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

New Definitions

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

Malignancy of undefined origin: Detection of metastatic malignancy on clinical examination or by imaging, without an obvious primary site — **MUO**

↓

Provisional CUP: Metastatic malignancy on histology.
No primary detected despite initial investigations.
Specialist review and possible further investigations pending

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Confirmed CUP: Metastatic malignancy on histology.
Specialist review and all relevant investigations complete.
No primary detected. — **CUP**

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CUP

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

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The MUO + CUP MDT will be busy!

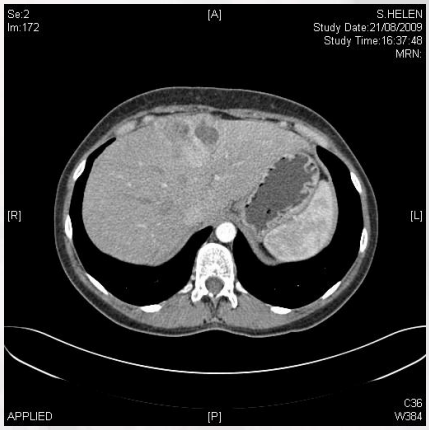
What is Cancer of Unknown Primary?

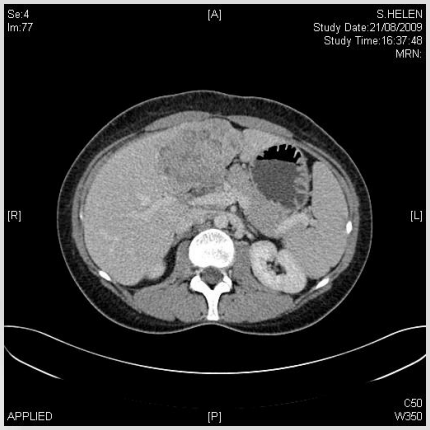
- Two cases to illustrate the problem

Case 1 – HS

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

Case 1 – HS





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 pancreatico-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

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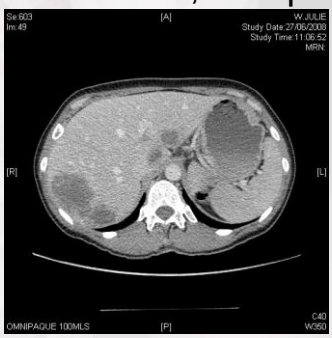
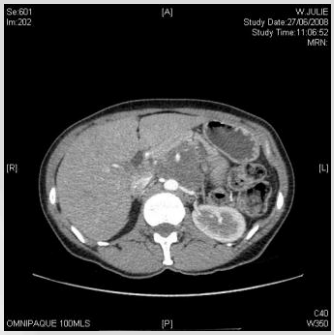
- CT: liver mets, retroperitoneal nodes 5x5cm





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?
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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?

- 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

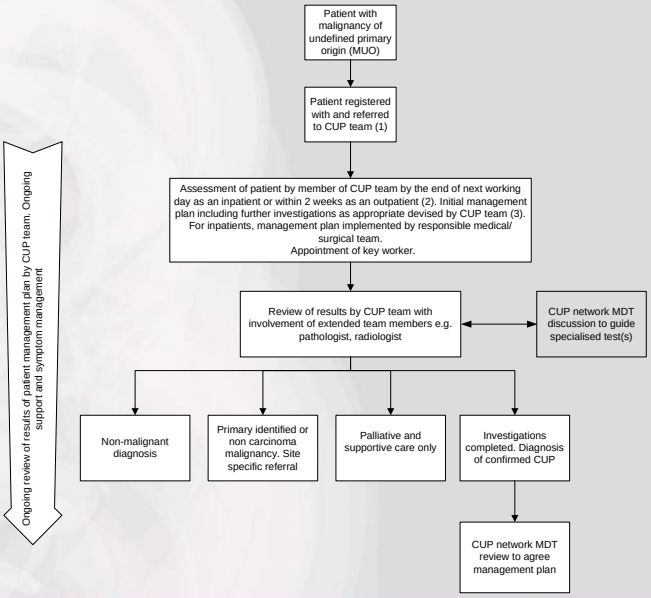
Key Components of CUP Care

- 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

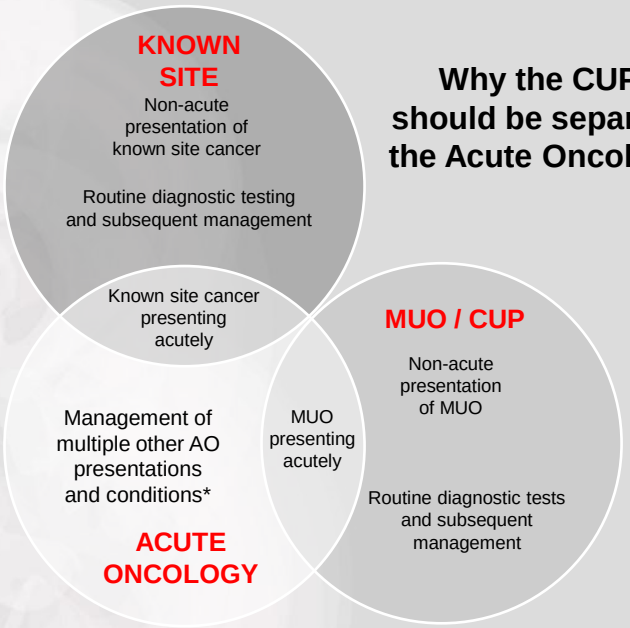
Organisation of CUP Services



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



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

Principles of Treatment

Principles of Treatment - 1

- 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

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