Cancer of Unknown Primary

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- What is Cancer of Unknown Primary?
- What problems do CUP patients have?
- How should CUP be managed?
- A faster, slimmer, better MDT for CUP
What is Cancer of Unknown Primary?

- A very common, but neglected condition
  - 4% of all cancers
  - 13,000 cases annually in UK

- **BUT**: “CUP” is an imprecise term which fails to recognise the spectrum between initial presentation and final diagnosis

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**New Definitions**

Based on clinical course, clinical findings and outcome of investigations, over time

- **Malignancy of undefined origin** (MUO): Detection of metastatic malignancy on clinical examination or by imaging, without an obvious primary site
- **Provisional CUP**: Metastatic malignancy on histology. No primary detected despite initial investigations. Specialist review and possible further investigations pending
- **Confirmed CUP**: Metastatic malignancy on histology. Specialist review and all relevant investigations complete. No primary detected.
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### CUP is common

- 4% of all cancers in UK = 13,000 cases / yr
- 8% of cancer deaths in UK
- 4\textsuperscript{th} most common cause of cancer death
  - Lung 34,500 deaths annually
  - Colorectal 16,000 deaths annually
  - Breast 12,500 deaths annually
  - CUP 12,000 deaths annually
CUP is common

• 4% of all cancers in UK = 13,000 cases / yr
• 8% of cancer deaths in UK
• 4th most common cause of cancer death
  – Lung    34,500 deaths annually
  – Colorectal 16,000 deaths annually
  – Breast   12,500 deaths annually
  – CUP      12,000 deaths annually

MUO is very common

The MUO + CUP MDT will be busy!
What is Cancer of Unknown Primary?

- Two cases to illustrate the problem

Case 1 – HS

- ♀ 34
- 8/09: RUQ pain
- CT – Multiple liver metastases, no primary
Case 1 – HS

- ♀ 34
- 8/09: RUQ pain
- CT – Multiple liver metastases, no primary
- All serum markers normal
- OGD = NAD
- Mammograms = NAD
- Liver biopsy
  - “Adenocarcinoma ?Upper GI ?pancreatic”
H.S. Female 34.
Needle biopsy of liver.
Hospital number F2916xx; biopsy number F12751/xx

• CK7, CEA positive

• CK20, TTF-1, ER, Hep Par 1, neuroendocrine markers all negative

• “Suggestive of an upper GI or pancreatice-biliary origin”

Case 1 - HS - Management

• Empirical EOX for presumed “upper GI 1°”

• Progressive disease
Case 1 - HS - Management

- Empirical EOX for presumed “upper GI 1°”
- Progressive disease
- ? pancreatico-biliary on histology review
- 2nd line Gemcitabine – static disease 3/12
- 3rd line phase I study
- 4th line Tamoxifen. No response

Case 2 – JW

- ♀ 50
- 6/08 – Upper abdominal pain, anaemia
Case 2 – JW

• ♀ 50
• 6/08 – Upper abdominal pain, anaemia
• CT: liver mets, retroperitoneal nodes 5x5cm

• Biopsy – Adenocarcinoma, “? GI origin”
• All serum tumour markers normal
• PET-CT: no primary identified
• OGD negative
• Colonoscopy negative
Case 2 – JW

- ♀ 50
- 6/08 – Upper abdominal pain, anaemia
- CT: liver mets, retroperitoneal nodes 5x5cm
- Biopsy – Adenocarcinoma, “? GI origin”

- All tests for primary were negative – True CUP
- Oxaliplatin + Capecitabine chemotherapy
- Complete remission January 2009
- No relapse since end of treatment 36 months ago

What is Cancer of Unknown Primary?

- Clinical overview
  - In general, outcomes are very poor
  - Avoid extensive tests which will not help
  - Recognise limitations of treatment
  - Recognise “treatable syndromes”
  - Recognise frequent need for symptom control
• What is Cancer of Unknown Primary?

• **What problems do CUP patients have?**
  • How should CUP be managed?
  • A faster, slimmer, better MDT for CUP

The problems with CUP / MUO…

• Lack of agreed definitions of the clinical entity.
• No referral guidelines for suspected cancer relevant to patients without an obvious or strongly suspected primary.
• No system to rapidly identify patients and to ensure early specialist review.
• Lack of efficient arrangements to manage the initial diagnostic phase.
• Uncertainty about appropriate tests, including the use of new technologies.
• Lack of a team structure to efficiently care for newly presenting patients.
• Insufficient specialist oncology expertise.
• Lack of dedicated key workers or specialist nurses.
• Referral to inappropriate site-specific cancer teams.
• Lack of support and information for patients.
• Delays in involvement of specialist palliative care.
• Lack of an overall organisational structure to ensure high-quality care.
• Uncertainty about optimal treatment.
• Lack of adequate epidemiology data.
• No research or research organisation
• JC – ♂ – age 78 – at a hospital near here…
  • 6/10/11 – Life threatening GI bleed – IP under cardiology
  • 6/10/11 – CT: malignant mediastinal nodes, no primary seen
  • 8/10/11 – OGD – blood in stomach, colonoscopy NAD
  • 17/10/11 – “Referral” to Upper GI MDT by cardiologist
  • 17/10/11 – Upper GI MDT suggest biopsy. EUS referral
  • 20/10/11 – Discharged. 1 month FU in cardiology. No CNS
  • 2/11/11 – EUS: FNA + biopsy. Limited information to patient
  • 2/12/11 – Cardiology OP. “FNA cytology negative”
  • 6/12/11 – Bone marrow
  • 12/12/11 – Upper GI MDT – no histology results available
  • 19/12/11 – Review of new CT by UGI MDT
  • 20/12/11 – Seen by GI physician. “For Mediastinoscopy”
  • 10/1/12 – Lung MDT: surgeon to book mediastinoscopy!!!!!

There has to be a better way!
• JC – ♂ – age 78 – the near future….
  • 6/10/11 – Life threatening GI bleed – IP under cardiology
  • 6/10/11 – CT: malignant mediastinal nodes, no primary seen
  • 7/10/11 – OGD, colonoscopy planned
  • 7/10/11 – Referral to CUP Team
  • 8/10/11 – Seen on the ward by CUP CNS within 24 hours
  • 8/10/11 – OGD – blood in stomach, colonoscopy NAD
  • 9/10/11 – CUP Team review. EUS / biopsy advised
  • 9/10/11 – Discharged with CUP CNS contact
  • 14/10/11 – EUS / FNA / biopsy
  • 18/10/11 – Results pursued by CNS. Non-diagnostic
  • 18/10/11 – CUP Team discussion - For Mediastinoscopy
  • 25/10/11 – Mediastinoscopy and biopsy
  • 29/10/11 – Results pursued. Lymphoma. FT Haem appt.

What problems do CUP patients have?

Top 5 problems

• No-one “owns” MUO / CUP patients
• There are no CUP specialists or CNSs
• Care is ad hoc, fragmented, disorganised
• Wrong tests in the wrong patients, too slowly
• Lack of support and information
• What is Cancer of Unknown Primary?
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• **How should CUP be managed?**
• A faster, slimmer, better MDT for CUP

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**How should CUP be managed?**

• **Recognise the problems**
  – Including

  • No-one “owns” MUO / CUP patients
  • There are no CUP specialists or CNSs
  • Care is ad hoc, fragmented, disorganised
  • Wrong tests in the wrong patients, too slowly
  • Lack of support and information

• **Devise a new, better system to meet gaps**
How should CUP be managed?

• NICE CUP Guideline (2010)
  – Put CUP on a “site-specific” footing
  – Deliver specialist care as for other sites
  – Understand limitations of treatment
  – Improved clinical system – faster, slimmer

Key Components of CUP Care

• Clinical “site-specific” organisation at hospital level
• Limited, appropriate investigation
• Rapid specialist decision making
• High quality, timely palliative care
• CNS support and information
Key Components of CUP Care

- Formation of CUP teams in all hospitals
  - Oncologist
  - Palliative care physician
  - CUP specialist nurse
  - Radiology and Pathology links

- Prompt assessment of patients by CUP team
  - Advise on management plan / investigations
  - Symptom control / psychological support
  - Provide information to patient
  - Act as patient advocate / liaise with other teams & GP

Organisation of CUP Services
At Network level

• Set up Network CUP MDT
  – Review difficult cases
  – Lead on treatment of Confirmed CUP
  – Facilitate clinical trials

• Set up Network CUP Site Specific Group
  – Oversee formation of CUP teams / Network MDT
  – Ensure local pathways in accordance with Guideline
  – Maintain database / undertake audit

Why the CUP SSG should be separate from the Acute Oncology SSG

KNOWN SITE
Non-acute presentation of known site cancer
Routine diagnostic testing and subsequent management
Known site cancer presenting acutely

MUO / CUP
Non-acute presentation of MUO
Routine diagnostic tests and subsequent management

ACUTE ONCOLOGY
Management of multiple other AO presentations and conditions*

*MSCC, treatment toxicity, symptom control, complications of known cancer, admission avoidance
Principles of Treatment

- Expert CUP management involves distillation of all the clinicopathologic features to define a “tissue-like” diagnosis

- New, major diagnostic role for Oncologists
Principles of Treatment - 2

• It’s just metastatic adenocarcinoma stupid…..

Principles of Treatment - 3

• It’s just metastatic adenocarcinoma stupid…..
  – Know limits of what is achievable in known-site disease
  – Then reduce expectations by about 50%
    • Poor performance status
    • Lack of certainty about organ of origin
    • ? Specific poor responsiveness of CUP ?
  – Then discuss aims and limitations with the patient
Selecting Treatment

• Special clinical entities
• Recognised “chemotherapy treatable syndromes”
• Confirmed CUP without special features

Special clinical entities

– Axillary nodes containing adenocarcinoma
– Squamous carcinoma in upper or mid-neck nodes
– Squamous carcinoma in inguinal nodes
– Solitary metastases
  • Avoid investigation which may compromise outcome
  • Consider radical treatment
Systemic treatment - 1

- Recognised “chemotherapy treatable syndromes”
  - Midline disease, poorly differentiated carcinoma
    - Consider treating as extragonadal germ cell tumour
  - Women with peritoneal adenocarcinoma
    - Consider treating as ovarian cancer

Systemic treatment - 2

- Other Confirmed CUP (ie no recognised “treatable syndrome”)
  - No trial evidence to support benefit from chemotherapy
    - However, some patients respond well
  - Poor outcomes from treatment overall
  - Specialist MDT / peer discussion helpful
    - Includes involvement of palliative care specialist in discussions
  - Consider trials
Key recommendations

• In confirmed CUP
  – Specialist management is required
  – Know when to stop investigation
  – Aim to “distill” a “tissue-like” diagnosis
    • This is complicated, so don’t rush, discuss, and think twice!
  – Have conservative expectations about outcome
  – Explain diagnosis and limitations of treatment honestly
  – Involve palliative care throughout
  – Recognise special presentations and treatable syndromes
  – Consider trials

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Now - there is a better way

A faster, slimmer, better MDT….

• Real-time working, NOT week-to-week meetings

• Acute Oncology reinforces this new approach

• Rapid, easy referral process – email to AO hub

• Prompt input of oncology + palliative care expertise

• EPR for Team communication + record keeping
“MDT v.2”

• What we need:
  • Accurate, comprehensive data collection
  • Efficient organisation
  • Tracking patients on more rapid pathways
  • Seamless, easy communication
  • Effective liaison between CUP Team
  • (Re-engineering of other traditional MDTs)

MDT v.2

• What we need:

COORDINATION
MUO / CUP – the future of MDTs

• 2012 CUP Measures mandate this new approach
• Efficient coordination of a lithe, slim Team
• Development of real-time “Virtual” MDT meetings
• MDT Coordinator integral to effective functioning

Now - there is a better way