



The Origin of Liver Metastatic Adenocarcinomas, a Single Center Experience from the South of Iran

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Abstract

Background: Liver is one the most common sites of metastasis, and metastatic liver cancers are the most common liver malignancies. Metastatic adenocarcinomas are the most common metastatic liver cancers, which have different origins. The liver biopsy is a very important step to find the origin of metastatic cancer by immunohistochemistry.

Objectives: In this study, we aimed to find the primary origin of metastatic adenocarcinomas in the liver biopsies.

Methods: In this study, 210 liver biopsies with the primary diagnosis of metastasis with unknown origin in the liver were investigated from 2008 to 2017 that 126 cases (60%) of which have proved to be metastatic adenocarcinoma with unknown origin. Histologic studies and immunohistochemical (IHC) stains were performed. Also, a complete endoscopic, radiologic, clinical, and paraclinical studies were carried out besides the liver biopsy to find the origin of the adenocarcinoma.

Results: Among these 126 liver biopsies, the origin of 94 cases (74.6%) was definitely determined by IHC and other examinations mentioned above. All efforts for thirty-two cases (25.4%) failed to find the primary origin despite a complete examination. Most common primary origins were colon (23.8%), lung (19%), pancreas (13.9%), and breast (11.2%).

Conclusions: Performing a liver biopsy is a very helpful modality to find the origin of liver metastatic adenocarcinoma but needs to be combined with other clinical findings and diagnostic modalities to find the origin of metastasis to the liver. By combining these methods, our study showed that the origin of 74.6% of metastatic liver adenocarcinomas can be found, which is most commonly from colon, lung, and pancreas.

Keywords: Liver, Metastatic Adenocarcinoma, Origin

1. Background

The most common liver malignancy is metastatic cancer. Metastasis from lymphoma, malignant melanoma, gastrointestinal stromal tumors, sarcomas, and many other cancers are very common in the liver; however, adenocarcinomas constitute more than 50% of metastatic cancers. Finding the origin of metastatic adenocarcinoma is very important and vital. By discovering a metastatic tumor in the liver, the next step is to find the origin of the metastasis to plan for the best treatment modality (1). The routine workup consists of measuring the serum levels of tumor markers, endoscopy, imaging studies, and liver biopsy (2). Recently, genetic profiling is also recommended by some studies, but it is still far from being routine (3).

2. Objectives

In this study, we discussed our experience with 126 patients who underwent liver biopsies with the pathologic

diagnosis of metastatic adenocarcinoma. To the best of our knowledge, this is the first report about the origin of liver metastatic adenocarcinoma in Iran.

3. Methods

In this study, 210 liver biopsies have been performed with the primary clinical diagnosis of metastatic liver cancer of unknown origin in our center from 2008 to 2017. Among these liver biopsies, 126 patients were confirmed to be metastatic adenocarcinoma, by the exclusion of intrahepatic cholangiocarcinoma, neuroendocrine tumors, mesenchymal tumors and so on. It is also worthy to note that rarely some liver biopsies were performed with known primary adenocarcinoma to confirm the metastatic tumor in the liver, which were removed from this study. After the primary diagnosis of metastatic adenocarcinoma, complete immunohistochemical (IHC) panel was stained for the biopsies to find the origin of the

tumor. Clinical chart of the patients was thoroughly reviewed and evaluated. All imaging modalities, including ultrasonography, CT scan and magnetic resonance imaging (MRI), were assessed. Clinical, pathologic, imaging, and laboratory studies were evaluated together and compared to find the exact origin of the metastatic adenocarcinoma in all of the 126 patients. Most common tumor markers were comprised of carcinoembryonic antigen (CEA), CA-125, CA15-3, CA 19-9, and alpha-fetoprotein (AFP). Immunohistochemical markers were variable, but most common markers were cytokeratin (CK), CK7, CK19, CK20, Estrogen/progesterone receptors (ER/PR), GATA-3, Thyroid transcription factor (TTF-1), Prostatic specific antigen (PSA), CDX-2, MUC5AC, and MUC-6; however, the type of markers was variable according to the clinical findings and histopathology of the liver biopsy (4).

4. Results

All 210 liver biopsies with the primary clinicoradiologic findings suspicious of metastasis were evaluated in our center. Among these 210 cases, 126 (60%) cases were confirmed to be metastatic adenocarcinoma, which is the most common metastatic cancer type in the liver. There were 59 female and 67 male patients (F/M = 0.88). The age range was 24 to 93 (56.5 ± 15.6) years. The origin of the tumor was definitely identified in 94 (74.6%) patients and in 32 (25.4%) cases no definite origin could be found despite complete clinical, imaging, paraclinical, and histopathologic evaluations.

Pathologic and IHC evaluation of the cases confirmed the primary origin of liver metastatic adenocarcinoma in 70 patients (55%) in the order of 30 (23.8%) colon adenocarcinomas, 24 (19%) lung adenocarcinomas, 14 (11.2%) of breast carcinomas, and 2 (1.6%) endometrial adenocarcinomas. Although, in 24 (19%) cases, pathologic and IHC studies were not definite, precise clinical, endoscopic, and radiologic studies helped to find the primary origin. In this regard, the cases have been originated from pancreas [17 cases (13.9%)], stomach [4 cases, (3.2%)], and gall bladder [3 cases (2.4%)].

Table 1 shows the origin of metastatic adenocarcinoma in these 126 cases of liver biopsies.

5. Discussion

The liver is the location of metastasis in more than 25% of malignancies, and the liver metastatic cancers are more common than primary malignancies (5, 6). Among metastatic cancers, the most common and important group is metastatic adenocarcinoma. About 50% - 60% of metastatic malignant liver tumors in previous studies

Table 1. The Incidence of the Primary Origin of the Metastatic Liver Cancer in the Biopsied

Origin	No. (%)
Colon	30 (23.8)
Lung	24 (19)
Pancreas	17 (13.9)
Breast	14 (11.2)
Stomach	4 (3.2)
Gall bladder	3 (2.4)
Endometrial	2 (1.6)
Unknown	32 (25.4)
Total	126 (100)

have been adenocarcinoma; this percentage in this study was also very similar (60%) (1-5).

Origin of metastatic adenocarcinoma is very important for the treatment decisions, because chemotherapeutic, radiation, and surgical approaches are different according to the origin of the metastatic adenocarcinoma (6). Discovery of metastasis in the liver needs clinical, endoscopic, imaging, and pathologic studies to find the origin of the adenocarcinoma, which is a time-consuming process (7). One of the most important steps in finding the origin of the metastatic adenocarcinoma is a liver biopsy. However, histologic findings of metastatic adenocarcinoma from different organs are very similar; thus IHC assessment, such as cytokeratin pattern (CK7/CK20 positivity) and specific markers related to each organ (such as PSA, TTF-1, ER/PR, and so on), is necessary on the liver biopsy. Histology and clinical, and imaging studies per se are not adequate for finding the origin of metastasis, but the combination of them can clarify the origin of metastasis in the majority of Liver metastases (8-11).

The reported origin of adenocarcinoma in this study is very similar to reports from other countries. Common cancers have been colon, lung, pancreas and breast in different orders. In most Western countries, colon and lung origins have been the most frequent metastatic adenocarcinomas to the liver followed by pancreas and breast (10, 11). Also, in our center, colon has been the most common origin followed by lung and pancreas. The breast was the fourth common origin of metastatic adenocarcinoma to the liver. It is worthy to note that the origin of 24.6% of the metastatic adenocarcinomas could not be found despite all investigations. This percentage is very similar to previous experiences from Western countries i.e. in previous reports, the origin of 25% - 35% of metastatic liver cancers was unknown (11, 12).

In conclusion, our study as the first report from Iran

showed that the origin of liver metastatic adenocarcinoma in this center is very similar to the report from Western countries. This study also showed that in most cases, the combination of liver histology and clinical findings, as well as imaging and other paraclinical information, can be helpful to find the origin of metastasis to the liver. Further studies are recommended to compare the outcomes of the patients with known and unknown metastasis to the liver regarding the primary origin and the treatment modalities.

Footnotes

Conflict of Interests: The authors declare that there is no conflict of interests.

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