CHOLANGIOCARCINOMA (CCA)

Deepak Hariharan
MD (Research), FRCS,
Locum Consultant HPB Surgeon
AIM

Outline essential facts & principles

Present 4 cases

Discuss - Challenges / Controversies
INTRODUCTION

Most common biliary tract malignancy

2nd most common primary hepatic malignancy

15-20% of all HPB malignancy

13% of cancer related deaths are due to HPB cancers
RISK FACTORS

• ESTABLISHED
  Choledochal cyst / Carolis disease
  Liver flukes
  Hepatolithiasis
  PSC
  Toxin - Thorotrast

• OTHERS
  Age, obesity, diabetes, HBV, cirrhosis
95% adenocarcinomas
mucin expressing desmoplastic stroma
CLINICAL PRESENTATION

- iCCA
  
  19-43% incidental,
  symptoms advanced disease
  (25% vs 58% resected asymptomatics)

- pCCA & dCCA
  
  Painless Jaundice / weight loss - 90%
DIAGNOSTIC TOOLS

- **CROSS-SECTIONAL IMAGING**
  - CT chest / abdomen - Liver triple phase
  - MRI liver / MRCP
  - PET

- **ENDOSCOPY**
  - ERCP, EUS, Cholangioscopy-Spyglass

- **PTC**

- **CYTOLOGY / BIOPSY**

- **STAGING LAPAROSCOPY**
MANAGEMENT

• SURGERY only treatment offering cure
• Large Majority have advanced unresectable disease

Contraindications -
  patient unfit for GA
  Metastatic disease
  Multifocal disease
  Bilateral arterial / venous encasement
  Inadequate Future liver remnant
CASE 1

64/F
Painless Jaundice 2 weeks
No weight loss
Weight 55 kgs

PMH - fit and well

Hb12.4, WCC-5.3
U&Es normal
Bilirubin - 121, Alp369, ALT-219
CA19-9 - 73.8

What next?
Contrast: Omnipaque 100mls
Gantry: 0°
Time: 500 ms
Slice: 1.5 mm
Couch: 573.6
Pos: FFS
FoV: 377 mm

100 kV
F: B20f
Image 120 of 373
Abdo/Pelvis 1.5
22/05/2018, 11:02:29
DIAGNOSTIC DILEMMA

• Benign Vs Malignant
  Presentation
  IgG4 levels
  CA 19-9

• Non PSC biliary stricture
  CA19-9 <100 U/L NPV of 92%

• In PSC patients
  CA19-9 < 129 U/L
  PPV of 57% & NPV of 99% for CCA
Cancelled ERCP, organised PTC and triple phase CT liver and chest

No aberrant vascular anatomy
RHA encased,
No hilar mass or metastases
BISMUTH CORLETTE - pCCA
PREOPERATIVE RESULTS

PTC biopsy - moderately differentiated adenocarcinoma

FLR - CT volumetry -
S1 - 4 - 495ml
S2 & 3 - 341ml

Calculation of adequate volume?
5x55kg = 275ml or 0.3(191.8+18.51x55)=363ml

No functional assessment of liver function done

Staging laparoscopy - clear

No PET scan
What surgery?
Caudate lobe?
Extd lymphadenectomy - Coeliac, SMA, Aortic

Dated within 40 days of presentation

Surgery Done -

Periportal Lymphadenectomy, extra hepatic biliary excision, Right hepatectomy, caudate lobe excision, Frozen section of left duct and left Hepatico-Jejunostomy

Complications?
LOS - 18 days
SOB - Right chest clear effusion drained
Histology - T2No R0

Survival - R0 and Nodal state
Adjuvant chemo ?
ADJUVANT THERAPY - BILCAP TRIAL

>80% of patients followed up for 36 months

- **Median OS**
  - **Capecitabine**: 51.1 (34.6, 59.1) months
  - **Observation**: 36.4 (29.7, 44.5) months
  - **HR (95% CI)**: 0.81 (0.63, 1.04)
  - **p = 0.097**

Sensitivity analyses adjusting prognosticators:
- **HR 0.70 95% CI (0.55, 0.91)**: p = 0.007

$Nodal status, Disease Grade, Gender
CASE 2

81 /F
ongoing pain in the RUQ
Non quantifiable weight loss

PMH - osteoporosis, Hypercholesterolemia

Hb-12.3, WCC-7.7
U&Es Normal
Bilirubin 5, ALT22, ALP184
Hep screen - Negative

CA19-9 - 2687
AFP3.4

What next?
Heterogenous contrast enhancement, no wash out in PV/delayed phases
WHAT NEXT?

PROGNOSIS - Tumour number, grade, nodal disease, vascular invasion
Tumour Size - controversial

Anaesthetic fitness -
Mortality 3.3, morbidity 55%

Staging laparoscopy done no mets PET not done

SURGICAL PLANNING -
? Do u routinely resect caudate, extent of lymphadenectomy
OPERATIVE FINDINGS:
1) Big left lobe tumour S 2, 3 and 4;
2) pressing on top of middle hepatic vein.
3) Caudate lobe is free from tumour - preserved.

OPERATION:
Extended left Hepatectomy as middle vein taken

LOS - 8 days

HISTOLOGY:
-Intrahepatic cholangiocarcinoma, 109 mm
-No vascular invasion or perineural infiltration
- completely excised
- pT1b N0 R0

Referred for Chemotherapy
CASE 3

67F
Obstructive Jaundice & weight loss 6 weeks

PMH - Open cholecystectomy
endometrial cancer and had a hysterectomy

Bilirubin 243
Biliary cytology inconclusive
Double duct sign
CA 19 -9 - NA

Options - ?
dCCA

- Pancreateo duodenectomy with reconstruction

HISTOLOGY Poorly differentiated cholangiocarcinoma of the common bile duct. T2N1 (2 of 22 lymph nodes)

LOS - 8 days

Referred for chemo - on Capecitabine
<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Case, n</th>
<th>R0, %</th>
<th>Morbidity, %</th>
<th>Mortality, %</th>
<th>5-Year survival, %</th>
<th>R0 5-year survival, %</th>
<th>N+ 5-year survival, %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>iCCA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weber <em>et al.</em></td>
<td>2001</td>
<td>33</td>
<td>88</td>
<td>19</td>
<td>3.9</td>
<td>31</td>
<td></td>
<td>25 (at 3-year)</td>
</tr>
<tr>
<td>Morimoto <em>et al.</em></td>
<td>2003</td>
<td>49</td>
<td>69</td>
<td>35</td>
<td>3.8</td>
<td>32</td>
<td></td>
<td>41</td>
</tr>
<tr>
<td>DeOliveira <em>et al.</em></td>
<td>2007</td>
<td>44</td>
<td>45</td>
<td>35</td>
<td>4.5</td>
<td>40</td>
<td></td>
<td>63</td>
</tr>
<tr>
<td>Konstadoulakis <em>et al.</em></td>
<td>2008</td>
<td>54</td>
<td>78</td>
<td>11</td>
<td>7.0</td>
<td>25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Choi <em>et al.</em></td>
<td>2009</td>
<td>64</td>
<td>86</td>
<td>22</td>
<td>1.6</td>
<td>40</td>
<td></td>
<td>54</td>
</tr>
<tr>
<td>Lang <em>et al.</em></td>
<td>2009</td>
<td>83</td>
<td>64</td>
<td>44</td>
<td>7.1</td>
<td>21</td>
<td></td>
<td>30</td>
</tr>
<tr>
<td>Murakami <em>et al.</em></td>
<td>2011</td>
<td>21</td>
<td>62</td>
<td></td>
<td></td>
<td>37</td>
<td></td>
<td></td>
</tr>
<tr>
<td>de Jong <em>et al.</em></td>
<td>2011</td>
<td>449</td>
<td>81</td>
<td></td>
<td></td>
<td>31</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ribero <em>et al.</em></td>
<td>2012</td>
<td>434</td>
<td>85</td>
<td>35</td>
<td>5.3</td>
<td>33</td>
<td></td>
<td>40</td>
</tr>
<tr>
<td><strong>pCCA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DeOliveira <em>et al.</em></td>
<td>2007</td>
<td>281</td>
<td>19</td>
<td>62</td>
<td>5.4</td>
<td>10</td>
<td></td>
<td>30</td>
</tr>
<tr>
<td>Hirano <em>et al.</em></td>
<td>2010</td>
<td>146</td>
<td>87</td>
<td>45</td>
<td>3.4</td>
<td>36</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lee <em>et al.</em></td>
<td>2010</td>
<td>302</td>
<td>71</td>
<td>43</td>
<td>1.7</td>
<td>33</td>
<td></td>
<td>47</td>
</tr>
<tr>
<td>Ercolani <em>et al.</em></td>
<td>2010</td>
<td>51</td>
<td>73</td>
<td>51</td>
<td>9.8</td>
<td>34</td>
<td></td>
<td>44</td>
</tr>
<tr>
<td>Unno <em>et al.</em></td>
<td>2010</td>
<td>125</td>
<td>63</td>
<td>49</td>
<td>8.0</td>
<td>35</td>
<td></td>
<td>46</td>
</tr>
<tr>
<td>Shimizu <em>et al.</em></td>
<td>2010</td>
<td>172</td>
<td>66</td>
<td>44</td>
<td>6.4</td>
<td>29</td>
<td></td>
<td>39</td>
</tr>
<tr>
<td>Saxena <em>et al.</em></td>
<td>2011</td>
<td>42</td>
<td>64</td>
<td>45</td>
<td>2.4</td>
<td>24</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Young <em>et al.</em></td>
<td>2011</td>
<td>83</td>
<td>46</td>
<td>64</td>
<td>7.2</td>
<td>20</td>
<td></td>
<td>33</td>
</tr>
<tr>
<td>Murakami <em>et al.</em></td>
<td>2011</td>
<td>50</td>
<td>74</td>
<td></td>
<td></td>
<td>37</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Matsuo <em>et al.</em></td>
<td>2012</td>
<td>157</td>
<td>76</td>
<td>59</td>
<td>7.6</td>
<td>32</td>
<td></td>
<td></td>
</tr>
<tr>
<td>de Jong <em>et al.</em></td>
<td>2012</td>
<td>305</td>
<td>65</td>
<td></td>
<td></td>
<td>5.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nagino <em>et al.</em></td>
<td>2013</td>
<td>574</td>
<td>67</td>
<td>57</td>
<td>4.7</td>
<td>33</td>
<td></td>
<td>67</td>
</tr>
<tr>
<td><strong>dCCA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yoshida <em>et al.</em></td>
<td>2002</td>
<td>27</td>
<td>85</td>
<td>22</td>
<td>3.7</td>
<td>37</td>
<td></td>
<td>20</td>
</tr>
<tr>
<td>Sakamoto <em>et al.</em></td>
<td>2005</td>
<td>55</td>
<td>84</td>
<td></td>
<td></td>
<td>3.6</td>
<td>24</td>
<td>34</td>
</tr>
<tr>
<td>DeOliveira <em>et al.</em></td>
<td>2007</td>
<td>239</td>
<td>78</td>
<td>56</td>
<td>3.0</td>
<td>23</td>
<td></td>
<td>27</td>
</tr>
<tr>
<td>Shimizu <em>et al.</em></td>
<td>2008</td>
<td>34</td>
<td>-</td>
<td>21</td>
<td>2.9</td>
<td>45</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Murakami <em>et al.</em></td>
<td>2011</td>
<td>56</td>
<td>80</td>
<td></td>
<td></td>
<td>43</td>
<td></td>
<td>21</td>
</tr>
</tbody>
</table>
Case 4

72/F
Asymptomatic, Iron deficiency anaemia

PMH - Asthma and thorocotomy for cystic lung disease

Refused endoscopy

CT colonoscopy done

Bilirubin - 15, ALT15, ALP67
Persistent and unchanged dilatation of the left lobe intrahepatic biliary radicles with internal cast formation. No mass
Tumour markers, Hepatology screen, IgG4 all normal

DIFFERENTIAL -

a) intrahepatic papillary neoplasm of the biliary tract

a) intra-ductal cholangiocarcinoma

a) Underlying cholangiopathy, such as PSC & associated hepatolithiasis.
1) Wait and watch – surveillance
2) Spyglass cholangioscopy
3) Surgical resection

Cholangioscopy - Multiple stones within a dilated Segment III duct. No abnormality of biliary mucosa.

If symptomatic from these stones then she should have a lobectomy.
ORTHOTROPIC LIVER TRANSPLANT

1) iCCA - not a standard of care as recurrence - 35% - 75% and 5 yr survival 34 - 51%

2) pCCA - PSC/cirrhotics de novo hepatocarcinogenesis

Mayo clinic protocol stringent selection criteria neo-adjuvant chemo-radiation recurrence free 5 yr survival - 68%

OTHER TREATMENT OPTIONS CCA
Endoscopic, Percutaneous, Vascular, Radiation treatments

local control and increase survival in locally advanced irresectable CCA

Guidelines do not support its use

Palliative biliary metal stenting
referral for chemotherapy - Gemcitabine / Cisplatin based treatments
ABC o2 trial standard of care
CONCLUSION

• Aggressive disease with poor prognosis

• 5 yr survival possible with radical resection

• Diagnostic pathways need improvement and standardisation

• New trials needed

• Future molecular oncology – aid early diagnosis
SUMMARY SURGICAL CHALLENGES

pCCA

Complexity of Hilar anatomy

Assessment of tumour extent

Objective assessment of FLR

Technical demands of surgery
  Ro resections
  Extended Liver resection
  Vascular resections
  Simultaneous Pancreas & Liver resection
VITAL QUESTIONS

CPEX testing - all, selective or none

Biliary drainage - ? need and ERCP or PTC

Sampling - cytology / biopsy

Functional study - ICG clearance ?

Remnant Volume - PVE or no

Staging laparoscopy / PET - ? Value

Lymphadenectomy & caudate lobe resection - iCCA ?

Extended vascular / pancreatic & liver resections