An Overview of Childhood Cancer and the Early Warning Signs

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People Development Centre (PDC) and CHOC Childhood Cancer Foundation
Childhood Cancer Awareness Indaba Programme
ONE DAY INDABA: 20 September 2017
What are we going to cover?

- What’s the scope of the problem?
- What makes paediatric malignancies different to adult malignancies?
- What’s the importance of early diagnosis?
- What are the warning signs?
How Common is it?

- Rare!

- Northern Hemisphere data
  - 100–150 new cases per million children < 15 per year

- Western Cape Only 75–80 cases per million are reported in the Western Cape each year …
  - Different epidemiology or Underreporting or both?

- Bottom line
  - 1 new case per paediatrician per year
  - A handful of cases per GP per career
LEUKAEMIAS
- ALL / AML / CML

BRAIN TUMOURS
- Separate textbook!

BONE TUMOURS
- Osteogenic Sarcoma
- Ewing’s Sarcoma

EMBRYONAL TUMOURS
- Neuroblastoma
- Nephroblastoma
- Rhabdomyosarcoma
- Hepatoblastoma
- Retinoblastoma
- PNET
- Germ Cell Tumour

RARE TUMOURS
- Thyroid Ca / Melanoma
US figures show total of 146 cancers per million children aged 0–14 per year

- ALL: 34.6
- BRAIN TUMOURS: 32.4
- NEUROBLASTOMA: 11.3
- NHL: 8.7
- WILMS TUMOUR: 8.6
- AML: 7.1
- HODGKIN’S DISEASE: 5.3
- RHABDOMYOSARCOMA: 5
- RETINOBLASTOMA: 4.6
- OSTEOSARCOMA: 3.7
- EWING’S TUMOUR: 2.1
- OTHERS: 23.2
Why this dramatic change?

- The introduction of multiagent chemotherapy
- Multidisciplinary care in dedicated units (POUs)
- Better health infrastructure $\Rightarrow$ earlier diagnosis
- Better diagnostics allowing for risk adaption
- New treatments, radiation modalities and surgical techniques.
- Improvements in supportive care allowing for more intensive the therapies e.g. stem cell transplantation
Childhood Cancer in a Nutshell

- Almost never runs in families
- Is not caused by diet / ROH / smoking
- Has a much better prognosis than cancer in adults ...
  - for example ...
    - Leukaemia: 75% 5 year survival
    - Wilms Tumour: 50–95% 5 year survival
- EARLIER diagnosis = BETTER outcome
Adult tumours are mainly carcinomas (epithelial in origin). These are often slow growing. Response to chemotherapy is relatively poor.

Childhood tumours are embryonal tumours and sarcomas. Childhood leukaemias and lymphomas are usually high grade and present acutely. They have a high mitotic rate, are fast growing and respond well to chemotherapy.
Childhood vs Adult Cancer

- Adult tumours occur in lining cells e.g. adenoCa of the breast and GIT, bronchial or uterine carcinoma. Classic warning signs are useful. **Screening tests** pick up early or pre-malignant lesions.

- Childhood tumours are deep seated. Warning signs are different. **Screening tests** are generally unhelpful.
Childhood Cancer at RCCH

- Approximately 130 new cases per year
- Many present with advanced disease
- Many have presented to the health service several times over the preceding weeks or months
- These delays make treatment more difficult and decrease the chances of success ...
WILMS’ TUMOUR

- **Stage I** ... confined to kidney
- **Stage II** ... through capsule
- **Stage III** ... residual tumour
  - Local spread
  - Nodes
  - IVC Thrombus
- **Stage IV** ... metastatic disease
- **Stage V** ... bilateral disease

Improved Prognosis
“What a Difference a Day (or two) Makes”
Wilms Tumour

Cumulative Proportion Surviving

- Stage I: 94.4%
- Stage II: 96.2%
- Stage III: 84.9%
- Stage IV: 54.2%

Chi-square = 22.898    df = 3    p = 0.00004
Burkitt Lymphoma

Overall 5-year Survival
LMB Chemotherapy
1988-2004
[Log Rank p value 0.06]

Complete  Censored
Stage II and III  88.2%
Stage IV  66.0%

Cumulative Proportion Surviving

Time - months
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0

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Ewing Sarcoma

Figure 1. Event-free Survival According to Study Group and the Presence or Absence of Metastatic Disease.
WILMS’ TUMOUR TREATMENT...

- Surgery (primary or delayed) for all

- Chemotherapy
  - Stage I or II: Vincristine + Dactinomycin
  - Stage III or IV: Add DOXORUBICIN

- RENAL BED RADIOTHERAPY for local Stage III
- PULMONARY RADIOTHERAPY for lung metastases
What Are the Warning Signs?

- **CLINICAL CRITERIA!**
  - Signs and symptoms that should alert one to the possibility of a malignancy

- **WHAT DOES ONE NEED?**
  - History and Examination BUT NO special tests!

**St Siluan Warning Signs Childhood Cancer:**

- **S** – *Seek* medical help early for ongoing symptoms
- **I** – White spot in the *eye*, new squint, sudden blindness or bulging eyeball
- **L** – *Lump* on the stomach, pelvis, head, arms, legs, testicle or glands
- **U** – *Unexplained* fever present for over two weeks, weight loss, fatigue, pale appearance, easy bruising & bleeding
- **A** – *Aching* bones, joints, back and easy fractures
- **N** – *Neurological* signs, a change in walk, balance or speech, regression, contiguous headaches with/without vomiting & enlarged head
What Are the Warning Signs?

- Pallor plus Bleeding
- Fever / Apathy / Weight Loss
- Bone Pain
- Adenopathy
- Unexplained Neurological Signs
- Unexplained Mass
- Eye Changes
1. Pallor PLUS Bleeding

- Pallor
  - buccal mucosa
  - conjunctivae
  - nailbeds

- Bleeding
  - bruises
  - nosebleeds
  - gumbleeds

Red flag for **PANCYTOPAENIA** implying involvement of the bone marrow ...
1. Pancytopaenia

- LEUKAEMIA
- LYMPHOMA or NEUROBLASTOMA

- ASK ABOUT …
  - bone pain

- WATCH OUT FOR …
  - swollen gums
  - lymph nodes
  - abdominal masses
  - proptosis

Gum hypertrophy
1. Pancytopenia

- MUST exclude HIV infection …

**LEUKAEMIA (or LYMPHOMA)**
- FBC: Hb↓ Plt ↓ WCC ↑/↓ … look for blasts
- Chemistry: LDH ↑ (with a normal ALT) and Urate ↑
- CXR: mediastinal mass in T–cell lymphoma

**NEUROBLASTOMA**
- Look for an Abdominal Mass !
- FBC: typically anaemic with preserved platelets
- Chemistry: LDH ↑ (with a normal ALT) and urinary HVAs
- Xrays: lytic bone lesions or calcified abdominal mass
2. Fever / Apathy / Weight Loss

- Non-specific picture

- MUST exclude ...
  - HIV/ AIDS
  - Urinary Tract Infection
  - Tuberculosis

- Review the patient systematically looking for other WARNING SIGNS ...
3. Bone Pain

- NOT localised
- Wakes the child
- Limp or Reluctance to bear weight
- A toddler who stops walking
- Backache!!
3. Bone Pain

- Again, malignancies involving the bone marrow...

- LEUKAEMIA or LYMPHOMA
- NEUROBLASTOMA

- Remember ... if local pain and swelling (especially around the knee joint)...

- BONE TUMOURS  eg. OSTEOGENIC SARCOMA
4. Lymphadenopathy

Most important aspect: What’s Normal?

- **SITE**
  - Cervical > 2cm
  - Axillary / Inguinal > 1cm
  - Supraclavicular

- **NATURE**
  - No regional infection
  - Non – tender
  - NOT responding to antibiotics

● Always think about TB and HIV infection

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5. Unexplained Neurological Signs

- Headache > 2 weeks
- Early morning vomiting
- Ataxia / unsteady gait
- Cranial Nerve Palsy

**BRAIN TUMOURS**
- Posterior fossa ... ataxia and cranial nerve palsies
- Supratentorial ... headache and vomiting ⇨ hemiplegia

**RHABDOMYOSARCOMA** (often occult in the sinuses)
- Lower cranial nerve palsies eg. VI, VII, IX, XII

**NEUROBLASTOMA** (secondary to skull infiltration)
- Commonly VI nerve palsy
6. Abdominal Masses

- from 6 months to 6 years ...

ABDOMINAL MASS

is a tumour until proven otherwise

ALWAYS CONSIDER SEDATING THE PATIENT IF YOU CAN’T PALPATE THE ABDOMEN!
6. Abdominal Masses

- **WILMS TUMOUR**
  - flank mass / overgrowth syndromes / hypertension / ↑ LDH

- **HEPATOBLASTOMA**
  - hepatomegaly / ↑ αFeto–protein

- **NEUROBLASTOMA**
  - adrenal / calcification on plain films / ↑ LDH and HVAs
  - Pancytopaenia and bone pain / SC compression / sweating, D&V, ↑BP / skin lesions / Opsoclonus–myoclonus

- **BURKITT LYMPHOMA**
  - central abdominal mass / nodes on imaging / ↑ LDH
6. Pelvic Masses

- GERM CELL TUMOUR
  - ↑ αFeto-protein

- BURKITT LYMPHOMA
  - ↑ LDH and urate

- RHABDOMYOSARCOMA
  - ↑ LDH

- NEUROBLASTOMA
  - ↑ LDH
7. Eye Changes

- White Reflex
- Recent Onset Squint
- Loss of Vision

- **RETINOBLASTOMA**

- Proptosis

- **LEUKAEMIA** especially Acute Myeloid Leukaemia
- **NEUROBLASTOMA**
- **RHABDOMYOSARCOMA**
7. Eye Changes

- Leukocoria

- REFER to an Ophthalmologist urgently for slit lamp examination
7. Eye Changes

- Proptosis

- CONSIDER Leukaemia / Neuroblastoma / Rhabdomyosarcoma ... abnormal FBC means diagnosis might be made on BM examination ... REFER / ARRANGE

- OTHERWISE REFER to an Ophthalmologist for urgent biopsy
In Summary

- History and examination are the KEY!

- Appropriate plain films and labs may be very helpful

- NEVER let special investigations (scans) delay transfer of an urgent case! Always discuss FIRST.

- **Leukaemia / lymphoma:**
  - FBC with differential count, Chemistry with ALT, LDH and urate.
  - CXR, ESR, Coagulation screen, HIV.
In Summary

- **Solid tumours**: (LDH and ultrasound)
  - NBS: Measure the BP!, LDH, Ferritin, HVAs
  - Wilms: Measure the BP!, urine dipstix
  - Hepato / HCC: αFP, (Hep B sAg)
  - Germ cell tumours: αFP, β–HCG

- **Brain tumours**: 
  - CT or MRI. Discuss with neurosurgeons about definitive surgery or biopsy.

- If you are suspicious CALL FIRST and discuss the case.
Cancer in children is RARE but eminently TREATABLE!

- Early diagnosis improves outcomes
- There are Warning Signs that can alert us to the diagnosis...
It’s all about Relationships

Better relationships

Less treatment related morbidity and less mortality

Stronger referral chain

CHILD

Lower stage disease

Earlier diagnosis