12 Clinico-Pathological Features of Hepatocellular Carcinoma

Massimo Colombo and Guido Ronchi

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12.1 Introduction

Hepatocellular carcinoma (HCC) is a major health problem worldwide due to its high incidence (approximately 600,000 new cases in 2000), and severe natural history. Indeed, the incidence and mortality rates associated with this disease significantly overlap worldwide (Parkin et al. 2001). The identification of chronic liver disease as the relevant risk factor for this tumor has made surveillance aimed at early detection of HCC possible and surveillance is now universally recognized to be the practical approach for improving the treatment of HCC patients (Bruix et al. 2001). The few cases (<5%) of HCCs that do not develop with a background of chronic liver disease present late and usually have poor prognosis (Bralet et al. 2000). The understanding of both the natural history and staging of HCC is hampered by the epidemiologic and clinical variability of the tumor. This, in turn, is influenced by the concurrence of multiple co-morbidity factors in the same patient as well as by the presence of multiple distinct cell lines in the liver that may develop into liver cell cancer (Sell 2002).

12.2 The Pathological Classification

HCC is classified as nodular, massive or diffuse. The nodular type occurs as a nodule sharply delineated from the surrounding liver. The massive type occupies a large area and infiltrates the neighboring hepatic tissue with satellite nodules. The diffuse type is characterized by the diffuse involvement of the liver (Kojiro 1997). All three forms of HCC occur with a background of chronic liver disease or of an otherwise normal liver. The growth pattern of HCC may be infiltrative, expanding, multinodular and mixed type. Based on histology, the WHO proposed a classification of HCC into trabecular, acinar, compact and scirrhoues (Gibson and Sobin 1978). In the trabecular type, tumor cells are arranged in cords of variable cell thickness separated by sinusoids, with minimal or no fibrosis (Fig. 12.1). The acinar (pseudoglandular) type is characterized by cells arranged in gland-like structures, filled with cellular debris, exudates and macrophages (Figs. 12.2, 12.3). The compact type shows tumor cells that are packed in a solid mass with inconspicuous sinusoids (Fig. 12.4). In the scirrhoues type, significant fibrous tissue separates cords of tumor cells. Each histological type is

Fig. 12.1. Trabecular hepatocellular carcinoma. Trabecular pattern of well-differentiated neoplastic hepatocytes arranged in plates which are between three and four cells in thickness (×30)
further classified according to different grades of cell differentiation. Well differentiated HCC is a trabecular tumor with two- to three-cell thick cords. The anaplastic tumor usually shows a solid growth pattern, with pleomorphic and giant syncytial cells (Fig. 12.5).

12.3 Early Detected Tumors

Surveillance of patients with cirrhosis has led to an increasing number of cancers detected early in the form of small nodules that first appear as well-differentiated tumors and proliferate along with gradual dedifferentiation (Kojiro 1998). A sizable number of tumors arising in cirrhotic livers seem to occur in a multicentric distribution and a certain proportion of them may arise from dysplastic nodules (International Working Party 1995). HCCs ranging from 1–2 cm in size may present with a fibrous capsule and/or fibrous septa in contrast to other indistinct nodular small cancers that have indistinct margins despite such tumors being clearly detected as hypoechoic or hyperechoic focal lesions on ultrasound (US) examination. The latter have been considered carcinoma in situ of the liver due to the absence of invasion into the portal vein branches and intrahepatic metastases (Kojiro 2002). Minute HCCs of the indistinct nodular type are difficult to differentiate from high grade dysplastic nodules. The majority of small (less than 1.5 cm) HCCs of the indistinct nodular type are not detected as hypervascular tumors by contrast imaging, whereas distinct nodular type tumors almost invariably show hypervascular features during the arterial phase of contrast imaging (Kojiro 2002). A combination of the lack of fibrotic capsule and reduced number of unpaired arteries per square millimeter in less than 1.5 cm tumors accounts for many false negative diagnoses of HCC with contrast imaging. Since well-differentiated tumors in the early stages proliferate along with the occurrence of gradual dedifferentiation (Kojiro 1998), more histological grades are seen in tumors greater than 1 cm in size. A “nodule-in-nodule”