Case histories in Urological cancers

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Outline of talk

Case histories for:

- Localised prostate cancer
- Active surveillance
- Metastatic disease
- Bladder cancer
Early diagnosis

Difficult in prostate – often no symptoms

“Democracy is the worst form of Government, except for all the rest”
Winston Churchill

Same true for PSA

Stick to referral criteria for PSA levels unless obvious cause

Think of prostate cancer in LUTS, Bone pain. More common with increasing age, but still possible in 40s and 50s.
Localised prostate cancer
Case history - localised prostate cancer

72 year old man presents with PSA of 12

MRI (always first!) stage T2NoMo (pelvis)

Gleason 3+4 in 7/12 cores (TRUS)

Patient otherwise well

T1 not visible on MRI
T2 confined to prostate
T3a Into/beyond prostate capsule
T3b Into seminal vesicles
T4 into surrounding structures (bladder, rectum, uro-genital diaphragm)
MDT

Every case discussed in local hospital (Epsom, Croydon, Kingston, Georges)

Every new radically treatable cancer discussed again in the Central MDT (Marsden/Georges)

Review pathology or pathology result, review each scan (radiology and nuclear medicine)

Clinicians (Surgeons, Oncologists, specialist nurses) decide on treatment plan or options
MDT discussion

Surgery probably not optimal at 72

Options

• Androgen deprivation therapy plus radiotherapy
• Brachytherapy

Whatever he chooses cure rate around 90%
We have made colossal progress in radiotherapy
Bowel side effects

2 D: 56%

3 D: 37%
33% 13%

CHHiP trial vs RT01 trial
Hard-and-fast prostate radiotherapy 'a win-win for NHS'

21 June 2016

David Dean, Zofar Malik, Andrew Story, Julia Pugh, The Royal Marsden
**CHHiP**: Phase III Trial of Conventional or Hypofractionated High Dose Intensity Modulated Radiotherapy in Prostate Cancer

- Histologically proven prostate cancer
  - T1b-T3a N0 M0
  - Estimated risk of seminal vesicle involvement = 30%
  - PSA ≤30ng/ml
  - Due to receive radiotherapy

- **Hormone therapy**

- **Randomisation**
  - 74 Gy / 37# in 7.4 weeks (standard)
  - 60 Gy / 20# in 4 weeks
  - 57 Gy / 19# in 3.8 weeks
60 Gy in 20 non-inferior to 74 Gy in 37
Very little toxicity – 4% Gd 2+ GI at 2 years
PSA follow up - increasingly Primary care led

PSA 6-monthly to 5 years, then annually

Side effects rare but may occur many years later – GI, GU, ED (ask!)

Refer each to relevant speciality

After prostatectomy – PSA should be undetectable for life, definitely refer back if reaches 0.1

After radiotherapy – PSA should be below nadir+2 ng/ml for life, otherwise please refer back
So how do we do radiotherapy?
Don’t worry, I’ll leave out the geeky bits
- You don't take any radiotherapy with you
- No risk to pregnant family members
- No sensation associated
- Probably a small risk of secondary cancers (prob <1:250)
Fiducial placement under trans-rectal ultrasound guidance - outpatient procedure
A fiducial in situ
Risks

• Pain
• Bleeding (GI, GU, Haematospermia)
• Infection

Rectal swab, targeted antibiotics

IF FEVER – STRAIGHT TO A +E, NEED IV Abx (risk 0.3%)
So what does the patient experience each day?

Empty bladder and take Microlet enema one hour before treatment  
(enema only first 5-10 treatments to keep rectum empty)

Drink 325 mls of water/squash and hold bladder – 1 hour

Change into gown

Lay on treatment couch (hard!) and get moved into the correct position (CT).

Radiographers leave the room, so patient is alone, but can be seen and heard

Machine moves around patient but doesn’t touch. No sensation during treatment
Brachytherapy
Active surveillance
Case history

- 53 years, PSA 0
- Presents to GP with PSA 5.1
- Referred to local hospital – has TRUS biopsy
- Gleason 6 (3+3), 2/10 cores positive, cT1c (DRE)
- MRI T1c or now PIRADS 2
What would you do for him?

A. Radical prostatectomy
B. Radical radiotherapy with Androgen Deprivation Therapy
C. Radical radiotherapy alone
D. Active surveillance
MDT discussion

- 53 not 73 years old
- But otherwise very favourable disease

- Recommend TP biopsy (can be in 6 months) and Active surveillance if no upstaging
# Watchful waiting is not active surveillance

<table>
<thead>
<tr>
<th>Rx indication</th>
<th>Symptoms</th>
<th>MRI!!</th>
<th>PSA trends (Biopsy results)</th>
<th>Rx timing</th>
<th>Rx intent</th>
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<tr>
<td>Watchful waiting</td>
<td>Rx timing</td>
<td>Late/Never</td>
<td>Early</td>
<td>Rx intent</td>
<td>Palliative</td>
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Royal Marsden Active surveillance cohort

- 471 men, 81% low risk
- 70% remain free of treatment at 5 years, 50% at 10 years
- 0.4% prostate cancer specific mortality at 5 years (5.3% non prostate cancer deaths at 5-years)

*Selvadurai et al, 2013*
82,429 men agreed to PSA test
2664 had localised prostate cancer
1643 agreed to be randomised
Around 500 in each group
FRCR (NICE) AS schedule

- PSA 3 monthly for 2 years
- **Repeat MR** (and biopsy) at 12-18 months
- Then repeat MR (and biopsy) 2 years later
- PSAs 6 monthly years 2-4

- Path or MR upgrade - treat
Locally advanced prostate cancer
Case history

- Fit 52 year old barrister, PMH of left nephrectomy for oncocytoma in 2008.
- GP had been monitoring PSA:
  - Dec 2009 – 3.7 ng/ml
  - Dec 2011 – 4.7 ng/ml
  - Sept 2012 – 13 ng/ml – pt referred to a Urologist
- Trus Bx – Gleason 4+5=9 in 10/10 cores, max length 12mm
- MRI – T3b N1 (several suspicious LN up to 14mm in pelvis)
- Bone scan – normal.
- IPSS = 2
MRI and biopsy

Gleason **4+5=9** (GG5) in 10/10 cores, up to 12mm length, PSA 7.0
- MRI spine – negative
- Choline PET – Several bilateral choline avid pelvic LN
  - left internal iliac
  - right and left external iliac
  - right obturator
• Commenced ADT with bicalutamide and LHRHa in Nov 2012-Aug 2015

• PSA fell from 15 in Oct 2012 to 0.13 by April 2013

• Radical EBRT in the IMRT Phase I/II trial with 74Gy in 37# to prostate, 60Gy in 37# to lymph nodes, 5Gy boost to LN
Androgen deprivation therapy

- Starting treatment
  - Bicalutamide 50mg or 150mg od for 28 days
  - LHRH analogues start 7-14 days after starting Bicalutamide (flare)
  - Usually start monthly
  - Can switch to monthly in those needing >12 months of therapy (T recovery 9 months)
ADT side effects

- Fatigue
- Hot flushes
- Loss of muscle bulke/weakness
- Mood swings – grumpy/teary/change in personality
- Almost complete erectile dysfunction/loss of libido (exceptions)
- ?Cardiovascular risk

Long term
- Loss of bone density
- Cardiovascular risk
What about chemo?

Addition of docetaxel, zoledronic acid, or both to first-line long-term hormone therapy in prostate cancer (STAMPEDE): survival results from an adaptive, multiarm, multistage, platform randomised controlled trial

Nicholas D James, Matthew R Sydes, Noel W Clarke, Malcolm D Mason, David P De Bree, Melissa R Spears, Alastair W S Ritchie, Christopher C Parker, J Martin Russell, Gerhardt Attard, Johann de Bono, William Cross, Rob J Jones, George Thalmann, Claire Amos, David Matheson, Robin Millman, Myrona Alzouabi, Sharon Beesley, Alison J Birtle, Susannah Brock, Richard Cathomas, Prabir Chakraborti, Simon Chowdhury, Audrey Cook, Tony Elliott, Joanna Gale, Stephanie Gibbs, John D Graham, John Hetherington, Robert Hughes, Robert Laing, Fiona McKinna, Duncan B McLaren, Joe M O’Sullivan, Omi Parikh, Clive Peedell, Andrew Protheroe, Angus J Robinson, Narayanan Srihari, Rajaguru Srinivasan, John Stafford, Santhanam Sundar, Shaun Tolan, David Tsang, John Wagstaff, Mahesh K B Parmar, for the STAMPEDE investigators*

6 cycles (=18 weeks) of Docetaxel chemotherapy = 10 months more survival
Side effects of radiotherapy

- Bowels – diarrhoea, proctitis, bleeding (? Second primary)
- GU – dysuria, LUTS, 1% acute retention
- Fatigue

- Rarely see skin reaction now, ED probably takes years to develop.
Is radiotherapy curative in node positive disease?

James et al, JAMA 2016
Metastatic disease
**Metastatic disease**

- 72 year old man
- Previously fit and well
- Presents to A+E with weak legs

- O/E Power 3/5 left hip flexion and extension, 4/5 right side
- No dermatomal sensation loss
- A+E bloods OK, PSA pending.
EMERGENCY!
Activate the spinal cord compression pathway

- Ring AOS team
- Order urgent MRI – minutes mean neurons
- Dex 8mg bd +PPI

- PSA comes back as 2658
- Start Degarelix 240mg sc
Tumour growing into spinal canal

Spinal cord shape distorted
Patient declined for neurosurgery

- Given emergency radiotherapy 20 Gy in 5 fractions to the spine
- Staged with a bone scan and CT chest abdomen pelvis
- Metastases in several bony areas, and widespread metastatic lymphadenopathy
How long is his median survival?

- Median survival of newly diagnosed metastatic prostate cancer 5-6 years at present
- Currently start with ADT and Docetaxel, then at progression cycle through a range of new generation hormonal therapies (Abi, Enza) and other active agents (Cabazitaxel, Radium)
- Who knows what is next..
Metastatic disease

- **LHRH analogues**
- **Add anti-androgens**
- **Consider Casodex withdrawal, stilboestrol, steroids**
- **Radium 223**
- **Docetaxel**
- **Abiraterone**
- **Enzalutamide**
- **Cabazitaxel**
Bladder cancer
Searching for a needle in a haystack?

Referral for suspected bladder cancer

When should I refer a person with suspected bladder cancer?

- Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) for bladder cancer if they are:
  - Aged 45 and over and have:
    - Unexplained visible haematuria without urinary tract infection or
    - Visible haematuria that persists or recurs after successful treatment of urinary tract infection, or
  - Aged 60 and over and have unexplained non-visible haematuria and either dysuria or a raised white cell count on a blood test (new NICE recommendation for 2015).
- Consider non-urgent referral for bladder cancer in people aged 60 and over with recurrent or persistent unexplained urinary tract infection (new NICE recommendation for 2015).
62 year old woman

- Presents to GP with visible haematuria
- MSU: E Coli sensitive to Trimethoprim
- 2 weeks later returns to GP
- Dysuria and visible haematuria returned
- MSU – no growth
You are the GP seeing her in clinic - do you?

A. Try another course of Trimethoprim and see if it clears up
B. Try a different antibiotic
C. Send a repeat MSU in 2 weeks
D. Refer on a 2 week rule pathway for visible haematuria
Patient undergoes a Haematuria work up

- Cystoscopy (flexi, rigid)
- CT KUB
- May do urine cytology if no primary in bladder
- Consider retrograde ureter studies
Other things bladder tumours can do

- Obstruct one ureter (rarely both)
- Present with sterile dysuria only
What next?

- Biopsy at cystoscopy - TCC into muscle
- Referred to oncology
- Patient otherwise well, no comorbidities
- Advised to have 3 cycles of chemotherapy with Gemcitabine and Cisplatin
The ABC meta-analysis

5% survival advantage

Figure 2: Survival in combination chemotherapy (CT) trials
Bladder preservation

- TUR BT
- Chem o
- Cystoscopy

RT

Cystectomy
What next?

- Cystoscopy shows complete response
- Patient elects to have bladder preservation
- 64 Gy in 32 fractions daily over 6.5 weeks with concomitant chemo

**MMC 12mg/m²**

**5FU 500mg/m²**

**RT 64 Gy/32fx**

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BC 2001 study CI Robert Huddart

Local control 67% vs 54%
3 months post radiotherapy

- Check cystoscopy – no sign of recurrence.

- Follow up – regular CT scans and cystoscopies

- What to watch out for:
  - Haematuria – muscle-invasive or non-muscle invasive recurrence
  - Hydronephrosis
  - Metastases (commonly lymph node, bone, lung)