MALIGNANT HEPATIC NEOPLASMS: USING ULTRASONOGRAPHY AS A MEANS OF DEFINING HEPATIC LESIONS

1.5 Contact Hours

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Malignant Hepatic Neoplasms: Using Ultrasonography as a Means of Defining Hepatic Lesions

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Learning Objectives

1. Define the term "neoplasm" and differentiate this term from "tumor".

2. Explain the difference between primary and secondary liver tumors.

3. List the two types of primary liver cancer and explain the differences between them.

4. Explain what is thought to be the cause of many cholangiosarcomas in Africa and Asia.

5. Define what a hepatoblastoma is, and who it is most likely to affect.

Malignant liver tumors are among the most frequent cancers that occur in adults.[1] In the United States, well over 1 million individuals are diagnosed with some type of cancer each year. According to the American Cancer Society, cancer caused approximately 538,000 deaths in 1997, accounting for about 23% of all deaths in America.[2] The word "cancer" comes from the Latin word for crab, presumably because a cancer adheres to any tissue it seizes upon in a stubborn manner.

Any new growth is termed a neoplasm; neoplasia literally meaning "new growth". The term "tumor" was originally applied to the swelling caused by inflammation. Neoplasms also may induce swellings, but by long precedent, the non-neoplastic usage of "tumor" has passed into limbo; thus, the term is now equated with neoplasm. Oncology (Greek "oncos" meaning "tumor") is the study of tumors or neoplasms.[2]

Malignant hepatic neoplasm refers to cancerous tumors of the liver. Malignant liver tumors are classified as primary (starting in the liver itself), or secondary from a cancer that has

started in another part of the body and has spread (metastasized) to the liver. Metastatic disease is the most common form of neoplastic involvement of the liver. The most common primary sites are the colon, breast, and lung. Metastatic spread to the liver occurs as the tumor erodes the wall and travels through the lymphatic system or through the bloodstream to the portal vein or hepatic artery to the liver.[3]

In North America, primary hepatic neoplasms are uncommon and metastatic tumors are commonly seen, whereas worldwide, especially in areas such as the Far East, hepatocellular carcinoma (HCC) is much more prevalent than metastatic disease; [4] about half of the malignant tumors in children which occur before the age of five years-old are HCC.[5]

Primary liver cancer is quite rare in the United Kingdom and the rest of the western world, but the number of people developing it is increasing. Approximately 1500 people are diagnosed with this type of cancer each year in the United Kingdom. In other parts of the world, such as tropical Africa and some parts of Asia, it is one of the most common cancers. It is twice as common in men as in women.[4]

There are two types of primary liver cancer. The most common kind is hepatocellular carcinoma (HCC), and arises from hepatocytes (which are the main cells of the liver), and occurs mostly in people with cirrhosis. The other type of primary liver cancer is called cholangiocarcinoma (bile duct cancer) because it starts in the cells lining the bile ducts.[6]

In the western world, most people who develop hepatoma usually also have cirrhosis of the liver. This is a fine scarring throughout the liver which is due to a variety of causes including infection and heavy alcohol drinking over a long period of time; however, only a small proportion of people who have cirrhosis of the liver develop primary liver cancer.[7]

Case study: A 78-year-old woman was admitted to the hospital with severe weight loss, right upper quadrant pain and heartburn that had lasted for 8 weeks. She had mild bilateral lower extremity edema. Her medical history included Hepatitis A 50 years ago and chronic hepatitis B, which was successfully treated with alfainterferon. Computer tomography showed a tumor of approximately 20.0 cm in diameter in her liver. Liver function tests were within reference range, and blood tests showed antibodies against hepatitis A and hepatitis B. The tumor was surgically removed, the immediate postoperative course was uneventful, and all her liver functions remained in the reference range. Two months later, the patient developed cardiovascular failure and died.[1]

Infection with either the Hepatitis B or Hepatitis C virus can progress to hepatoma.[8] People who have a condition called hemochromatosis, which causes excess deposits of iron in the body, have a higher chance of developing hepatoma. In Africa and Asia a poison called aflatoxin, found in moldy peanuts and grain, is an important cause of hepatoma.[4]

Cholangiocarcinomas are less common than hepatomas. The cause of most bile duct cancers is unknown, but they are slightly more likely to occur in people with conditions which cause inflammation of the bowel, such as ulcerative colitis. In Africa and Asia, infection with a parasite known as the liver fluke is thought to cause many cholangiocarcinomas.[6]

Hepatocellular carcinoma is far and away the most common primary tumor of the liver, even in those parts of the world where its incidence is low. In nations where the prevalence of hepatitis B infection is high, it is a very common neoplasm and one of the leading causes of death. Hepatocellular carcinoma arises from the hepatocytes in a liver which is almost always chronically diseased and often cirrhotic. In the United States, as many as 80% of hepatocellular

carcinomas arise in cirrhotic livers, with alcohol as the most common underlying disease, followed by hepatitis B infection.[3]

There are a number of variants of hepatocellular carcinomas. The most important of these is fibrolamellar hepatocellular carcinoma. These usually occur in otherwise normal liver, and occur in a younger age group than typical hepatocellular carcinoma, with the average age of affected individuals being in the mid-twenties.

Hepatoblastoma is a type of liver cancer which consists of embryonic hepatic tissue and is the most common primary malignant hepatic tumor in children. It occurs in the younger age group, being virtually unheard of after the age of three years. This helps in differentiation from hepatocellular carcinoma of childhood which occurs in an older group (average age nine years), and is usually seen in association with some metabolic abnormality.[9]

Kaposi's sarcoma frequently involves the liver in patients with AIDS. It is uncertain whether these lesions represent spread from elsewhere in the body (metastases) or had originated at multiple sites in the liver (multifocal primaries).

Metastatic tumors outnumber primary tumors by 15- or 20-to-one in most series. Virtually any tumor can metastasize to the liver. The access to the portal venous system is an important factor in determining the frequency of metastasis. For this reason, a much higher percentage of neoplasms of colon, pancreas, and gallbladder metastasize to liver than neoplasms from other primary sites. Neoplasms without direct access to the portal venous system that seem to have a particular propensity for metastasizing to liver include breast, melanoma, testes and lymph nodes.[3]

Initially, patients with metastasis or primary liver cancer may have no clinical symptoms. Hepatomegaly (enlargement of the liver) may or may not be initially present. Some patients may

notice a vague discomfort in the upper abdomen that may become painful as liver enlarges. Loss of appetite, weight loss, nausea, weakness and lethargy are common symptoms. Jaundice may occur late as more of the liver is replaced by tumor or if the bile ducts become blocked. Ascites may occur in abdomen as back pressure in the veins which lead into the liver causes fluid to build up and collect in abdomen.[7]

In the past two decades, hepatocellular carcinoma (HCC) has emerged as a growing health threat in the developed world. In the United States alone, the incidence has almost doubled. In addition, the explosion in the number of Hepatitis C cases, which peaked in the late 1980s, will be expected to produce a similar peak in HCC approximately twenty to thirty years later. Although surgical resection has traditionally been considered the gold standard of treatment, long-term survival is generally disappointing.[4]

There are many different tests and procedures available to determine the type of cancer and how far it is advanced as well as the particular area of involvement. This allows staging of a cancer to determine its size and whether it has spread to other areas of the body. Knowing the particular type and the stage of cancer helps clinicians decide on the most appropriate treatment.

Many imaging modalities are utilized to screen for and to evaluate liver tumors. Computerized tomography (CT) scanning and magnetic resonance imaging (MRI) are both frequently performed as well as hepatic arteriography (the use of contrast medium to image the vasculature of the liver). Advantages of ultrasound as a screening test for metastatic liver disease include its relative accuracy, speed, lack of ionizing radiation and availability. Furthermore, the multiplanar capability of ultrasound allows for excellent segmental localization of masses with the ability to detect proximity to or involvement of the vital vascular structures.[3]

With the rapidly improving technology used in diagnostic imaging, the diagnosis and characterization of lesions have improved significantly. Diagnostic imaging techniques help to differentiate lesions, distinguishing benign from malignant lesions and defining the precise anatomical location of the lesions. Because surgical resection remains the mainstay of treatment of many of the liver lesions, definition of the extent of the mass lesion and its relationship to hepatic segmental anatomy is essential.[9]

Hepatic masses in children are usually malignant tumors or abscesses. Hepatic tumors are the third most frequent neoplasm in children after Wilm's tumor and neuroblastoma. Malignant hepatic tumors account for about two thirds of all primary hepatic tumors in children. These are usually hepatoblastomas or hepatocellular carcinomas. Pathologically, HCC occurs in three forms: solitary tumor, multiple nodules, and diffuse infiltration. There is a propensity toward venous invasion. The portal vein is involved more commonly than the hepatic venous system.[7]

The sonographic appearance of HCC is variable. The masses may be hypoechoic (appear less dense than the surrounding tissue), hyperechoic (appear more dense than the surrounding tissue), complex (a mixture of hypoechoic and hyperechoic) or isoechoic (same texture as the surrounding tissue with only subtle differences). Most small (less than 5.0 cm) HCCs are hypoechoic. The sonographic findings of hepatoblastomas and hepatocellular carcinomas are similar, so the definitive diagnosis has to be made by biopsy of the lesion. Both tumors are usually confined to a single lobe, with the right lobe affected twice as often as the left; however, the tumors may involve both lobes of the liver. On sonography the tumors may appear as solitary masses, a dominant mass with smaller satellite lesions, or multiple nodules throughout the liver. Most tumors are hyperechoic relative to normal parenchyma and heterogeneous, reflecting the presence of partial necrosis and hemorrhage.[3]

Because of its ease of performance, ultrasound (US) is the most commonly used initial imaging technique used to evaluate a suspected hepatic mass in a child. Ultrasound accurately identifies or excludes a mass, identifies the organ of origin, and characterizes it as a cystic or solid. These initial US findings help the radiologist to determine the remainder of the child's imaging work-up. Intraoperative US (ultrasound used during surgery) using high frequency transducers are very helpful in detecting focal hepatic lesions.[9]

Duplex and color Doppler flow ultrasound is excellent for evaluating focal liver lesions. Vascular invasion can be evaluated adequately using color Doppler with conventional gray scale ultrasound. Color Doppler has been reported to be highly sensitive and specific in detecting blood flow in a tumor thrombus (a clot in the vessels of the tumor) and hence can distinguish tumor thrombus from bland thrombus (a clot not related to cancer). Microbubble-enhanced sonography is highly superior to conventional Doppler for characterization of HCC in the cirrhotic liver in the detection the vascularity of HCC lesions, but as yet is untested in terms of its role in the detection of HCC.[3]

References

1. Suriawinata AA, Thung SN. Malignant liver tumors. *Clin Liver Dis* 2002;6:527-554.

2. Aloha Laboratories. http://www.alohalabs.com/cancer_&_disease.htm Accessed January 4, 2008

3. Elsevier CL. (2005) Imaging Children. 2nd ed. v 2. Mosby, Philadelphia.

4. Pawlik TM, Poon RT, Abdalla EK, et al. (2005) Critical Appraisal of the Clinical and Pathologic Predictors of Survival After Resection of Large Hepatocellular Carcinoma. *Arch Surg*; 140:450-458.

5. Hans-Udo K, Longerich T, Stippel DL, et al. Mixed hepatoblastoma in an adult. *Arch of Path Lab*

Medicine 129;2:234-237.

6. Netter FH (2001). The Netter Collection of Medical Illustrations. Volume 3. Digestive System. Part III; Liver, Biliary Tract and Pancreas. Icon Learning Systems, 295 North Street, Teterborough, New Jersey.

7. Hagen-Ansert SA. (2001) Textbook of Diagnostic Ultrasonography. v 1; 5th ed. St. Louis, Missouri. Mosby, Philadelphia.

8. First Principles of Gastroenterology. http://gastroresource.com/GITextbook/En/Chapter14/14-16.htm Accessed January 8, 2008.

9. Siegel MJ. (ed) (1996) Pediatric Sonography. 2nd ed. Philadelphia. Lippencott-Raven.