Fine Needle Aspiration Cytology of Liver Tumors

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ABSTRACT

Fine needle aspiration cytology has undergone increasing utilization in the evaluation of hepatic neoplasms. Experience with liver aspirates has demonstrated that problems in differential diagnosis require thorough understanding of criteria for distinguishing different tumor types. The present report describes the cytologic presentation of primary and metastatic hepatic tumors with emphasis on characteristic nuclear and cytoplasmic features encountered in fine needle aspiration biopsy specimens.

Introduction

Fine needle aspiration cytology of the liver is now well recognized as a diagnostic procedure. The method has been utilized extensively in institutions where experience in the interpretation of such specimens is available. Aspiration cytology has been applied in the diagnosis of hepatic cancer and benign conditions, including parasitic diseases, granulomatous lesions, and diffuse liver disorders. The principal application has been in the evaluation of malignant neoplasms.

Since fine needle aspiration cytology is finding increasing use in the diagnosis of hepatic neoplasms, criteria for distinguishing different types of tumors need to be clearly understood. Several reports have described the cytologic features of primary liver tumors and metastatic tumors. Experience with liver aspirates has indicated that problems can occur in the classification of tumor type. The present report describes the characteristic cytologic findings in primary and metastatic hepatic tumors, with emphasis on specific nuclear and cytoplasmic features seen in fine needle aspiration cytology specimens.

Hepatoma

Cytologic presentation of hepatoma depends on the degree of differentiation. As indicated in table I, the cellular features of well differentiated hepatoma closely resemble those of normal hepatocytes. Nuclei are round and regular with evenly distributed chromatin (figure 1). In hepatoma, there is, in addition, evidence of increased nucleocytoplasmic ratio and enlargement of nucleoli. Significant pleomorphism is not found. The presence of binucleation is not a helpful feature, since this may be seen in hepatocytes under a variety of conditions.
TABLE I

<table>
<thead>
<tr>
<th></th>
<th>Normal Hepatocytes</th>
<th>Well Differentiated Hepatoma</th>
<th>Poorly Differentiated Hepatoma</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Arrangement</strong></td>
<td>Side by side, no overlapping</td>
<td>Overlapping present, mixed with normal cells</td>
<td>Overlapping present, mixed with normal cells</td>
</tr>
<tr>
<td><strong>Nucleus</strong></td>
<td>Round, uniform chromatin, may be binucleated</td>
<td>Large, indented, high N/C ratio; prominent nucleoli; even chromatin pattern</td>
<td>Large, indented, greatly increased N/C ratio; prominent nucleoli</td>
</tr>
<tr>
<td><strong>Cytoplasm</strong></td>
<td>Polygonal, eosinophilic; lipofuchsin, fat, bile may be seen</td>
<td>Similar to normal hepatocytes; may contain fat, bile</td>
<td>Scant, undifferentiated; fat, bile rarely present</td>
</tr>
</tbody>
</table>

Similarly, cytoplasmic features in well differentiated hepatoma resemble those in benign hepatocytes. Normal hepatocytes generally show clear definition of cells arranged in cords and groups with evident separation of nuclei. In hepatoma, there is cellular crowding which results in overlapping and close grouping of nuclei of adjacent cells.

In poorly differentiated hepatoma, malignant features are clearly evident (figure 2). Nuclei are large and irregular with densely distributed chromatin and prominent nucleoli. The nucleocytoplasmic ratio is greatly increased. Cells show marked crowding and overlapping within groups present. Cytoplasm is generally scant without specific evidence of hepatocellular features. A helpful finding in such cases is the mixture of malignant cells with normal hepatocytes indicating cell of origin. In those instances in which the appearance is anaplastic and precise classification is uncertain, electron microscopy can be useful in demonstrating hepatocellular origin. For example, the presence of bile canaliculi or cytoplasmic

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**Figure 1.** Well differentiated hepatoma, liver aspirate, showing resemblance to normal hepatocytes and minimal pleomorphism (×550).

**Figure 2.** Poorly differentiated hepatoma, liver aspirate. Note macronucleoli (×550).
TABLE II
Cytologic Features of Metastatic Tumors in Liver Aspirates

<table>
<thead>
<tr>
<th></th>
<th>Metastatic Adenocarcinoma</th>
<th>Metastatic Islet Cell Tumor</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Arrangement</strong></td>
<td>Depends on primary site</td>
<td>Overlapping, grouped arrange-</td>
</tr>
<tr>
<td><strong>Nucleus</strong></td>
<td>Large, pleomorphic, irreg-</td>
<td>ment arrangement</td>
</tr>
<tr>
<td></td>
<td>ular; coarse chromatin</td>
<td>Oval, slightly indented;</td>
</tr>
<tr>
<td><strong>Cytoplasm</strong></td>
<td>Depends on type of tumor</td>
<td>uniform appearance;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>nucleoli not prominent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Scant, finely granular</td>
</tr>
</tbody>
</table>

Metastatic Tumors

The cytologic features of metastatic hepatic tumors are indicated in table II. The most frequently encountered are adenocarcinomas. Characteristic features include large pleomorphic nuclei with prominent nucleoli and grouped arrangement with overlapping (figure 3), although the particular arrangement depends on tumor type. Similarly, the cytoplasmic appearance is related to the type of tumor. In cases in which the primary site is unknown or indefinite, electron microscopy and/or immunoperoxidase studies may be needed to indicate cell of origin.

Metastatic islet cell tumors have a characteristic cytologic presentation. These features, which are also seen in other endocrine tumors, include cellular crowding, oval, slightly indented nuclei with generally even chromatin distribution and scant, finely granular cytoplasm (figure 4). As indicated previously, if precise origin is unclear, ultrastructural and

![Figure 3. Metastatic adenocarcinoma, liver aspirate. Considerable pleomorphism is evident (×550).](image)

![Figure 4. Metastatic islet cell tumor, liver aspirate, showing moderate nuclear irregularity and abundant granular cytoplasm (×550).](image)
immunohistochemical studies can be utilized. Electron microscopic evidence of typical cytoplasmic secretory granules together with immunohistologic demonstration of specific islet cell products will confirm the diagnosis.

Summary

The principal problems in the differential diagnosis of fine needle aspirates of the liver include distinction between well differentiated hepatoma and benign hepatocytes and between poorly differentiated hepatoma and metastatic tumors. Hepatomas of well differentiated type can be distinguished from benign liver cell groups by their overlapping arrangement, increased nucleocytoplasmic ratio, and prominent nucleoli. Poorly differentiated hepatomas are recognized by their association with groups of normal hepatocytes and generally anaplastic appearance. Distinguishing features of metastatic adenocarcinomas include their pattern of cellular arrangement and cytoplasmic appearance. When the precise diagnosis is not clear, appropriate additional studies, such as electron microscopy and immunoperoxidase analysis, should be employed.

References