Morphology of liver diseases in The Gambia: first pathology report from the "Gambia Hepatitis Intervention Study"

International Agency for Research on Cancer
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Outline

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• Brief review of GHIS program
• Set up of the pathology workflow
• Observations during 4-Y period
Conflict of Interest

[ ] YES
[✓] NO
Liver cancer in *The Gambia*

- Reports from The Gambia, West Africa, in the 80s
  - Liver cancer, the most common malignancy
  - Curability rate near zero
  - Endemic infection with HBV
    - Very high rate of childhood infection with HBV
  - High prevalence of HBsAg carrier
  - High level of exposure to aflatoxin
  - Known association of aflatoxin and HCC from other areas with high incidence of HCC (Thailand)
The Gambian Hepatitis Intervention Study (GHIS)

- Large-scale vaccination program in The Gambia to be added to the expanded program of immunization (EPI), initiated in 1979
- National hepatitis B (HBV) vaccination of young infants over a 4-year period (stepped-wedge design), initiated in July 1986
- Cohort of 120,000 children, to receive/not-receive a course of HBV vaccine
- Installation of a national surveillance system to detect new cases of HCC and chronic liver diseases over 30 to 40 years
  - Site of BCG vaccination as a proxy for receiving HBV vaccine (application of two different sites)
  - Handprint and footprint of each child at 4 months
- Creation of a population-based cancer registry
IARC in charge of the pathology in 2015

- To access a reliable and continuous confirmed diagnosis of liver diseases
- To create a reliable pathology database to be linked with the other data
- To support the budget and the expertise
Established pathology workflow since 2015

FNLB in the EFSTH hospital in Banjul

Transfer to the pathology lab at the same day

Processing and paraffin embedding during the week

Shipment of the FFPE blocks to IARC

Processing in the pathology lab. at IARC

Preparation of the pathology reports

Sending back the reports by e-mail

Team of pathology lab. in the Edward Francis Small Teaching Hospital (EFSTH), Banjul, Gambia

Ramatoulie Njie
Sheikh Omar Bittaye
Christine Carreira, Research assistant in the pathology lab. at IARC
Diagnostic parameters

• To diagnose chronic hepatitis
  • Sufficiency criteria
  • Routine use of special stains
    • Masson’s trichrome, PAS, Reticulin
  • Scoring of hepatitis activity by two methods
    • Modified hepatitis activity index (Ishak)
      • Grade: 0 to 18
      • Stage: 0 to 6
    • METAVIR
      • Activity: 0 to A3
      • Stage: 0 to 4

• To diagnose HCC
  • Sufficiency criteria
  • Confirmation by IHC
    • HepPar 1
    • Arginase 1
  • Grading based on two scoring methods
    • Four-tier Edmondson-Steiner
    • Three-tier well to poorly differentiated
Findings from 2015 to 2019

<table>
<thead>
<tr>
<th></th>
<th>No significant finding</th>
<th>Chronic Hepatitis</th>
<th>HCC</th>
<th>Liver metastasis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of biopsies</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Total= 314</td>
<td></td>
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<tr>
<td>Accepted for reporting=215 (68.5%)</td>
<td>26 (12.1%)</td>
<td>83 (38.6%)</td>
<td>77 (35.8%)</td>
<td>29 (13.5%)</td>
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<tr>
<td><strong>Mean age</strong></td>
<td>38</td>
<td>39</td>
<td>47¹</td>
<td>44</td>
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<tr>
<td><strong>Male %</strong></td>
<td>77%</td>
<td>86%</td>
<td>82%</td>
<td>59%</td>
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<tr>
<td><strong>HBs-Ag positive/Tested (%)</strong></td>
<td>17/26 (65%)</td>
<td>64/79 (81%)</td>
<td>32/70 (46%)</td>
<td>14/27 (52%)</td>
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<tr>
<td><strong>Mean of α-FP (Tested)</strong></td>
<td>3765 (9 cases)</td>
<td>13026 (20 cases)</td>
<td>11021 (32 cases)</td>
<td>12174 (7 cases)</td>
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<tr>
<td><strong>Scoring of Hepatitis</strong></td>
<td></td>
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<tr>
<td>HAI (ISHAK)</td>
<td></td>
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<tr>
<td>Grade Mean (SD)</td>
<td>9.0 (4.0)</td>
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<tr>
<td>Stage Mean (SD)</td>
<td>4.0 (2.0)²</td>
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<tr>
<td>METAVIR</td>
<td></td>
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<tr>
<td>Activity Mean (SD)</td>
<td>2.0 (1.0)</td>
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<tr>
<td>Stage Mean (SD)</td>
<td>3.0 (1.0)</td>
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<tr>
<td><strong>Grade of HCC</strong></td>
<td></td>
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<tr>
<td>WD (I, II)</td>
<td>10 (16%)</td>
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<td>MD (III)</td>
<td>41 (66%)</td>
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<td>PD (IV)</td>
<td>11 (18%)</td>
<td></td>
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<tr>
<td><strong>Elastography score Mean (SD)</strong></td>
<td>13(8) for 21 cases</td>
<td>22(20) for 74 cases</td>
<td>62(40) for 60 cases</td>
<td>46(30) for 17 cases</td>
</tr>
</tbody>
</table>

¹18/77 (23.4%) <=35
²50% stage 5 and 6
Cirrhotic liver confirmed by special stain

Masson’s-Trichrome & Reticulin
Confirmation of HCC by IHC

HCC with variable differentiation express HepPAr1 but in different percentage and intensity
Metastatic cancers

I. No expression of HepPar1, indicative of metastatic adenocarcinoma
II. Internal positive control to confirm the efficiency of the antibody
Conclusion

• Did IARC succeed to support pathology workflow in a low-income country?
  • Establishing and maintenance of a standardized protocol remain the main challenge in low-income countries
    • Fondation constraints
    • No permanent supervision
    • No secure budget
    • Essential need for continued education
    • High level of will and interest to learn and to be better