Introduction to sarcoma

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The Royal Marsden
Overview

General overview

IOG/ NICE guidelines

General management with case studies

Useful resources
Sarcomas - what are they?

- Sarcomas are solid tumours of connective tissue, i.e. resemble muscle, nerve, fat, bone, fibrous tissue

- They are extremely variable in behaviour and treatment and can occur anywhere in the body

- They can occur at any age, with a median age at presentation of 65 but can affect young people, including children

- Soft tissue sarcoma (STS) incidence 5 per 100,000 per annum, bone sarcomas even more rare
What are the advantages of centralising the care of sarcomas?

- Rarity
- Diversity - >100 subtypes of sarcoma
- Expertise in all areas of management requires considerable cumulative experience
Guidance on Cancer Services

Improving Outcomes for People with Sarcoma

The Manual

March 2006

Developed by the National Collaborating Centre for Cancer
NICE\textsuperscript{1} Improving Outcomes Guidance (IOG) for People with Sarcoma

Consultation exercise lead to publication of guidance in 2006 covering early referral, diagnosis, centralisation of care and all aspects of multidisciplinary management

http://guidance.nice.org.uk/CSGSarcoma

National Institute for Health and Clinical Excellence
The Royal Marsden

NICE IOG - key recommendations

- All sarcoma pts must be managed by a sarcoma MDT
- Designated Diagnostic Centres
- Provisional sarcoma diagnosis must be reviewed by sarcoma expert pathologist
- Treatment Centre must manage $\geq 100$ new cases of soft tissue sarcoma a year – 50 for bone (implications for numbers of surgeons and other staff)
- Sarcoma operations must be done by appropriately skilled surgeons, in sarcoma MDT or specialist MDT in consultation
Management of primary STS - the Multidisciplinary Team

- Pathologist
- Radiologist
- Surgeon
- Clinical oncologist
- Medical oncologist
- Specialist nurse
- Physiotherapist
- MDT coordinator

- accurate diagnosis essential
- surgery only curative modality
- neo/adjuvant radiotherapy often required
- chemotherapy sometimes necessary
- support services vital
Tumours requiring shared management i.e. sarcoma and site-specific MDT

- Limb soft tissue sarcomas
- Retroperitoneal sarcoma
- Bone sarcomas
- Gynaecological sarcomas
- Head and neck sarcomas
- Chest wall/intrathoracic sarcomas
- Skin sarcomas
- Central nervous system sarcomas
- Gastro-intestinal stromal tumours (mainly GIST)
- Adult-type soft tissue sarcomas arising in children.
The London and South East Sarcoma Network (LSESN) was established to ensure that patients from London and the South East of England who have been diagnosed with or have a suspected sarcoma can access world-class diagnostic and treatment services at one of two specialist sarcoma centres serving the network.

Multidisciplinary clinical teams work at The Royal Marsden, treating soft-tissue sarcomas, and at University College Hospital and Royal National Orthopaedic Hospital, treating both bone and soft-tissue sarcomas.

The LSESN works with London Cancer, London Cancer Alliance and NHS England Specialised Commissioning to deliver care that is consistent and of the highest quality, based on efficient and effective pathways of care from primary care to treatment and follow-up.

Details of how to refer, the services available at the sarcoma centres, our pathways and our guidelines can be found by following the links to the right and above.

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For referrers

- 2WW contact details for GPs
- 2WW referral guidelines for GPs
- LSESN 2WW form for GPs outside of London
- LSESN referral guidelines for hospital referrals
- UCLH/IRNOH information
- RMH information

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2ww contact details for GP

- **The Royal Marsden**
  - Tumour types: Soft tissue
  - Tumour sites: All tumour sites
  - Fax: 020 8661 3149
  - Tel: 020 8661 3630
  - Email: rmh-tr.referrals@nhs.net

- **Royal National Orthopaedic Hospital**
  - Tumour types: Soft tissue & bone
  - Tumour sites: Limb, trunk & spine
  - Fax: 020 8909 5709
  - Tel: 020 8909 5603
  - Email: rno-tr.LondonSarcomaService@nhs.net

- **TRM: soft tissue sarcoma centre**

- **RNOH: bone and soft tissue sarcoma centre**
Criteria for urgent referral of a patient with a suspicious lump:

- >5 cm
- Increasing in size
- Deep to deep fascia
- Painful
Sarcoma UK has developed this diagnostic tool and golf ball keyring to help GPs recognise the presenting signs and symptoms of sarcoma. The guidance aims to assist GPs in referring patients with suspected sarcoma quickly and easily to specialised sarcoma services for diagnosis and treatment.
Case study 1

- 44 year old man
- Lump on lower leg following energetic football match

- On examination- 6 cm+ lump
  - non tender
  - appears fixed

- First investigation...
What would you do next?

1. Send to local surgical team
2. Refer to orthopaedic team
3. Request an USS scan
4. Refer via 2ww
5. Refer to local diagnostics service
USS scan

‘solid mass- possible lipoma but sarcoma can’t be excluded’
Next steps...

Refer via ‘2 week wait pathway’

First investigation at The Royal Marsden

Core needle biopsy and further imaging
MRI scan
Test results

- Biopsy confirms high grade sarcoma
- Staging CXR is normal
- Treatment:
  - Surgery
  - Radiotherapy
- Follow up
- Surgical resection with **clear margins** offers the best chance of cure in the absence of metastatic disease.

- **Function-preserving limb conservation** is the goal
  - Marginal excision, wide local excision,
  - margins usually defined by adjacent vital structures, e.g. vessels
  - compartmental resection: taking subtype/biology into account

- Amputation is rarely necessary < 5%

- **Radiotherapy** is indicated high grade deep seated tumours
Improving outcomes in extremity sarcoma by surgery

The Treatment of Soft-tissue Sarcomas of the Extremities

Propective Randomized Evaluations of (1) Limb-sparing Surgery Plus Radiation Therapy Compared with Amputation and (2) the Role of Adjuvant Chemotherapy

STEVEN A. ROSENBERG, M.D., Ph.D.,* JOEL TEPPER, M.D.,† ELI GLATSTEIN, M.D.,† JOSE COSTA, M.D.,† ALAN BAKER, M.D.,* MURRAY BRENNAN, M.D.,* ERNEST V. DeMOSS, M.D.,* CLAUDIA SEIPP, R.N.,* WILLIAM F. SINDELAR, M.D., Ph.D.,* PAUL SUGARBAKER, M.D.,* ROBERT WESLEY, Ph.D.,§
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Survival identical between amputation and limb conservation
The Royal Marsden

Femoral artery
Femoral nerve
Increased wound complications with pre-op RT but lower incidence of long term side effects

With improved techniques, pre-op RT preferable
Sensitivity to radiotherapy

Myxoid liposarcoma

Pleomorphic liposarcoma
What’s the main reason for wanting to diagnose sarcomas early?
Impact of tumour size on survival in STS
(data from ROH courtesy of R Grimer)
Histological diagnostic discrepancies

- Audit of 277 cases referred to The Royal Marsden with a diagnosis of sarcoma in a 12 month period
- Overall discrepancy rate 26.6%
- 10.9% major, i.e. could lead to significant change in management
  - 7 “sarcomas” proved to be carcinoma or germ cell
  - 7 cases wrongly diagnosed as GIST, 1 GIST as LMS
  - 3 malignant tumours diagnosed as benign
  - 2 benign tumours diagnosed as malignant
  - 2 others were fibromatosis
- 15.7% minor, i.e. mainly changes in STS subtype

Impact of referral to specialist centres

- Canadian study: patients with limb STS referred to cancer centre within 3 months of diagnosis had improved OS and reduced risk amputation.

- Swedish study: patients with limb or trunk STS referred to a specialist centre before surgery had improved DSS but not OS

- Five studies, 1 UK, 1 France and 3 Sweden, compared surgical margins. 4 found adequate margins more likely for patients treated at specialist centres.

- Consistent evidence of reduced risk of local recurrence at specialist centres
Impact of inappropriate surgery

- Patients with extremity or trunk STS 2001 to 2005 with median follow-up = 51 months

- **Study group**: patients who underwent an inappropriate operation of a sarcoma elsewhere, and then referred immediately for further management at TRM (n=134)

- **Control group**: stage matched patients who underwent planned surgery at TRM after a core needle biopsy (n=209)
**Disease-specific survival**

![Graph showing cancer specific survival for stage 3 patients. The graph compares survival rates between inappropriate and appropriate treatments. The x-axis represents months ranging from 0 to 120, and the y-axis represents survival percentage ranging from 0 to 100. The graph shows two lines: one for inappropriate treatment (red) and one for appropriate treatment (blue). The p-value for the difference in survival rates is 0.0362.](image)
Metastatic Disease in Grade 3 STS

Metastatic Disease Stage 3

- Inappropriate
- Appropriate

$P = 0.0033$
Summary of Practice guidelines for localized STS*

- Planned biopsy first
- Planned surgery resection with a goal of R0-R1
- Re-operation if unplanned ("whoops") initial surgery
- Pre or Post operative RT
- No systematic adjuvant chemotherapy
- Follow up after initial treatment

*SOR 2004, Casali et al, Ann oncol 2010/2015
Case study 2

- 68 year old man
- Presenting with upper GI bleed
- Hb 80g/dl, MCV 65
- First investigation?
What are the next steps?

1. Send off haematinics
2. Request CT scan
3. Colonoscopy
4. Gastroscopy
5. Prescribe Feso4
CT scan
Biopsy: CD117
Gastrointestinal stromal tumour (GIST)
GIST treatment options:

- Surgery – potentially curative
- Drug treatment (Imatinib)
Case study 3

- 56 year old woman
- Menorrhagia and fatigue
- Abdominal distention
What investigations would you do?

A. FBC
B. TV USS
C. MRI abdomen
D. CT scan
E. Thyroid function tests
First steps

• Haemoglobin 78g/dl

• Ultrasound of abdomen: ‘expanded uterus with multiple degenerating fibroids’

• Referred to gynaecology team
Pre op MRI scan
Options?

Patient proceeds to Total Abdominal Hysterectomy and BSO

Histology- unexpected finding of uterine leiomyosarcoma
The Royal Marsden

Staging post op CT scan
Treatment options for metastatic disease

- Palliative chemotherapy
- Consider hormone status of tumour
- Role of other palliative treatments - radiotherapy
- Importance of palliative care
Case study 4

- 36 year old woman
- Long standing lump on shoulder
- Concerned about cosmetic appearance
- ? Changing in size over time
Clinical appearance
What investigations would you do?

1. Excision biopsy
2. USS scan
3. Refer via 2ww
4. Referral to local surgical clinic
5. Observe
Next steps in management?

- Referral
- Imaging
- Biopsy

- lipoma
The Royal Marsden

Surgical excision

Wide excision margins not required - no long term follow up
In summary
Role of Imaging and Biopsy

• The major purpose of imaging is to define the anatomical position of a tumour and its relationship to surrounding (vital) structures.

• The purpose of biopsy is to provide a histological diagnosis.

• It is an ERROR to assume that CT or MR can predict the histological diagnosis or differentiate benign from malignant.
Role of surgery

- Optimal outcome when performed at specialist centre

- 5yr local recurrence free survival: limbs 80 – 90%, RPS 50 – 60%

- 5yr overall survival: 50-60%
Role of radiotherapy

Pre-operative or post operative in high grade soft tissue sarcoma
Conformal radiotherapy
Complex radiotherapy
  IMRT
  SABR
  Proton therapy

Palliative radiotherapy
  Local control
  Symptom control
Role of chemotherapy: important facts

- Palliative chemotherapy in metastatic sarcoma
  - Main benefits are disease control and QoL

- Curative chemotherapy in paediatric subtypes
  - Eg Ewing sarcoma and rhabdomyosarcoma

- Risk of neutropenia and sepsis can be high
  - If in doubt check FBC or send to A+E
Access to clinical trials

- Evidence that patients treated within the context of clinical trials have better outcomes
- Access to trials very limited for rare disease outside specialist centres
- Specialised centres have numbers to conduct pilot studies and coordinate research into ultra-rare diseases, e.g. ASPS, clear cell sarcoma
Questions?

Thank you for listening