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Barcelona Clinic Liver Cancer Classification and Treatment of Hepatocellular Carcinoma in a Côte d'Ivoire University Hospital

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Abstract

Context/Objectives: Hepatocellular carcinoma occurs mainly and increasingly in developing countries, where the prognosis is particularly poor. The Barcelona Clinic Liver Cancer classification is used to guide the treatment of hepatocellular carcinoma. The aim of this retrospective study was to describe the Barcelona Clinic Liver Cancer classification and the treatment of hepatocellular carcinoma in a University Hospital in Côte d'Ivoire. **Methods:** Patients with hepatocellular carcinoma hospitalized in the hepato-gastroenterology unit of the University Hospital of Yopougon from 01 January 2012 to 30 June 2017 were included. The diagnosis of hepatocellular carcinoma was based on the presence of hepatic nodules on the abdominal ultrasound scan, typical images with the helical scanner associated or not with an increase of the α-fetoprotein higher than 200 ng/ml or with histology. Demographic, clinical, biological and radiological data were determined at the time of diagnosis. Patients were classified according to the Barcelona Clinic Liver Cancer classification. Their treatment was specified. **Results:** There were 258 patients whose median age was 48.1 years. Viral hepatitis B virus was the primary cause of hepatocellular carcinoma in 64.7% of cases. The severity of the underlying cirrhosis was Child-Pugh A in 12.1%, B in 63.6% and C in 24.3% of cases. The median size of the tumor was 63 mm. The α-fetoprotein level was higher than 200 mg/ml in 56.03% of cases. The Eastern Cooperative Oncology Group (ECOG)/World Health Organization (WHO) system was ≥2 in 82.9%. The Barcelona Clinic Liver Cancer classification was A in 1.3%, B in 0%, C in 55.2% and D in 43.5% of patients. There was no transplantation or hepatic resection. Very few patients (1.9%) received radio-frequency curative therapy.

The treatment was predominantly symptomatic in 97.8% of patients. During hospitalization 43.7% of patients died. **Conclusion:** Hepatocellular carcinoma occurs on a liver with severe cirrhosis at a late stage. This does not allow cure treatment and explains a high mortality rate during hospitalization. Hepatitis B virus is the main risk factor and immunization at birth will reduce the incidence of this cancer in Africa.

Keywords

Hepatocellular Carcinoma, Barcelona Clinic Liver Cancer Classification, Viral Hepatitis B, Africa

1. Introduction

Hepatocellular carcinoma (HCC) accounts for more than 90% of primary liver cancer and is a major public health problem [1]. It is the fifth most common cancer in men and the seventh in women worldwide [2]. HCC occurs frequently and increasingly in developing countries where the prognosis is particularly poor [3]. In 2020, 915,677 new cases were estimated globally, 83% of which occurred in the least developed regions [4]. In Côte d'Ivoire, according to Globocan 2020, liver cancer has an incidence of 7.9/100,000 inhabitants and a mortality of 7.5/100,000 inhabitants respectively [4]. Liver cancer is the second most common cause of cancer death worldwide; the prognosis of liver cancer is poor [3] [4] [5] [6]. Patients with HCC are a special case in oncology because their prognosis doesn't depend only on the stage of the tumor but also on the underlying liver disease [7] [8]. The diagnostic strategy and treatment of the Barcelona-Clinic Liver Cancer (BCLC) group is based on the analysis of several cohorts and randomized control studies that have shown the continued improvement of the therapeutic indication and its application [7] [9]. This classification uses variables related to the stage of the tumor, the status of the liver function, the physical condition of the patient and links the stages to a treatment algorithm. The objective of the BCLC classification is to incorporate the prognostic estimation and the potential therapeutic advances into a single unified proposal [7] [10] [11]. The BCLC classification is approved by the European Association for the Study of Liver (EASL) [1] and the American Association for the Study of Liver (AASLD) [12]. This classification divides patients into 5 stages [very early (0), early (A), intermediate (B), advanced (C) and terminal (D)] providing a simultaneous information distribution on the prognosis and treatment [13] [14]. Treatment strategies for HCC are categorized in curative, palliative and symptomatic [8]. Despite the high prevalence and mortality of HCC in Côte d'Ivoire, few studies have assessed the BCLC classification and treatment in a cohort of Ivorian patients. This manuscript examines retrospectively in a descriptive study the BCLC classification and the treatment of HCC in our hepatology and gastroenterology unit at the university hospital of Yopougon.

2. Method

2.1. Type and Period of Study

This is a descriptive retrospective study from January 2012 01st, to June 2017 30th.

2.2. Inclusion Criteria

Patients hospitalized consecutively during the period for HCC were included. Clinical arguments were: pains in the right hypochondrium, tumor liver, painful liver cirrhosis. Radiological diagnosis was based on the presence of hepatic nodules on cirrhosis liver on abdominal ultrasound scan or abdominal CT scan (wash-out image) with or without the presence of portal thrombosis. An alpha fetoprotein level of ≥200 ng/ml was considered significant but a level <200 ng/ml did not eliminate the diagnosis. The microbiopsy of the liver nodules allowed the histological diagnosis of HCC and the fine needle aspiration of hepatic nodules allowed the cytological diagnosis by the presence of malignant hepatic cells.

2.3. Exclusion Criteria

Patients with benign or secondary malignant hepatic tumors were excluded. Incomplete HCC files without radiological examination (abdominal ultrasound or abdominal CT scan) were not retained. Files with cirrhosis and HCC diagnosis based on unconvincing arguments were excluded from the study.

2.4. Parameters Studied

We collected the data in the hospitalization register of the hepatology and gastroenterology department of the University Hospital of Yopougon.

Epidemiological data (frequency, age, gender), clinical data (presence of pains in the right hypochondrium, jaundice, cirrhosis or tumor liver, ascites) were collected. The Eastern Cooperative Oncology Group (ECOG)/World Health Organization (WHO) system classification was used for the assessment of the general condition of the patient [15]. The grade varies from 0 to 5:

0: Fully active, able to carry on all pre-disease performance without restriction

1: Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work

2: Ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours

3: Capable of only limited self-care; confined to bed or chair more than 50% of waking hours

4: Completely disabled; cannot carry on any self-care; totally confined to bed or chair

5: Dead

Biology included blood count, transaminases, prothrombin level (PT), albumin, bilirubin, alpha fetoprotein, viral markers of hepatitis B and C. Radiological examinations (abdominal ultrasound, abdominal computed tomography) speci-

fied the characteristics of the tumor (the number, size and seat of the nodules). The helical scan was performed with triple arterial, parenchymal and portal acquisition: the most evocative sign of HCC was the existence of a hyper vascularized nodule at early arterial time with lavage (wash-out: (hypo-density) at the portal phase or at the late phase with respect to the non-tumor parenchyma. The diagnosis of HCC was made on the basis of clinical, biological and radiological evidences (nodules > 2 cm giving a "wash-out" image on CT scan) on cirrhosis liver. Histological confirmation by hepatic and cytological microbiopsy was performed by an ultrasound-guided fine needle aspiration of hepatic nodules. The diagnosis of cirrhosis was based on clinical criteria (sharp bottom edge of liver), biological factors (low prothrombin levels, platelet decrease, hypo-albuminemia, Fibrostest-Actitest®), Fibroscan®, morphologic criteria (hepatic dysmorphism and signs of portal hypertension on ultrasound or CT scan) and endoscopic criteria (esophageal varices, varices of cardia and gastric tuberosity or portal hypertension gastropathy).

The BCLC stages were: Stage 0: Patients with very early HCC are optimal candidates for resection. Stage A: Patients with early HCC are candidates for radical therapies (resection and ablation, liver transplantation; or percutaneous treatments). Stage B: Patients with intermediate HCC may benefit from chemoembolization. Stage C: Patients with advanced HCC may receive new agents in the setting of a RCT. Stage D: Patients with end-stage disease will receive symptomatic treatment.

2.5. Statistical Analyzes

The data collected was recorded in an EXCEL file. Statistical analysis was done by calculating the averages and percentages of the different variables. These results were presented in tables. The quantitative variables were expressed as an average. The qualitative variables were expressed by their number and frequency.

2.6. Ethical Aspects

The ethical aspects and deontology have been respected. The anonymity and respect for the confidentiality of information gathered has been guaranteed. The research was done according to the principles of the Helsinki Declaration.

3. Results

During the study period, 2061 patients were hospitalized in the hepato-gastroenterology department of the University Hospital of Yopougon, including 293 cases of HCC. There were 35 files excluded, which made 258 cases of HCC. The mean length of hospital stay was 8.4 days with extremes of 1 to 37 days. The mean HCC frequency in our unit was 5.8%. Our patients had an average age of 48.1 ± 13.4 years with extremes of 19 to 86 years. The male-female sex ratio was 2.95. The date of onset of symptoms was on average 2.5 months and varied from

1 to 10 months, while 82.6% of patients consulted after more than 3 months of the evolution of the disease. Table 1 summarizes the different demographic and clinical characteristics of patients. HCC occurred on a cirrhotic liver whose etiology was dominated by viral hepatitis B with a level of HBs antigen in 62.6% of cases and total anti-HBc antibodies in 90.9% of cases, followed by viral hepatitis hepatitis C in 13.1% of cases. The Child-Pugh score was A in 12.1%, B in 63.6%, and C in 24.3% of cases. The ultrasound was performed in 95.5% of cases. The liver had increased in size with an average size of 170.2 mm. There was 1 nodule in 25.2% [13.5 - 129 mm]; there were 2 nodules in 8.4% [12 - 144 mm], 3 nodules in 2.5% of the cases [6.1 - 129 mm] and more than 3 nodules in 63.9% of cases [9.4 - 144 mm]. The median diameter was 63.2 mm and the largest nodule was 144 mm. We noted 01 ascites in 62.6% of cases, 01 portal thrombosis in 30.4% and 01 splenomegaly in 26.2% of cases. The abdominal computed tomography performed in 62.3% of cases showed a hepatomegaly in 76.9% of cases. There was 01 nodule in 22.5% of cases; there were 02 nodules in 3.9%, 3 nodules in 4.9% and more than 3 nodules in 68.7% of cases. The mean size of nodules on the scan was 91.4 mm in diameter. There was 01 ascites in 67.8% of cases, 01 thrombosis in 30.4% of cases. The different radiologicical signs are in Table 2. For the histological diagnosis of HCC, microbiopsy was performed in 4 cases (2.4%), which returned fibrous liver tissue in 2 cases, not interpretable in 1 case and in favor of HCC in 1 case. There were 3 cases (1.9%) of fine needle aspiration of hepatic nodules that were in favor of HCC. Pulmonary X-ray in search of a secondary localization showed pleurisy in 17.2% of cases and nodules in 14.1% of cases. The BCLC classification was A in 1.3%, B in 0%, C in 55.2%, and D in 43.5% of patients. There was no liver transplantation or hepatic resection. The radiofrequency curative treatment was performed in 2 patients. No patient had palliative treatment by chemoembolization. One patient was treated with sorafenib for 2 months and was unable to continue treatment for lack of financial means. Palliative treatment was mainly support care by analgesics level 2 (%) and 3 (%), blood transfusion (%), rehydration. Table 3 shows the BCLC stages and the different types of treatment. During hospitalization 43.7% of patients died. The causes of death when specified were hepatic encephalopathy (33.9%), digestive hemorrhage (12.5%) and terminal evolution (8.9%).

Table 1. Demographic and clinical characteristics.

Parameters	Number	Percentage
Median age (range), years	48.1 (19 - 86)	
Sex ratio	2.95	
ECOG Classification 0/1/2/3/4	2/27/120/105/4	0.6/10.5/46.5/41/1.4
Hepatomegaly	204	79.2
Jaundice	152	58.9
Ascitis	156	60.4

Table 2. Radiological characteristics of the tumor.

Parameters	Number (N)	Percentage (%)
Nodules number 1/2 - 3/>3	58/23/177	22.5/8.8/68.7
Median tumor size (range), mm	71.4 (17 - 144)	
Ascites	175	67.8
Portal thrombosis	79	30.4

Table 3. BCLC stage and treatment.

Variable	Number (N)	Percentage (%)
BCLC Stage A/B/C/D	3/0/142/112	1.3/0/55.2/43.5
Liver resection	0	0
Liver transplant	0	0
Ethanol percutaneous injection	0	0
Radiofrequency ablation	5	1.9
Transarterial chemoembolization	0	0
Sorafenib	1	0.3
Supportive care	252	97.8

4. Discussion

Our patients are young men with a disease at an advanced stage on presentation manifesting itself in slimming (95%), abdominal pains (94%) and hepatomegaly (93%). This description is the same in the other African studies [16] [17] [18] [19] [20]. In the West, male predominance is also found, but patients are older and diagnosis is made most often during the monitoring of cirrhosis [21] [22]. There is a significant difference in the diagnostic stage between low and high incidence countries. In developed countries, HCC is frequently diagnosed at the symptomatic phase because of the routine instrumental control performed in patients at risk. In developing countries, diagnosis is often delayed by lack of regular control leading to the diagnosis of HCC at an advanced stage [5]. We had no accidental discovery of HCC. Our patients had cirrhosis predominantly classified Child B (63.6%) and C (24.3%). Only 12.1% of patients had Child A cirrhosis. This is due to late consultation of patients who are symptomatic at an advanced stage with severe cirrhosis. It is the opposite in the West where patients are mostly classified Child A [22] [23] [24]. Regardless of the etiologic agent, HCC in West Africa manifests itself at a very advanced stage [17]. HBV is the leading cause of HCC accounting for % of cases in our study, 60% in the Gambia [17] and 65.8% in the African multicentre study [18]. Most of our patients had multi-nodular livers and 84% of patients did not meet the Milan criteria. The choice of treatment is guided by the stage of cancer, the resources available and the level of expertise of the practitioner [25]. Our patients were mostly classified as BCLC C or D because they were symptomatically advanced, which is not the case in Europe [21] [22] [24]. This difference can be explained by the poor general condition of our hospitalized patients, mostly WHO system classi-

fication ≥2. As for curative treatment, we have very few resources because only hepatic resection is possible in our country. Hepatic transplantation and radiofrequency are not performed in our country. Our patients with severe cirrhosis and with portal hypertension are mostly ineligible for surgery, which explains the reason why we have not recorded any case of hepatic resection in our department. Radiofrequency was carried out outside the country. Chemoembolization is also not carried out in the country. Sorafenib is not available and the only patient who received this treatment brought it from the outside. Only the palliative treatment is performed consisting of a symptomatic treatment by level 2 analgesics and support care. HCC in Africa appears to be a more aggressive and incurable tumor than in developed countries, although this assertion may be challenged by the tendency of patients to consult late. Management of liver disease is low in West African countries. The lack of resources leads to the use of untested alternative medications [25]. Prognosis is poor in low-income countries because optimal management of HCC requires resources that are rarely available in developing countries [3] [25]. Our mortality rate was very high because the majority of our patients were at an advanced stage limiting any curative possibilities. Cancer mortality in sub-Saharan Africa is high because of the lack of advanced infrastructures, advanced stage of disease, and dependence of patients on traditional therapies with low therapeutic potential [26]. The Overall survival could not be estimated in our study because very few patients are followed up after hospitalization.

Our current investigation presents the limitations inherent in a retrospective study, including selection bias due to incomplete medical records. As patients underwent different types of treatment, we were unable to evaluate their follow-up due to a high number of patients lost to follow-up. Nevertheless, our results constitute a first study on HCC BCLC classification in our country.

5. Conclusion

HCC occurs on a liver with severe cirrhosis at a late stage in our hospital. What does not allow curative treatment and explains a high mortality rate during hospitalization. The viral hepatitis B is the main risk factor and vaccination at birth will allow reducing the incidence of this cancer in Africa.

Author Contributions

Kissi Anzouan-Kacou Henriette Ya wrote the article, made conception and design, data acquisition, or data analysis and interpretation. Kouamé Dimitri and Bangoura Aboubacar Demba filled and analyzed the database. Mahassadi Kouamé Alassane and Yao Bathaix Fulgence Mamert made the critical revision of the article. Attia Koffi Alain motivated the study.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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