Diagnosing Fibrolamellar Carcinoma
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Disclosure

• No conflicts of interest to disclose.
Utilization Management

As you view this presentation, you will see how PRKACA FISH can be appropriately used:

- To support diagnosis particularly in difficult cases and in small biopsies
- Guide clinical management
Objectives

• Describe a novel FISH test available from MML to assist in evaluation of primary liver carcinomas

• Describe our approach to the diagnosis of fibrolamellar carcinoma
• 32-year-old female
• 7.4-cm mass in right lobe of liver
• Invasion of the portal vein
Diagnosis: Fibrolamellar Carcinoma
Fibrolamellar Carcinoma is Positive for CK7 and CD68

Ross et al, Mod Pathol 2011
Fibrolamellar Carcinoma is Characterized by $\text{DNAJB1-PRKACA}$

- $\text{DNAJB1-PRKACA}$ identified initially in all FLC tested
- $\text{DNAJB1-PRKACA}$ is specific for FLC among primary liver tumors

$Graham$ et al, *Mod Pathol* 2015
Novel FISH Probe to Detect PRKACA Rearrangement

Normal Signal Pattern (2 fusion signals)
Abnormal Signal Pattern (1 green and 1 fusion signal)
Fibrolamellar Carcinoma Cases of FLC

- TMA
- 88 conventional HCC
- 6 fatty liver
- 7 normal liver

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• Independent histologic review
  • Typical FLC
  • Possible FLC
  • Unlikely FLC
• CK7 and CD68 performed
• PRKACA FISH performed

Graham et al, Mod Pathol 2015
Fibrolamellar Carcinoma

Typical
Fibrolamellar Carcinoma

Solid with intratumoral histiocytes
93 cases
All showed CK7 and CD68 expression
99% *PRKACA* rearrangement

Typical FISH pattern for *PRKACA*
Fibrolamellar Carcinoma

Possible FLC

Unlikely FLC
<table>
<thead>
<tr>
<th>Category</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases “possible FLC”</td>
<td>15 cases</td>
</tr>
<tr>
<td>PRKACA rearrangement</td>
<td>10 cases</td>
</tr>
<tr>
<td>CK7 and CD68 coexpression</td>
<td>9 cases</td>
</tr>
<tr>
<td>Cases “unlikely FLC”</td>
<td>6 cases</td>
</tr>
<tr>
<td>PRKACA rearrangement</td>
<td>0 cases</td>
</tr>
<tr>
<td>CK7 and CD68 coexpression</td>
<td>1 case</td>
</tr>
</tbody>
</table>

**PRKACA FISH**
PRKACA FISH is Useful for Diagnosis

- 93 cases where histology was typical
  - PRKACA FISH confirmed the diagnosis in 99% of cases
  - 1 negative FLC arose in the setting of the Carney Complex
  - Biallelic loss of PRKAR1A

- 21 cases where histology was not typical
  - PRKACA FISH allowed for accurate diagnosis in all 10 FLC

Terracciano et al, Arch Pathol Lab Med 2004
PRKACA Rearrangement is Specific for FLC

- No PRKACA rearrangement identified
  - Conventional HCC (N=113)
  - Fatty liver (N=6)
  - Normal liver (N=7)

Graham et al, Mod Pathol 2015
Conclusions

• Detection of PRKACA rearrangement by FISH (available from MML) is an excellent diagnostic tool

• Our approach to diagnosis of FLC:
  • Compatible morphology PLUS either
    • CK7 and CD68 coexpression
    • PRKACA FISH
Questions or requests…
Email to: MMLHotTopics@mayo.edu

For more information…
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