Tough to treat tumours in the elderly: sarcomas

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Sarcomas

• Malignant tumours of mesenchymal origin
  – Rare
  – Difficult to diagnose
  – Often late presenting
  – Anatomically unrestricted: involve diverse surgical teams
  – Require access to expert multi-disciplinary teams
  – Relatively less sensitive to radiotherapy
  – Relatively less sensitive to chemotherapy
  – Slow development of new therapies due to low trial recruitment
  – Overall 5 years survival rate ~ 50%
Sarcoma practice age profile

- 25%
- 20%
- 15%
- 10%
- 5%

Age ranges:
- 0 - 9
- 10 - 19
- 20 - 29
- 30 - 39
- 40 - 49
- 50 - 59
- 60 - 69
- 70 - 79
- 80 - 89
- 90 - 99
Age related aspects in the management of sarcoma

- Late diagnosis
  - Patient delay
  - Physician delay
- Access to specialist teams
  - Reluctance to refer (physician)
  - Reluctance to attend (patient)
- Adherence compliance with therapeutic advice
- Under-representation in clinical trials
- Generalisability of research findings
- Possibly different biology
  - host – PK, co-morbidity, con meds
  - tumour biology
- Danger of under or over treatment
Scenario 1: Non-metastatic soft tissue sarcoma

- **Presentation:** progressive mass in leg
- **Diagnosis:** cross sectional imaging, biopsy, staging
- **Management plan:** Wide local excision and post-operative radiotherapy
- **Expected outcome:**
  - Local control: 80%
  - Severe functional impairment: rare
  - Metastatic relapse: ~20% in 5 years
Points

• Clinical outcomes generally good
• Ability to tolerate surgical resection and long course RT may be reduced by frailty
• Less radical therapy may have a worse palliative outcome
• Options for tailoring
  – Immediate onco-plastic reconstruction
  – Pre- vs post- op radiotherapy
Scenario 2: Metastatic soft tissue sarcoma

• Presentation: relapse after resection or metastatic at presentation
• Diagnosis: assessment of extent of disease and fitness for therapy
• Management plan: Doxorubicin, ifosfamide, trabectedin cytotoxic chemotherapy
• Expected outcome:
  – Overall response rate: 25% or less
  – Average survival: 12 months
Overall survival in advanced STS
Outcome from first line chemo

Overall survival: doxorubicin

- Survival rate decreases over time from the start of chemotherapy.
- The graph shows the percentage of survivors against years from the start of chemotherapy.
- At 5 years, approximately 1 patient (93/132) remains.
Number of lines of chemotherapy

Number of lines of therapy in advanced soft tissue sarcoma

- 0 lines: 35%
- 1 line: 40%
- 2 lines: 20%
- 3 lines: 25%
- 4 lines: 10%

Lines
No chemo given at Christie

Patients not receiving chemotherapy for advanced soft tissue sarcoma

Age decade

%
Survival in STS

STS survival from advanced stage

$p < 0.0001$, logrank test
Points

• Palliative therapy often ineffective and associated with morbid toxicity
  – Both doxorubicin and ifosfamide known to be problematic in elderly patients
  – Less known about trabectedin

• Useful benefit in a minority

• Honest disclosure and optimal patient involvement in decision making. Early engagement of community supportive care services

• Options for tailoring
  – Avoid combination regimens
  – Less toxic chemotherapy regimens have been published but no RCTs to compare
Scenario 3: Gastrointestinal stromal tumour (GIST)

- Presentation: mass +/- upper GI haemorrhage or incidental
- Diagnosis: Post-op / radiological / biopsy
- Management plan:
  - Surgery
  - Tyrosine Kinase Inhibitor therapy (imatinib)
- Expected Outcome
  - Non-metastatic presentation: 5 yr survival 90%
  - Survival from metastases: median 5 years
Lines of therapy in advanced GIST

Number of lines of therapy in advanced GIST

- 0 lines: 5%
- 1 line: 45%
- 2 lines: 30%
- 3 lines: 15%
- 4 lines: 10%
Lines of therapy in advanced GIST

Number of lines of therapy in advanced GIST by age

- <65 years
- >65 years

Lines

0% 10% 20% 30% 40% 50% 60%

0 1 2 3 4

0% 10% 20% 30% 40% 50% 60%
Points

• Good outcomes can be obtained with correct management
• Tolerability of stomach resections is variable
• Use of TKIs has revolutionised the outlook for patients
  – Issues with drug-drug interactions (CYP450)
Scenario 4: Childhood type tumours presenting in the elderly

• Presentation: Solitary destructive bone lesion
• Diagnosis: Osteosarcoma / Ewing’s
• Management plan: Intensive pre-operative cytotoxic chemo; radical surgery; extended post-operative chemo +/- radiotherapy
• Expected outcomes:
  – Osteo: 60 – 80 % cured
  – Ewings: 55 – 65 % cured
Points

• Good outcomes can be achieved but is dependent on use of chemotherapy
  – treatment very morbid
  – age thought to be a poor prognostic factor
  – applicability in older patients
    • ? Different biology
Conclusions

- Let age be no bar
- Host and condition both need careful assessment
- Validated tools are required
- Cross disciplinary dialogue is very welcome
- Organisational co-ordination may be more effective than any clinical intervention

- Targeted therapies are better tolerated but have their own problems
- Current avenues being explored
  - Trabectedin
  - VEGF therapy (pazopanib)
  - mTOR inhibitors (radiforalimus as maintenance therapy)
  - Lower dose infusional ifosfamide
  - Single sub-type trials
Geriatric Oncology: Cancer in Senior Adults

11th Meeting of the International Society of Geriatric Oncology
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