
- 245 patients UM screened at diagnosis with FBC, LFT, CXR, Abdo US (only those undergoing enucleation
- Positive predictive value of liver ultrasound and CXR 100%, sensitivity poor 14% and 2% respectively
- LFTs had a positive predictive value of <50%
- Recommend staging all patients with CXR and liver ultrasound

- Good American review article:

Prospective cohort of 52 patients with primary UM staged with PET/CT
- 2 of 52 (3.8%) had metastatic disease detected with PET/CT
- 7 of 52 (13.4%) had benign inflammatory lesions detected with PET/CT detected using known SUVs
- False positive’s in 3 of 52 (6%) (investigated further with CT/MR/biospy)
- The detection of metastatic disease at diagnosis influences management. This is particularly important in patients with large choroidal melanomas in eyes that are not painful, where enucleation can be avoided.


Two randomised controlled trials medium and large uveal melanoma
- Among 7,541 patients screened for COMS trials, only 70 (<1%) had metastatic melanoma detected at the time of staging.
- Staging with LFTs and CXR (if LFTs abnormal liver imaging performed)
- The value of at least one abnormal LFT in predicting metastatic disease
- Sensitivity 14.7%, Specificity 92.3%, Positive predictive value 45.7%, Negative predictive value 71.0% (Alk Phos most useful)
- Conclusion UM patients should undergo screening with serial LFTs and CXR at baseline

I Kaiserman, R Amer, J Pe’er, Liver Function Tests in Metastatic Uveal Melanoma AJO Feb 2004

Retrospective cohort 30 patients with metastatic disease cf 80 controls
- Trends in liver enzyme changes at 36/24/12/6 months prior to diagnosis of metastatic disease
- All except bilirubin rose at least 6 months prior to detection of mets. Many stayed within normal range
- Supports need for staging LFTs
PREOPERATIVE STAGING OF UVEAL MELANOMA IN THE LONDON OCULAR ONCOLOGY SERVICE (2007-2011)

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Aim

• To report the incidence of metastatic disease at preoperative staging for uveal tract melanoma
• To correlate the incidence of metastatic disease with operation performed
• To assess the value of preoperative staging investigations.
Current Staging Protocol

• All patients receive a liver function test, chest x-ray and an abdominal ultrasound scan.

• Positron emission tomography (FDG/PET/CT) scan or Computed Tomography (CT) are performed if abdominal ultrasound results are abnormal.
Methods

• Single centre study - St Bartholomew’s Hospital
• All patients undergoing primary treatment for a new diagnosis of uveal tract melanoma
• Retrospective data analysis of the digital patient record
• Time period 2007 to 2011
Over 5 years, 911 patients underwent surgical treatment for uveal tract melanoma
Surgical procedures 2007-2011

- Plaque brachytherapy: 57%
- Enucleations: 40%
- Exenterations: 0.2%
- Insertion of tantalum markers: 3%
31 PATIENTS HAD METASTASES AT DIAGNOSIS (3.4%)
Patients with metastases at diagnosis 2007-2011

In 2007 50% of the surgery was undertaken at Moorfields.

Total number of patients with metastases 31/911 (3.4%)
Patients with metastases at diagnosis according to operation
Five year summary data

<table>
<thead>
<tr>
<th>Operation</th>
<th>Normal</th>
<th>Metastases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enucleation</td>
<td>336</td>
<td>28</td>
</tr>
<tr>
<td>Plaque</td>
<td>515</td>
<td>3</td>
</tr>
</tbody>
</table>

7.7% vs. 0.6%
## Abnormal Liver function tests

<table>
<thead>
<tr>
<th>Liver function test</th>
<th>Number of patients</th>
<th>Percentage abnormal</th>
</tr>
</thead>
<tbody>
<tr>
<td>γGT</td>
<td>74/860</td>
<td>8.6%</td>
</tr>
<tr>
<td>ALT</td>
<td>55/860</td>
<td>6.4%</td>
</tr>
<tr>
<td>Total bilirubin</td>
<td>53/860</td>
<td>6.1%</td>
</tr>
<tr>
<td>ALP</td>
<td>46/860</td>
<td>5.3%</td>
</tr>
</tbody>
</table>
• 40% (12/31) patients with metastatic disease had normal LFTs

• Of the remaining 19:
  • **Alkaline phosphatase** increased in 4 cases all with widespread metastases including bone involvement.
  • **γ-GT** was found increased in 2 cases all with widespread metastasis
  • Abnormal liver function tests in the remaining cases
Abdominal ultrasound results

Number of patients 837/911 (92%)

Normal or other 542/837 64.83%

Hepatic cyst 52/837 6.21%
Hepatic metastases 12/837 1.43%
Hepatic hemangioma 7/837 0.80%
Fatty degeneration 113/837 13.52%
Gall bladder calculi 47/837 5.61%
Kidney cyst 18/837 2.10%
Suspicious lesions 46/837 5.51%
• Abdominal ultrasound detected liver metastases in 40% of cases with metastases (12 out of 31)

• 46 patients required additional imaging as abdominal ultrasound was inconclusive
Additional imaging required

• **CT scans** (thorax and abdomen contrast enhanced and triple phase liver scans) were requested throughout 2007-2011 as additional imaging

• **PET/CT scans were introduced in 2009.**
Additional imaging results (46 patients)

- Metastases: 16/46 (35%)
- No metastases: 30/46 (65%)
CT scans 2007-2011
Total number of patients 77/911 (8.45%)

- Normal or other: 40%
- Metastases: 30%
- Liver cyst: 5%
- Fatty change: 3%
- Gall bladder calculi: 3%
- Mediastinal disease: 1%
- Adrenal adenoma: 5%
- Renal neoplasm: 5%
- Splenic hemangioma: 1%
- Pleural effusion: 2%
- Inconclusive: 5%
CT scans 2007-2011
Profile of metastases detected

- Liver (14/19) 74%
- Bone (2/19) 11%
- Lung (1/19) 5%
- Colon (1/19) 5%
- Peritoneum (1/19) 5%
PET scan results 2007-2011

Number of patients 207/911 (22.7%)

- Normal or other 153/207 (81%)
- Metastases 18/207 (9%)
- Pulmonary nodule 7/207 (4%)
- Liver hemangioma 2/207 (1%)
- Liver cyst 5/207 (3%)
- Liver cirrhosis 1/207 (1%)
- Subpleural nodule 2/207 (1%)
# PET scan results 2007-2011

Profile of metastases detected

<table>
<thead>
<tr>
<th>Location</th>
<th>Count/Total (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver metastases</td>
<td>14/207 (6.8%)</td>
</tr>
<tr>
<td>Cervical node metastasis</td>
<td>1/207 (0.5%)</td>
</tr>
<tr>
<td>Adrenal metastasis</td>
<td>1/207 (0.5%)</td>
</tr>
<tr>
<td>Bone metastases</td>
<td>1/207 (0.5%)</td>
</tr>
<tr>
<td>Lung metastases</td>
<td>1/207 (0.5%)</td>
</tr>
</tbody>
</table>
• Only 0.6% of patients scheduled for brachytherapy (7mm height and 17mm diameter) had metastatic disease

• Should preoperative staging be done for patients scheduled with plaque brachytherapy?
• 53% of patients with metastatic disease required additional imaging such as CT or PET/CT scans. LFTs were normal in 40% of patients with metastases.

• Should the current staging protocol change?

Who should have staging?

Current practice
- London stage everyone
- Sheffield stage everyone
- Liverpool stage only those with tumour >17 mm in diameter

Summary of evidence (question answered in only 2 of 722 articles sifted)
Incidence of metastases
COMS 2004  (1%) 70 of 7,5241 UMs 1987-1998
Finger 2005  (3.8%) 2 of 52 UMs 2003-2005
Cohen et al  (3.4%) 31 of 911 UMs 2007-2011 (unpublished data)

Incidence of metastases according to tumour size
Damato 10% for MM >17mm diameter (personal communication)
Cohen 7.7% for MM >17mm diameter or >6mm height unpublished data)
0.6% for MM <17mm diameter or <6mm height
How should we stage?

Current practice
London    CXR, LFTs, Abdominal ultrasound and PET/CT for MM >4mm
Sheffield CXR, LFTs, Abdominal Ultrasound
Liverpool LFTs, Abdominal Ultrasound only for MM >17mm diameter

Evidence from 3 papers in 722 sift
LFT’s high specificity low sensitivity (COMS, Hicks et al) fluctuation over time predicts onset of mets (Kaiserman et al)
CXR 100% specificity 2% sensitivity (Hicks et al)
MR no data for staging
Abdo U/S 100% specificity, 14% sensitivity (Hicks et al)
    Detected liver metastases in 40% (12 of 31) of cases with metastases (unpublished data)
PET/CT high specificity, false positives in 6% (Finger et al)

IGOR KAIERMAN, RADGONDE AMER,JACOB PE’ER, MD. Liver Function Tests in Metastatic Uveal Melanoma  AJO Feb 2004