Gastroentérologie Clinique et Biologique (2010) **34**, 191—199

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CURRENT TREND

Clinical presentation and management of intrahepatic cholangiocarcinoma

Présentation clinique et prise en charge des cholangiocarcinomes intrahépatiques

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Available online 4 March 2010

In both the International Union Against Cancer (UICC) and American Joint Committee on Cancer (AJCC), intrahepatic cholangiocarcinoma (IHCC) are considered as primary intrahepatic liver tumors, along with hepatocellular carcinoma (HCC). This differentiates them from malignancies of the biliary confluence (Klatskin tumors) that are stratified as extrahepatic tumors along with malignancies of the gallbladder and of the common bile duct. The definition of IHCC (primary tumor of the intrahepatic bile ducts) implies that it encompasses all malignancies developed from the intrahepatic bile ducts, starting from the second order branches and up to the Hering ducts.

This heterogeneity of origins readily explains that the clinical presentation and management of this tumor are quite variable depending on whether the tumor originates from the end-order peripheral branches or from the juxtahilar branches (Fig. 1A and B). The former is likely to be more frequent than the latter, at least in part because as bile structures divide, their number increases. However, the proportion of each is still ill-defined as mass forming type IHCC may behave as hilar malignancies as a result of their location in the vicinity of the biliary confluence (Fig. 1C) or centrifugal extension along the glissonian pedicles (Fig. 1D).

Two words of caution should be given on the source of informations available in the medical literature that will be used in this chapter. First, the figures that will be presented relate, as a rule, to patients who have been operated for an IHCC and not to the general population of IHCC. As a matter of fact, virtually all series or registries of IHCC-patients are surgical series. They have the advantage of focusing on patients with pathologically proven tumors but the disadvantage of dealing with a subgroup of patients (those referred to surgeons for resection) that probably account for less than 20% of all patients with IHCC. Second, most data originate from single surgical centers and usually include a limited number of patients (around 50) gathered over a fairly large period of time (typically 10—20 years). The few exceptions are in particular the Surveillance, Epidemiology and End Results Program (SEER) that collects information from

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0399-8320/$ — see front matter
doi:10.1016/j.gcb.2010.01.006

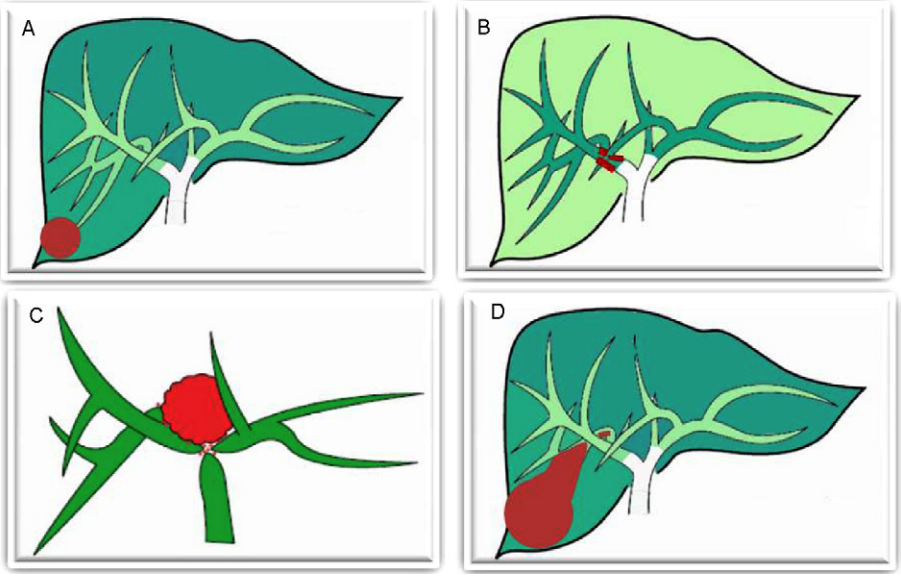

Figure 1. Heterogeneity of the morphological presentation of IHCC. The two extreme situations depending on the origin of the tumor are the mass forming type that originates from the end division of the intrahepatic bile ducts (A) and the periducal infiltrating type that originates from the proximal segmental or sectional bile ducts and resembles a Klatskin tumor (B). Some mass forming type IHCC may however behave as hilar tumor either when they develop from small bile ducts but in liver segments adjacent to the biliary confluence (C) or when they extend along the glissonian pedicles (D).

approximately 25% of the population of the United States [1], a Japanese registry of liver tumors which is declarative and likely not comprehensive [2] and a recent French multi-institutional survey of operated patients at the initiative of the French Association of Surgery [3].

Frequency

A specific chapter of this monography being dedicated to the epidemiology of IHCC, we will only attempt to highlight here how this tumor compares to extrahepatic bile duct tumors on one side and to HCC (the other and predominant intrahepatic primary tumor) on the other side.

IHCC in relation to other bile duct malignancies

It has been widely assumed in the past, in particular in surgical series, that IHCC account for a very small proportion (approximately 10%) of all bile duct malignancies [4]. This view is challenged worldwide by more recent epidemiological database and in particular the latest edition (published in 2007) of ''Cancer incidence in five continents'' that covers the period 1998—2002 [5]. In France for example, the incidence of IHCC in 11 regional registries ranged between 0.5 and 1.3 per 10^5 for men and between 0.2 and 0.9 per 10^5 for women whereas the respective incidences of all extrahepatic bile duct malignancies ranged between 0.6—1.3 and 0.7—2.3 per 10^5. Caution in interpreting these data are given in the first chapter of this monography but according to these figures, IHCC are almost as frequent as all extrahepatic bile ducts in men and only twice less frequent in women. The same holds true in most other countries, except in those where the incidence of gallbladder cancers is particularly high (in particular Chile, Peru and Korea).

IHCC in relation to primary liver malignancies

It has recently been estimated that in France IHCC is 15 times less frequent than HCC [6]. This figure is in between that observed in the Unites States (eight times) [7] and that reported in Japan where the prevalence of HCC is particularly high (23 times) [2]. These variations are indeed more influenced by the numerator (i.e. the incidence of HCC which is highly variable in different areas of the world) than by the denominator (i.e. the incidence of IHCC which is fairly constant, except in South East Asia where distomatosis is endemic). Interestingly, in the French analysis (performed in nine administrative regions accounting for one tenth of the population) there were (unexplained) geographical variations and the ratio actually also ranged between 8 and 22.

Further evaluations are warranted as these studies, although published recently, refer to patients registered 10 years ago whereas the incidence of IHCC is considered to have increased since then.

Circumstances of diagnosis

Age and gender

The peak incidence of IHCC occurs between the age of 55 and 75 years and this tumor is extremely rare before the age of 45 (< 10% of the patients). Although the sex-ratio may fluctuate slightly around 1 in different areas of the world (0.9 in the Western world and 1.5 in Asia) this may simply