Causation Issues

Delay in Diagnosis of Cancer Cases

Prof Pat Price
Imperial College London
office@patprice.co.uk
www.patprice.co.uk

Faculty of Advocates
Annual conference

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EVIDENCE BASED

Medicine

Research

Law
Medical Errors

• Delay in diagnosis cancer third largest medical negligence cases in the UK

• Medical error—the third leading cause of hospital death in the US (after cardiovascular and cancer. BMJ May 2016

http://www.bmj.com/content/353/bmj.i2139

• Call for more research and more recording
Cancer Facts

• 1 in 2 people get cancer at some time in lifetime

• 1 in 3 people die of their cancer

• Most cancers occur in the over 75 year olds

• Large body of research in tumour biology
What is Cancer

Basic Biology

• Cells grow uncontrolled and abnormally
  – Abnormalities in genes
  – Production of local growth factors
• Grow to develop a tumour. All tumours are different
• Tumour spreads locally
• Tumour metastases-lymphatics/blood/other
Main Causation Issues

• Delay in diagnosis
  • Most common issue
  • All cancers are different
  • Usually most difficult to assess

• Failure of screening
  • Cervical /breast/colon/follow up

• Side effects of treatment
  - Negligent or not/consent

• Life Expectancy

• Montgomery consent

• [Causes of cancer]
Main arguments in Cancer Cases

• What is stage of the cancer & prognostic factors → treatment & prognosis
  - medical records
  - radiology and detailed histopathology reports

• What is the natural history/behaviour/growth rate of the tumour
  - detailed serial chronology from medical records
  - symptoms - witness evidence
  - Litterature and opinion as to departure from average
Main arguments in Cancer Cases

• What is the treatment guidelines of individual cancer for stage/grade/prognostic features
  - literature

• What does the literature say about prognosis
  - literature

*Main evidence is medical records and literature
*Need to define natural history of individual tumour
  - needs time and full paper medical records
Natural History of Cancer

Pre-malignant → Malignant-localised → Metastatic

**Curable:** screening
- Cervical: 3-10yrs
- Breast: 3-10yrs
- Bowel: 5-10yrs
- Oesophagus: 2-3yrs

**Surgery/adjuvant therapy**

**Radical radiation**

**Curable:**
- Teratoma/Lymphoma

**Chemo increase survival**
- Lung: 2months
- Colon: 3.7+ months
- Gastric: 3months
- Ovary: years

**Chemo given early increase survival:** ???
Premalignant stage

-screening programmes
Adenoma-carcinoma sequence

• Classical “sporadic” colorectal cancer pathway

• 5 – 10 year time frame
Development of Cervical Cancer

- Normal
- CIN2/3
- Cervical Cancer

HPV Infection

Persistant infection (1-10 years)

Invasion (30% by 30 years)
Tumour cell growth
Colorectal cancer growth and spread
Staging of cancer

TNM classification
Cancer TNM

• Primary Tumour T

• Regional Lymph nodes N

• Blood borne spread M
Staging of cancer

TNM UICC classification 8th edition
- Absolute definition
- Clinical vs pathological
- Stage Determines treatment and prognosis

Alternative summaries
  - e.g Dukes classification in colon cancer

<table>
<thead>
<tr>
<th>TNM Classification (American Joint Commission on Cancer)</th>
<th>Dukes' Classification</th>
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<tbody>
<tr>
<td>Stages</td>
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<td>Stage I</td>
<td>T1</td>
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<td>T1, T2</td>
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<td>T3, T4</td>
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<tr>
<td>Stage IV</td>
<td>Any T</td>
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A comparison of TNM and Dukes' Classification
Clinical Staging of Tumours

• Assess
  – Local cancer spread / Distant metastatic spread
  – Decide on treatment at MDT meeting

MRI: Rectal cancer
CT: Liver metastases
Histopathology

Cancer under the microscope

- Prognosis and treatment
- Pathological staging pTNM
- Grading: G1/2/3
- Immunohistochemistry
Diagnosis & Management plan

Multidisciplinary Team Meeting

- MDT clinicians present
- TNM staging
- Histology
- Treatment plan
- Time to Treatment: TTT-31 days
Treatment Targets

1. Urgent GP referral
2. First seen for suspected cancers
3. Diagnostic phase (CT, MRI, endoscopy, biopsy etc.) and MDT
4. Decision to treat made
5. First definitive treatment

14 days

31 days for all cancers

62 days for all cancers from urgent GP referral

Source: Department of Health 2008
Delay in Diagnosis
Basic structure of arguments

Opinion on earlier tumour status
- **TNM stage**
- Grade
- Other biological factors-PSA level, ER and HER2 status
- In situ components

Earlier TNM stage based on:
- Clinical experience
- Known natural history-literture based and individual tumour information
- Back extrapolation of size of tumour
Tumour Growth & delay in Diagnosis

Below this line the tumour mass is not seen on scan

The slope of this line is the growth rate-steep for faster and shallower for slower

Growth slows as tumours get very large and necrotic
# Half empty glass

## Natural History of Growth

<table>
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<tr>
<th>Doublings</th>
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<th>Diameter</th>
<th>Detection</th>
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<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>10 µm</td>
<td>microscopic</td>
</tr>
<tr>
<td>20</td>
<td>$1 \times 10^6$</td>
<td>1 mm</td>
<td>microscopic</td>
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<tr>
<td>30</td>
<td>$1 \times 10^9$</td>
<td>1 cm</td>
<td>Detectable XR</td>
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<tr>
<td>35</td>
<td>$1 \times 10^{10.5}$</td>
<td>3 cm</td>
<td>Average Diagnosis</td>
</tr>
<tr>
<td>40</td>
<td>$1 \times 10^{12}$</td>
<td>10 cm</td>
<td>Death</td>
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</tbody>
</table>
Back extrapolation calculation

**Volume doubling time**: Literature average or individual serial measurements. Plus reality check
Volume doubling time

Based on literature based assessments

Or

Serial clinical measurements with no intervening treatment
Earlier nodal disease

- Based on nodal status at diagnosis
- Back extrapolation more difficult as clumps of cells and exiting cells
- Clinical experience
- Disease free interval
- Probability of spread to nodes based on T stage and prognostic factors
Earlier Metastatic disease

• Often extent of clinical metastatic disease can be underestimated

• Important to consider subclinical disease
Growth rate of metastases

• **Back extrapolation technique**

  Using known or literature based-only go so far
  Unknown use x2 primary growth rate

• **Disease free interval**

  Time to image metastases following resection
  = growth rate of subclinical disease

Gray et al 2007
Pitfalls in Back extrapolation of tumour

T stage

• Based on mathematical models of tumour biology – exact figure v.s broad guide

• Reality check from subsequent natural history

• Poor understanding of biology and mathematics confused with invalidity

• Concept vs maths. VDT vs growth rate
Estimate Previous TNM stage

- Know Clinical/pathological/subclinical TNM

- Treatment strategy at MDT based on TNM/prognostic factors - need guidelines

- M is rarely curable

- Prognosis based in TNM/prognostic factors/literature
Treatment of Cancer
-and results of delay in diagnosis
Development of surgery
Surgery

- 50% patients cure by surgery
- Open/laparoscopic/endoscopic/robotic
- Complete resection needed R0 (not R1 or R2)
- Complications of surgery
  - Premature death
  - Not allowing adjuvant therapy
  - Anastomotic leak
Adjuvant Therapy

• Definition
  – Treatment given at the same time as primary treatment

• Treatment of micro-metastatic disease

• Improves local control – Gynea/rectal/breast

• Improves survival-breast/colon

• Radiotherapy /chemotherapy/hormone
Radiotherapy

External Beam Radiotherapy

Brachytherapy
Medico Legal Issues: Radiotherapy

• Acute late side effects
  ——5% severe
• Given incorrectly
  ——IMER guidelines and regulations/medical physicists
• Overdose to critical structures
• Given unnecessarily
Medicolegal Issues: Chemotherapy

• Too late-delay in diagnosis
• Not given, given
• Over-dosage
• Toxicity of individual agents
• Acute side effects
• Long term side effects
Other Therapy

Hormone Therapy
• Breast and prostate

Immunotherapy
• Significant developments in melanoma
Prognosis and Life expectancy
Prognosis Issues:
Survival Rates

- TNM used to express the probability of survival (with range)
- For most legal cases 5 year survival without disease is taken as "cure", as probability of relapse after is < 50%. Some not
Web based tools to predict survival

Patient name
Age at diagnosis: 45
Mode of detection: Screen-detected
Tumour size: 40 mm (blank if unknown)
Tumour grade: 2
Number of positive nodes: 6
Overall survival at five and ten years (percent)

- Additional benefit of adding Trastuzumab to adjuvant chemotherapy and hormone therapy
- Additional benefit of adding adjuvant chemotherapy to adjuvant hormone therapy
- Benefit of adjuvant hormone therapy
- Benefit of adjuvant chemotherapy
- Survival with no adjuvant treatment
Life Expectancy
JD vs Mather 2012 EWHC 3063 (QB)
Conditional survival

- Prognosis at diagnosis vs prognosis at a later time
- Assess when most recurrences occur
- Loss of LE may disappear over time
When claims difficult to defend

Failure of Care

• Guidelines not adhered to
• Serial radiology is available
• Results not acted on
• There has been a SUI report identifying failure
When claims difficult to defend

Causation

• Incorrect treatment given
• Delays starting treatment (31 day ITT)
• Significant delay in diagnosis (often years)
  – tumour would have been pre-invasive
  – significantly different TNM stage eg not metastasised.
• Cant always trust SIR
Change in case profile - related to change in NHS last 10 years

Hospital

• Increase in administrative failure
  - Cancelled appointment/tests
• Results not communicated to team
• Lack of continuity of care
• Failure of responsibility e.g. MDT meeting
• X-rays not routinely reported

GP

• Interpretation of guidelines
References

Cancer and the Law: Waxman and Simons

Treatment of Cancer: Price & Sikora 6th edition on line

http://cancerhelp.cancerresearchuk.org/about-cancer/

http://www.cancer.gov/statistics/glossary

www.actionradiotherapy.org