a biopsy – a simple skin punch is adequate
Differential list is long and includes melanoma

KS 3

- General treatment
- Immune restoration – help! **cART – GP or ID**
- Stop immunosuppressive drugs if possible
- Encourage a watch and wait approach if disease is mild
- Warn patient and watch for IRD – IRD may cause a paradoxical flare and necessitate systemic treatment

KS 4

- Chemotherapy and other systemic options
- 1) Liposomal Doxorubicin 20mg/m2 q2w – SE
- 2) Paclitaxel – low dose q1-2w – SE
- 3) Anti-angiogenic agents: pomalidomide – promising and non-toxic
- 4) TKI: imatinib

NHL

- Usually high grade (low grade not ADC)
- If immune replete use same treatment, stage for stage, as non-HIV
- Several subtypes typical of HIV – eg: Plasmablastic and Burkitt's
- Adequate biopsy mandatory
- Adequate staging mandatory
- Generally chemotherapy, immune-therapy occasionally radiotherapy and intrathecal chemotherapy
- BMT possible – several HIV "cures" as proof of principle after BMT: HIV drugs withdrawn and ongoing negative VL

NHL rare

- Primary effusion NHL
- “Castlemans disease” – not a malignancy officially
- HIV reactive lymphadenopathy – Rx HIV and observe if possible – becoming rare

CNS NHL

- Was a common cause of of AIDS related death pre cART
- Generally presented when CD4 had been very low for a long period
- Presented very ill (low ECOG or poor performance status) with focal neurology and headache
- Single mass on CT and MRI
- LP +/- biopsy needed for diagnosis
- Treatment: radiotherapy and chemotherapy. Reports of high dose methotrexate working.
- Poor outcomes in the early days (MS 2-3 months) and improved later (MS months- years)

Cervical Carcinoma – prevent, screen, diagnose, treat

- HPV vaccinate the population to prevent this disease
- PAP screening as appropriate for HIV – PAP recommendations need review
- Significant burden among women with HIV
- Incidence is higher: late cART, older age and South Africa (SA), South America (Sam) vs Europe.
- Incidence after 5 years cART: 2-3x in SA and 11x in S Am vs Europe and NAm
- Starting cART does not seem to reduce incidence at 5 years in non-European populations
- Rohner: Int J Cancer 2019 – data 1996-2014 included over 64,000 women
- Please keep a close eye on these women

Cervical Carcinoma

- In HIV: CC tends to present late with high morbidity and mortality
- Treatment is the same as non-HIV stage for stage: surgery +/- radiotherapy +/- chemotherapy
- Modern radiotherapy please – may need to include stereo-tactic techniques
- I won't review staging and treatments further here
- Experienced MDT is proven to maximise benefit and minimize mortality – usually a major cancer centre (SA?? S Am?? – poor access to MDT)
- Make referrals carefully

Anal Carcinoma - review

- Advanced HIV is associated with higher risk of developing HPV related cancers
- Advanced HIV and MSM highest risk: 32x general population (ASCO 2018)
- Incidence increased 1996-2001, plateau 2001-2008 and declined 2008-2012(USA)
- Role for screening – unclear but under investigation in groups with a high cumulative incidence (Joel Polevsky et al)
- Anal PAPs – tricky to uniformly perform and assess cyto-pathologically

Anal Carcinoma - treatment

- T1-2 N0 M0 or T1-2 N1 M0 or T3 N0 M0
- Combined radiotherapy – 6 weeks to a total of 60Gy external beam with boost to tumuor bed
- With chemotherapy – 5FU infusions and Mitomycin C weeks 1 and 4
- Reasonable expectation of long-term cancer free survival (I am very careful of the cure word – anecdotally I have seen possibly too many relapses with this treatment)
- Toxic but sphincter saving – stories abound re why the sphincter needs saving but QOL studies support this idea
- The alternative is an AP resection – this not thought to be more successful but more observation needs to be done

HCC – prevent, screen, diagnose

- Treat HCV and HBV – post cART end stage liver disease in 50% with HIV and HBV or HCV
- Alcohol excess tricky to “treat”
- Screen if HIV+ and established cirrhosis (for all causes of CLD)
- Screening: remember the principles of early diagnosis allowing a better chance of cure with less toxic treatment. Radiology: Li RADS system may obviate need for a biopsy!
- Most with HCC die of it: 20% alive at 5 years (Aust 2020)(HIV worse survival than general)
- Hence the Australian consensus statement to simplify screening and management to improve outcomes (2020)

HCC – treatment

- Barcelona Clinic Liver cancer staging
- MDM
- Surgery
- Liver transplantation
- Ablative therapies: eg SRS
- Systemic for metastatic: latest lenvantinib (TKI) or atezolizumab (PD-L1 antibody) improve survival by months only

Lung Carcinoma - general

- Relationship to HIV unclear
- 2x risk general population
- 2x smoker as well confounds the figures
- Prevent: stop smoking - anecdote alert: my friend

Lung Carcinoma – treatment. Stage critical. GENOMICS critical

- III. Vastly improved outcomes with combined chemotherapy, radiotherapy and maintenance immune-therapy (PD1 inhibitors such as nivolumab and pembrolizumab)
- IV. EGFR mutation testing on samples is critical – GENOMIC testing
- If EGFR mutant: TKI first then other accordingly
- Many generations TKIs – ask the registrar – hard to keep up
- EGFR wild type and PD1 positive – chemotherapy and immunotherapy

NADC – Immune-suppression

- My anecdotes: A view from my office. Who knows how common this may be.
- Neurological conditions requiring longer term steroids or agents such as methotrexate may precipitate NEW KS – previously not part of HIV picture
- If a patient has HIV consider other options: eg: IvIg for CIDP or polymyositis
- If a patient has HIV be aware of it – even test for it – and beware risks KS.
- Do HHV8 viral load and PCR pre-Rx – if negative the risk is lower or nil

NADC – Immune-suppression & HIV

- Sarcoid Rx steroids – latent unknown Hep B flare
- CIDP and known KS – stop prednisolone and use apheresis
- Polymyositis and no KS on steroids – use IvIG

General tips for primary care physicians:

- Consider referrals carefully:
- Are they comfortable with HIV?
- Are they familiar with HIV?
- Do they work with an experienced team and participate in MDC?
- Should we be asking what our colleagues outcomes are?

General tips for specialists:

- Know your HIV medicine and ask for advice
- Before any anaesthetic check is propofol is preferred
- Before any drug treatment liaison with an expert pharmacist re drug interactions is mandatory
- Understand clearly why treatment should probably not vary in well controlled HIV with no other comorbidities

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General tips for specialists:

- Surgeons: are you comfortable if not take advice or refer on
- Surgeons: what are your needlestick injury protocols and who would you contact in that unlikely event
- Surgeons: what is your HIV status
- Physicians: screen for HIV in at risk populations – anecdote: KS on feet in a case of aggressive NHL in a 23 year old male
- Physicians: beware long term immuno-suppression in well controlled HIV

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- Thankyou for inviting me to speak
- May I try to answer any of your questions?