Esophageal Metastatic Sub-mucosal Lesion of Hepatocellular Carcinoma Diagnosed by EUS

Abstract
Esophageal metastatic lesions are rare particularly of hepatocellular carcinoma (HCC). The majority of reported cases were diagnosed post-mortem, only a few cases were identified by upper endoscopy. Endoscopic ultrasound (EUS) has never been reported as a diagnostic tool for esophageal metastasis from HCC, nor has EUS-FNA ever been used for this purpose. We reported a 59-year-old male who was under surveillance post liver transplant from HCC 4 years ago, had elevated alpha fetoprotein (AFP) at 258.3 ng/ml and a positron emission tomography–computed tomography (PET-CT) showing an increased uptake lesion of standardized uptake value (SUV) 7.5 at gastro-esophageal junction. EUS showed a homogeneous hypoechoic mass measuring 35x20 mm from the 3rd layer of the distal esophageal wall and EUS-FNA was performed. Cytopathology was consistent with metastatic HCC. The patient expired 20 months later from progressive disease with systematic bacterial infection despite multidisciplinary treatments.

Keywords: Endosonography; Endoscopic ultrasound; EUS; Hepatocellular carcinoma; Esophagus; Metastasis; Esophageal metastasis; EUS-FNA

Introduction
Esophageal metastatic lesions are rare particularly of hepatocellular carcinoma (HCC). The majority of reported cases were diagnosed post-mortem, only a few cases were identified by upper endoscopy. Endoscopic ultrasound (EUS) has never been reported as a diagnostic tool for esophageal metastasis from HCC, nor has EUS-FNA ever been used for this purpose. We recently used both EUS and EUS-FNA to diagnose esophageal metastasis.

Case Presentation
A 59-year-old male who was under surveillance post liver transplant from HCC 4 years ago, had elevated alpha fetoprotein (AFP) at 258.3 ng/ml and a positron emission tomography–computed tomography (PET-CT) showing an increased uptake lesion of standardized uptake value (SUV) 7.5 at gastro-esophageal junction (Figure 1). Upper endoscopy showed unremarkable esophageal mucosa so EUS was performed showing a homogeneous hypoechoic mass measuring 35x20 mm from the 3rd layer of the distal esophageal wall (Figure 2.1 & 2.2) and EUS-FNA was performed. Cytopathology was consistent with metastatic HCC (Figure 3.1 & 3.2). The patient expired 20 months later from progressive disease with systematic bacterial infection despite multidisciplinary treatments.

Discussion
Gastro-intestinal metastasis from HCC is rare with an incidence of only 2% [1]. Only 10 cases of the metastases have been reported in the PUBMED (Table 1) [2-11]. The majority of patients presents with gastrointestinal bleeding, dysphagia and elevated AFP. Diagnosis was mostly made by biopsy from endoscopy.
Figure 2a & 2b: Endoscopic ultrasound showed a sub-mucosal homogeneous hypo-echoic mass measuring 20x35 mm in diameter, being located at 34-39 cm from incisor. The lesion originated from third layer of esophageal wall as shown in figures.

Figure 3a & 3b: a) Malignant cells resembling hepatocyte present in trabeculae; b) Pseudoacinar pattern. They were stained with Papanicolaou stain with original magnification 400X.

Table 1: Clinical characteristics of patients with HCC with esophageal metastasis were shown in this table.

<table>
<thead>
<tr>
<th></th>
<th>Gender/Age</th>
<th>Presentation</th>
<th>Diagnostic Method</th>
<th>Shape</th>
<th>Tissue Diagnosis</th>
<th>AFP (ng/ml)</th>
<th>Survival Time* (months)</th>
<th>Note</th>
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<tbody>
<tr>
<td>Sohn et al. [3]</td>
<td>M/74</td>
<td>Anorexia</td>
<td>Esophagogram</td>
<td>Polypoid</td>
<td>EGD</td>
<td>ND</td>
<td>ND</td>
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<td>M/56</td>
<td>Dysphagia, tarry stool</td>
<td>EGD</td>
<td>Polypoid</td>
<td>Autopsy</td>
<td>12,200</td>
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<td></td>
</tr>
<tr>
<td>Sohara et al. [5]</td>
<td>M/54</td>
<td>Melena</td>
<td>EGD</td>
<td>SMT</td>
<td>EGD</td>
<td>4,987</td>
<td>3</td>
<td></td>
</tr>
<tr>
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<td>M/46</td>
<td>Hematemesis</td>
<td>EGD</td>
<td>Polypoid</td>
<td>Autopsy</td>
<td>990</td>
<td>7</td>
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</tr>
<tr>
<td>Cho et al. [6]</td>
<td>M/50</td>
<td>Dysphagia, hematemesis</td>
<td>EGD</td>
<td>Polypoid</td>
<td>EGD</td>
<td>Elevated</td>
<td>13</td>
<td>EUS was utilized</td>
</tr>
<tr>
<td>Tsubouchi et al. [7]</td>
<td>M/63</td>
<td>Epigastric pain</td>
<td>EGD</td>
<td>Polypoid</td>
<td>EGD</td>
<td>4,130</td>
<td>14</td>
<td>EUS was utilized</td>
</tr>
<tr>
<td>Choi et al. [8]</td>
<td>M/66</td>
<td>Hematemesis</td>
<td>EGD</td>
<td>SMT</td>
<td>EGD</td>
<td>3.47</td>
<td>7</td>
<td>EUS was utilized</td>
</tr>
<tr>
<td>Xie et al. [9]</td>
<td>M/50</td>
<td>Dysphagia, odynophagia</td>
<td>EGD</td>
<td>Polypoid</td>
<td>EGD</td>
<td>ND</td>
<td>More than 7</td>
<td>OLT 3y</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th></th>
<th>M/54</th>
<th>Hematemesis, tarry stool</th>
<th>EGD</th>
<th>Polypoid</th>
<th>BGD</th>
<th>ND</th>
<th>4</th>
<th>OLT 2y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hsu et al. [10]</td>
<td>M/63</td>
<td>Progressive anemia</td>
<td>EGD</td>
<td>Polypoid / SMT</td>
<td>BGD</td>
<td>ND</td>
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</tbody>
</table>

M: Male; ND: Not Described; EGD: Esophagogastroduodenoscopy; EUS: Endoscopic Ultrasound; SMT: Submucosal Tumor; OLT: Orthotopic Liver Transplant

*The duration between the diagnosis of esophageal metastasis and death.

It is hypothesized that esophageal metastasis from HCC came about through the tumor invading the portal vein through hepatofugal portal blood flow [12] or direct invasion of tumor cells to the left gastric vein to the esophagus. This case supports a hypothesis of hematogenous spread mechanism of HCC due to the detection of tumor in the submucosa without mucosal involvement.

Based on available information, the majority of esophageal metastases present either as polypoid masses or sub-mucosal lesions which mainly were discovered during endoscopy. EUS were applied in only 3 cases only after the lesions were detected by endoscopy [6-8]. In this case, the esophageal metastasis was incidentally suspected from the PET scan. Upper endoscopy did not detect any lesion. Nevertheless, EUS successfully identified the lesion with positive results of HCC from EUS-FNA. This suggests that patients with history of HCC with positive results of PET-CT in the gastrointestinal wall, EUS should be considered as an investigation of choice despite negative finding from endoscopy.

In general, prognosis of esophageal metastasis is extremely poor with an average survival time shorter than 1 month [8]. Given the fact that this current case was detected in earlier stage than other previously reported cases, his survival time was then longer than other ones.

**Conclusion**

This case report demonstrated that EUS can diagnose early esophageal metastasis despite negative endoscopic findings. It is hence a potential investigation of choices to search for gastrointestinal wall metastasis including esophagus in patients with positive PET scan. This current case report also supports a hypothesis of hematogenous spreading mechanism of hepatocellular carcinoma.

**Conflict of Interest**

None.

**Acknowledgement**

None.

**References**


