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Treatment of the patients were mainly palliative. Patients with massive ascites were treated with diuretics (usually spironolactone and frusemide). Complications such as bleeding from oesophageal varices were managed conservatively. None of the patients was treated with sclerotherapy.

At post-morterm, pathological findings were noted with a careful attention to the presence of liver cirrhosis, intravascular tumour thrombi and metastases both to the heart and to other organs. Data were analysed using Chi square, Fischer's and Mann Whitney tests where appropriate.

Results

A total of 81 patients (62 males and 19 females) satisfied the inclusion criterion of having autopsy examination. The ages of these patients ranged from 26 to 79 years with a mean of 44 years. Of these patients, 45 (56%) had no CVS tumour thrombi or metastases (Group A) while the remaining 36 (44%) had detectable metastases within the CVS (Group B).

Table 1 comprises the clinical findings in the two groups. There were no significant differences in the features. However, dyspnoea and ascites were more frequent in group B. In group A, 9 patients had a shock syndrome characterised by severe hypotension and oliguria. Bleeding oesophageal varices (2 patients), septicaemia (1 patient) disseminated intravascular coagulopathy (1 patient) and haemoperitoneum (1 patient) were responsible for this syndrome. The 2 patients with shock in group B had episodes of variceal bleeding and haemoperitoneum respectively.

Table 1: Comparison of clinical data in patients without (Group A) and with cardiovascular system tumour invasion (Group B)

	Group A (N = 45)	Group B (N = 36)		
Biodata				
No. of males	30	32		
Age Range (Years)	26 — 79	14 — 69		
Mean Age (Years) ± SD	45.3 ± 13.6	43.6 ± 12.6		
Clinical Features N (%)				
Dyspnoea	10 (22)	10 (28)	X^2=0.3;	P=0.6
Shock	9 (20)	2 (6)	Fisher's;	P=0.06
Ascites	24 (53)	26 (72)	X^2=0.6;	P=0.4
Haemorrhage	9 (20)	6 (17)	X^2=0.6;	P=0.4
Oedema	24 (53)	16 (44)	X^2=0.6;	P=0.4
Abnormal ECG	3 (7)	6 (17)	Fisher's;	P=0.17

The pattern of CVS involvement in group B is summarised in Table 2. The commonest system involved is the PV. It was singularly obstructed by tumour thrombi in 27.2% of the 81 patients. Tumour blockage of the hepatic vein above occurred in 4 (5%) of the patients, and in association with other CVS thrombi in additional 5 (6.2%). The IVC above was obstructed in 1 (1.2%) and as an extension of right atrial tumour in one additional patient. In both patients with pulmonary artery tumour invasion, the cardiac chambers were free of tumours.

Two patients with tumour thrombi in the right atrium were severely dyspnoeic prior to their deaths but there were no clinical characteristics which might have distinguished them from dysponea occurring in other patients, without CVS tumour invasion. Repeated electrocardiography was normal except in 3 and 6 patients in groups A and B respectively. In

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Cardiovascular systemic invasion by hepatocellular carcinoma: Incidence and pattern in a West African population

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Summary

To determine the frequency of cardiovascular systemic invasion by hepatocellular carcinoma (HCC). Eighty-one Nigerian patients who had autopsy examinations were studied. Of these, 36 (44%) had tumour thrombi within the cardiovascular system (CVS) or metastases to the heart itself. Compared with the patients without CVS invasion, no clinicopathologic findings distinguished these two groups from each other. Furthermore, CVS invasion did not worsen the generally bad prognosis of these patients with liver cancer. It is concluded that CVS invasion is frequent and difficult to diagnose by clinical examination. Patients who are selected to undergo hepatic resection must be assessed by imaging techniques to exclude CVS invasion. However, it is unlikely that frequent and routine imaging procedures will affect the generally bad prognosis of the majority of the patients.

Resume

Pour determiner la frequence du cardiovasculaire systeme par l'hepatocellulaire carcinoma, par etude 81 patients de la Nationalite Nigeriens ont subi l'examination de l'autopsie. Parmi 36 (44%) avaient tumeur thrombosis avec CVS ou bien metastase cardic. Cliniquement on trouve pas de destinctions si on fait la comparaison entre les malades qui sont atteints du CVS aux autres. Alors l'invasion du CVS n' a pas du mauvais pronostic par rapports aux patients de l'hepatocellulaire carcinoma. Il faut selecter par des techniques ma giques les patients qui ont subi une chirurgie du foie (ablation) pour exclure la CVS. En fin la ma joute de ces patients ont un mauvaie pronostic.

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Introduction

Hepatocellular carcinoma (HCC) has a tendency to invade the vascular system, particularly the portal vein (PV) and its branches[1-4]. The growth of this tumour from the hepatic vein into the inferior vena cava (IVC) and the right atrium (RA) may result in Budd- Chiari syndrome[5]. Cardiac metastases have been reported to occur from neplasms of various organs including the liver[6-8].

The biological characteristics of HCC differ appreciably in different geographical regions[1,9,10]. The incidence and frequency of cardiovascular metastases have been occasionally reported in Causasians[10] and orientals[11]. However, there is very little information on the invasion of the cardiovascular system by HCC in the Africans[1,12]. We report here the frequency and clinicopathologic pattern of cardiovascular metastases in Nigerians with HCC.

Materials and methods

The patients comprised Nigerians who were evaluated in the Liver Unit of the University College Hospital, Ibadan, Nigeria, from 1976 to 1982. They were histologically proven to have HCC with or without cirrhosis, and were included in this analysis if post-mortem examination were performed immediately after death.

Apart from careful documentation of clinical features, all patients had routine investigations which included complete blood count, liver function tests, electrolytes, urea, chest X-ray and electrocardiogram. Further investigations were performed as dictated by the clinical circumstances. These included hepatic angiography, cardiac echocardiography and abdominal ultrasound. The latter two tests were easily available during the latter half of the study period.

Table 4: Liver, spleen and heart weights, and ventricular thickness in patients with hepatocellular carcinoma without (Group A) and with (Group B) cardiovascular system invasion

Organ	Group A (N = 45)	Group B (N = 36)	Statistical Comparison
Liver: Range (gm)	610 — 6685	955 — 5825	MW2 = 1.2
Mean ± SD	2267 ± 1299	2464 ± 1116	P = 0.1
Spleen: Range (gm)	105 — 1160	88 — 605	MW2 = 0.23
Mean ± SD	384 ± 276	333 ± 135	P = 0.4
Heart: Range (gm)	175 — 485	200 — 785	MW2 = 0.72
Mean ± SD	270 ± 62	287 ± 100	P = 0.26
RV Thickness: Range (mm)	0.1 — 0.8	0.1 — 0.8	MW2 = 0.23
Mean ± SD	0.33 ± 0.2	0.38 ± 0.20	P = 0.4

RV = Right Ventricle; SD = Standard deviation

Discussion

Our study included only those patients in whom post-mortem examination was performed. This group represented only a small proportion of all the patients with HCC evaluated in our unit during the period covered by the study. As very common in most developing countries, consent for autopsy is frequently denied for socio-cultural and religious reasons. Furthermore, a sub-group of patients are lost to follow-up or they discharge themselves into other modalities of treatment outside the medical care system, and die at home.

Despite this limitation, the clinico-pathologic features of our patients are typical for Nigerian patients when compared with the pattern previously reported from our unit[13] and elsewhere in Nigeria[14]. The majority of patients usually present with right hypochondrial pain or mass, and frequently with hepatic decompensation. However, HCC is noted for its protean modes of presentation including spontaneous rupture into the peritoneal cavity. Local or metastatic spread may occasionally be the initial reason for medical consultation[15].

The exact frequency of CVS metastases in HCC is not known and may vary from one geographic area to another. In our study, 44 per cent of HCC patients had tumour thrombi in one or more of the great veins or within the cardiac chambers. This frequency is higher than the 30% documented by Ihde *et al.* in an autopsy study of 26 patients[10].

Metastases to the PV and hepatic veins have been estimated to be 37 and 23 per cent respectively, in patients with cirrhosis associated HCC. The frequency rates in non-cirrhotic HCC are reported to be 23 and 18 per cent respectively[16]. Our study in which 37 per cent of the patients had tumour thrombi (PVTT) confirms these estimates. The high frequency of PVTT in these patients is attributable to an increased flow of arterial blood into the portal vein through the neovascularisation of the tumour itself.

It has been reported that presence of PVTT in some populations may be associated with more severe liver dysfunction, worse prognosis and more advanced oesophageal varices[16]. This observation was not borne out by the experience with our patients. Prognosis as determined by the length of survival was not influenced by the presence of PVTT. Nearly all our patients had underlying macronodular cirrhosis and nodular multicentric type of HCC. In such patients, the prognosis is usually dismal with or without metastases[1,17].

group A, the ECG abnormalities comprised sinus tachycardia (1 patient) low voltage (1 patient) and left ventricular hypertrophy (1 patient). In group B, the ECG abnormalities comprised atrial fibrillation (in 1 patient with tumour invasion of the perimyocardium), incomplete right bundle branch block (1 patient) and sinus tachycardia in the remaining three patients.

Table 2: Cardiovascular involvement (tumour thrombi/metastases) in 81 patients with hepatocellular carcinoma

Site	No	%
Portal Vein (PV)	30	37.0
Hepatic Veins (HV)	9	11.0
Inferior Vena Cava (IVC)	5	6.1
Right Atrium (RA)	2	2.5
Pulmonary Artery (PA)	2	2.5
Heart	1	1.2

PV only (22) HV only (4) IVC only (1) PV + HV (2)
PV + HV + IVC (2) PV + IVC + RA (1) PV + HV + PA (1) PV + PA (1)
PV + Heart (1) IVC + RA (1).

Tables 3 and 4 compare the pattern of pathologic features and metastases in both groups. Liver and spleen weights as well as ventricular thickness were similar in both groups. Distant metastases were more common in group B (with CVS involvement) than in group A.

Table 3: Pathological findings in patients with hepatocellular carcinoma without (Group A) and with (Group B) cardiovascular system invasion

	Group A (N = 45)	Group B (N = 36)	
Lobes Involved			
Both Lobes	34	34	
Right Lobe	7	2	
Left Lobe	4	0	
Underlying Cirrhosis			
Macronodular	41	33	
Micronodular	1	0	
Mixed	3	3	
No Cirrhosis	0	0	
Metastases			
Lungs	5	7	X^2=1.1; P=0.3
CNS	1	1	Fisher's P=0.24
Others	2	4	Fisher's P=0.24

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Secondary Budd-Chiari syndrome caused by HCC is poorly defined and probably underdiagnosed clinically. Eleven per cent of our patients had this complication. This is much less when compared to the observation of Gustafson who found 19 (30%) of 62 cases of HCC to have secondary Budd-Chiari syndrome[18]. Whether this represents a true difference related to ethnicity is uncertain. In none of our patients was there a clinical suspicion of this complication, despite careful analysis of the clinical features. In cirrhotic associated HCC, the ascites is usually tense and intractable. The liver does not easily lend itself to palpation and very often the features of acute Budd-Chiari syndrome, such as tenderness are unidentifiable under the circumstances.

Malignant cardiac metastases may not be as uncommon as hitherto believed. Its incidence may be high as 10 per cent[6,7]. However, only rarely do they involve the cardiac chambers. In our study, only three per cent patients had intracardiac metastases. In one of them, the myocardium was involved with metastatic deposits. In none of these was anti-mortem diagnosis of cardiac metastases confirmed. The difficulty in clinical diagnosis of this complication has been highlighted by Kate *et al.*[7]. In none of their 5 cases with right atrial tumour thrombus, were they able to diagnose this CVS involvement before autopsy. Furthermore, we were unable to observe in any of our three patients fainting, posture related symptoms and oxygen hunger dyspnoea as described by Hanne and Climie in 26 patients with right atrial thrombi[19]. This discordance may be explained by the facts that the tumour thrombi in our patients were not mobile and therefore did not produce the so called ball-valve thrombus syndrome[6,19].

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