

Primary Carcinoma of the Liver in Zambia

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SUMMARY

A review of liver biopsies over a three year period revealed 166 cases of carcinoma of the liver. Hepatocellular carcinoma constituted the commonest malignant tumour in male Zambians. The different histologic sub-types were studied and compared with a study of liver cell cancer in Uganda. Trabecular carcinoma was the commonest histological type. A significant association of hepatocellular carcinoma with macronodular cirrhosis was noted.

INTRODUCTION

The incidence of primary liver cancer shows remarkable regional variations. It is a rare tumour in North America and Europe but it constitutes one of the commonest malignant neoplasms in certain parts of Africa (Doll et al, 1966, 1970). The varied histological patterns of hepatocellular carcinoma have been described by many workers (Edmondson, 1958, Anthony 1973).

The epidemiological and histopathological features of this tumour have not been previously reported from Zambia. The present study was conducted in order to elucidate the epidemiological and histopathological features of liver cell carcinoma and to compare the results with those available from other parts of Africa.

MATERIALS AND METHODS

The Department of Pathology and Microbiology, University Teaching Hospital, Lusaka provides the

diagnostic histopathological services to University Teaching Hospital and hospitals of Central, Southern, Eastern and Western Provinces. These cover approximately 55% of the population of Zambia (Republic of Zambia, Census 1973). All liver biopsies received during the three year period (1971–1973) were reviewed. A total of 166 cases of carcinoma of the liver were found. Aspiration needle biopsy was done in 132 and wedge biopsy in 34 cases. Haematoxylin and eosin (HE), Perl's Prussian blue reaction for iron and reticulin stain (Gordon and Sweet's method) were routinely done. Special stains, periodic acid-Schiff (PAS) before and after diastase, and Southgate's mucicarmine stain were supplemented where necessary.

RESULTS AND COMMENTS

One hundred and sixty six cases of carcinoma of the liver were encountered.

Age and Sex Distribution

This has been shown in Table 1. The age range varied from 18 to 77 years. The majority of the cases 110 (66.2%) were seen in 4th 5th and 6th decades. The peak incidence occurred in the 5th decade. Most of the African studies (Doll et al, 1966; 1970; Pavlica and Samuel, 1970; Gelfand et al, 1972 Anthony 1973) found a similar age distribution. In contrast, liver cell carcinoma had its highest peak in the sixth and seventh decades of life in United States

TABLE I

Age and Sex pattern of liver cell carcinoma.

Age in yrs.	Male	Female
0-10	—	—
11-20	3	—
21-30	9	—
31-40	32	4
41-50	38	6
51-60	24	7
61-70	13	1
70+	1	—
Adult	23	5
Total	143	23

and Europe (Doll et al, 1966; 1970).

Hepatocellular carcinoma occurred in 143 males and 23 females, giving a male: female ratio of 6.2:1. Male predominance is more marked in the present study than noted in Uganda (Anthony, 1973). However a pattern similar to the present study was seen in Ethiopia (Pavlica and Samuel, 1970) and Rhodesia (Gelfand et al., 1972).

Incidence

Hepatocellular carcinoma accounted for 8.2% of all malignant tumours encountered in our Department of Pathology and constituted the commonest malignancy in male Zambians. Our frequency figure of 8.2 per cent is higher than the figures of 6.8 in Uganda, 5.2 in Kenya, 3.0 in Tanzania (Linsell, 1968) and 4.3 in Malawi (Borgstein, 1968).

In contrast, the present figure is much lower than that of Mozambique, 65.5% (Prates and Torres, 1965).

Histopathological Features

Anthony's classification (1973) was used in the present study for comparison of our tumour pathology. Following subtypes were defined with hepatocellular carcinoma.

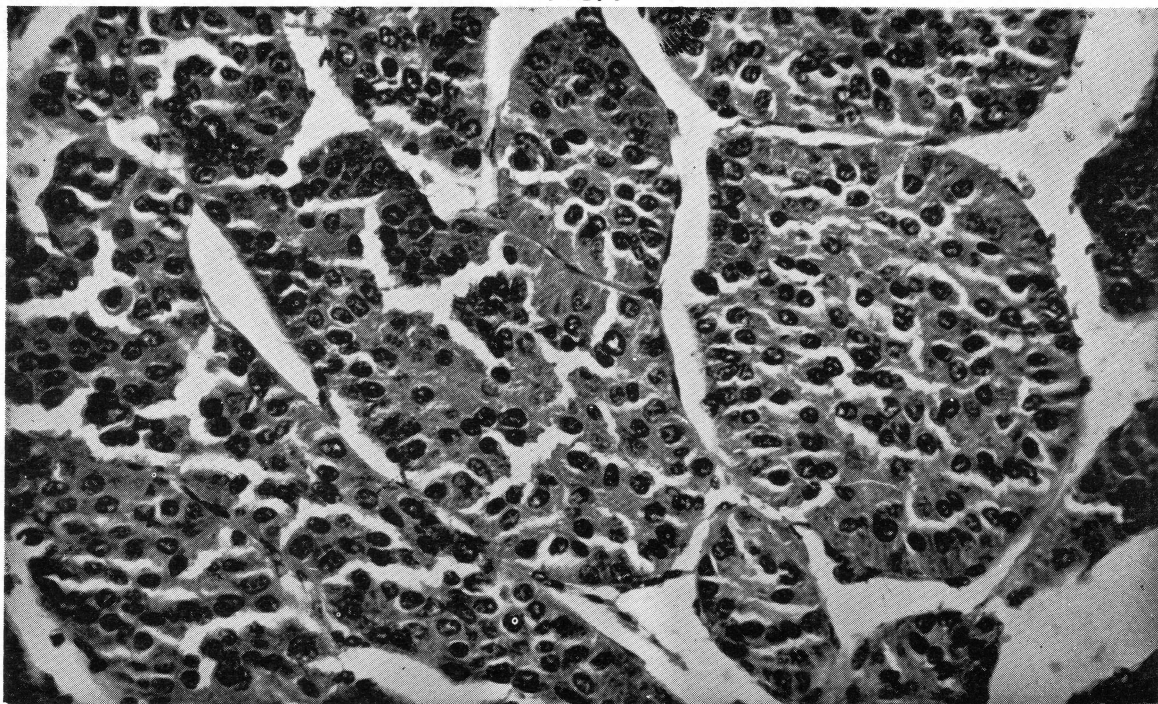
Trabecular Type

This histological type occurred most commonly and was noted in 145 (87.3%) cases. The histological appearance of this type was described by Anthony (1973) and is demonstrated in figures 1 and 2. In this study 72.9% of trabecular carcinoma were well differentiated while 14.4% were poorly differentiated.

Pleomorphic (Anaplastic) Type

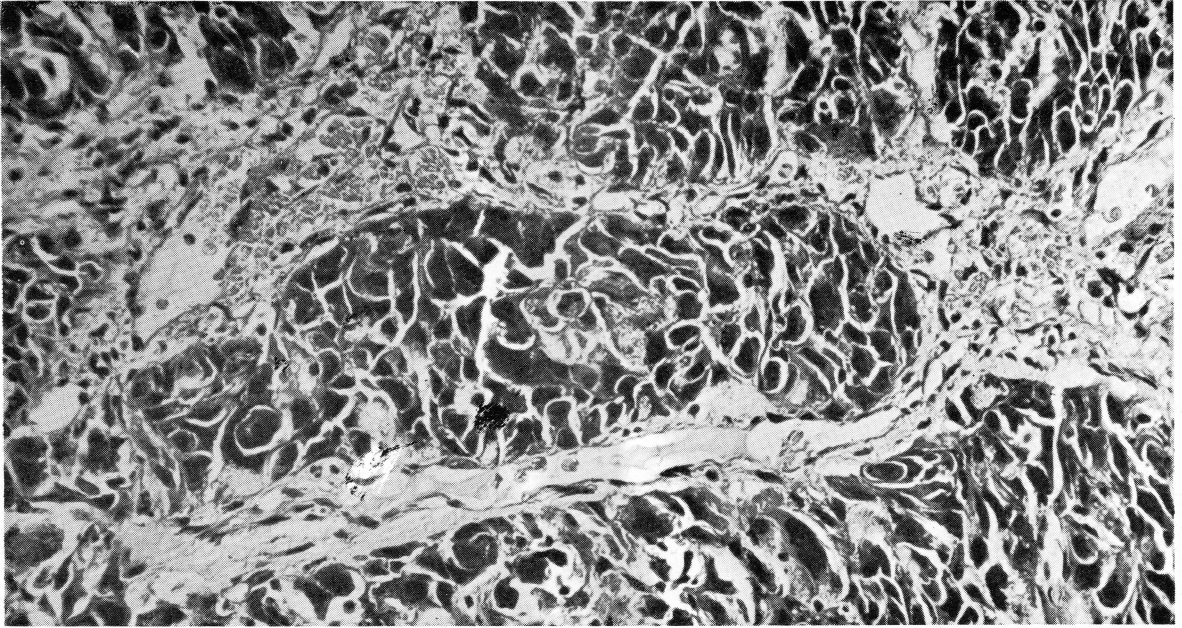
There were only 2 cases classified as pleomorphic carcinoma (Fig. 3). This is a much lower figure than noted in Uganda (Anthony, 1973).

FIG. I



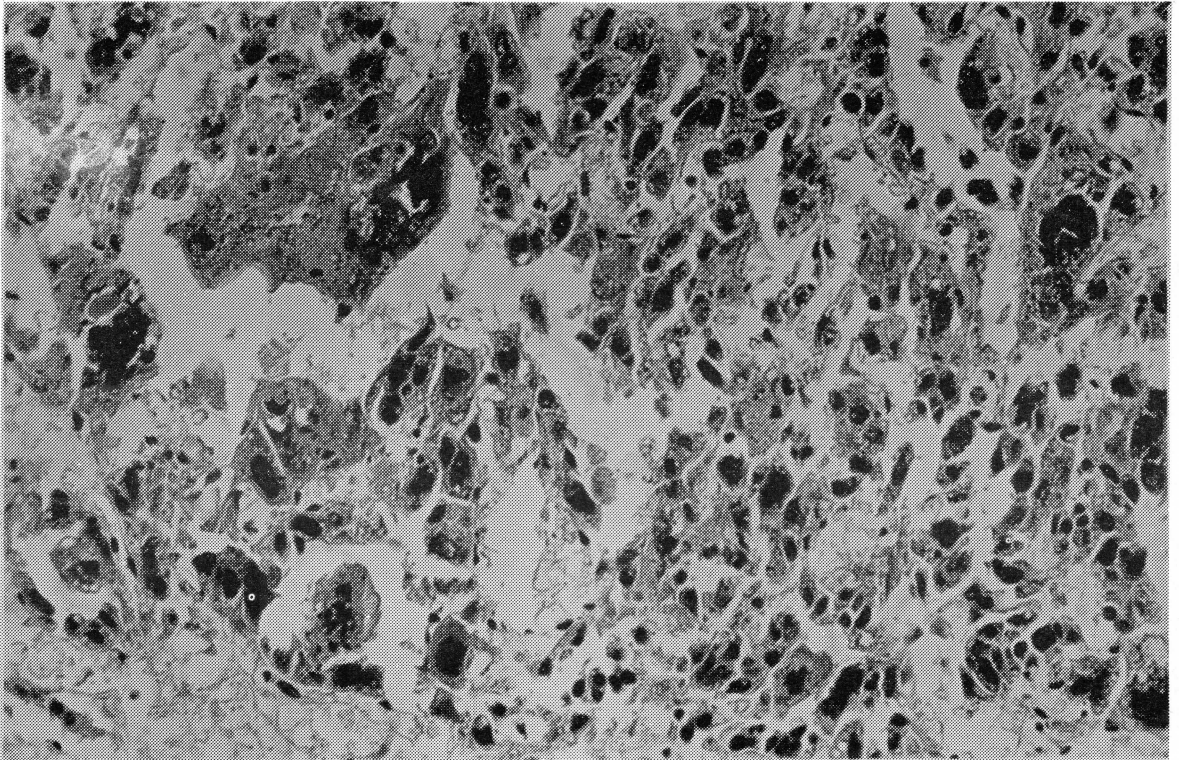
Well differentiated trabecular carcinoma. Tumour cells resemble the normal adult hepatocytes and arrange in trabeculae of more than one to several cells thick. Haematoxylin and Eosin (H & E) x 296.

FIG. II



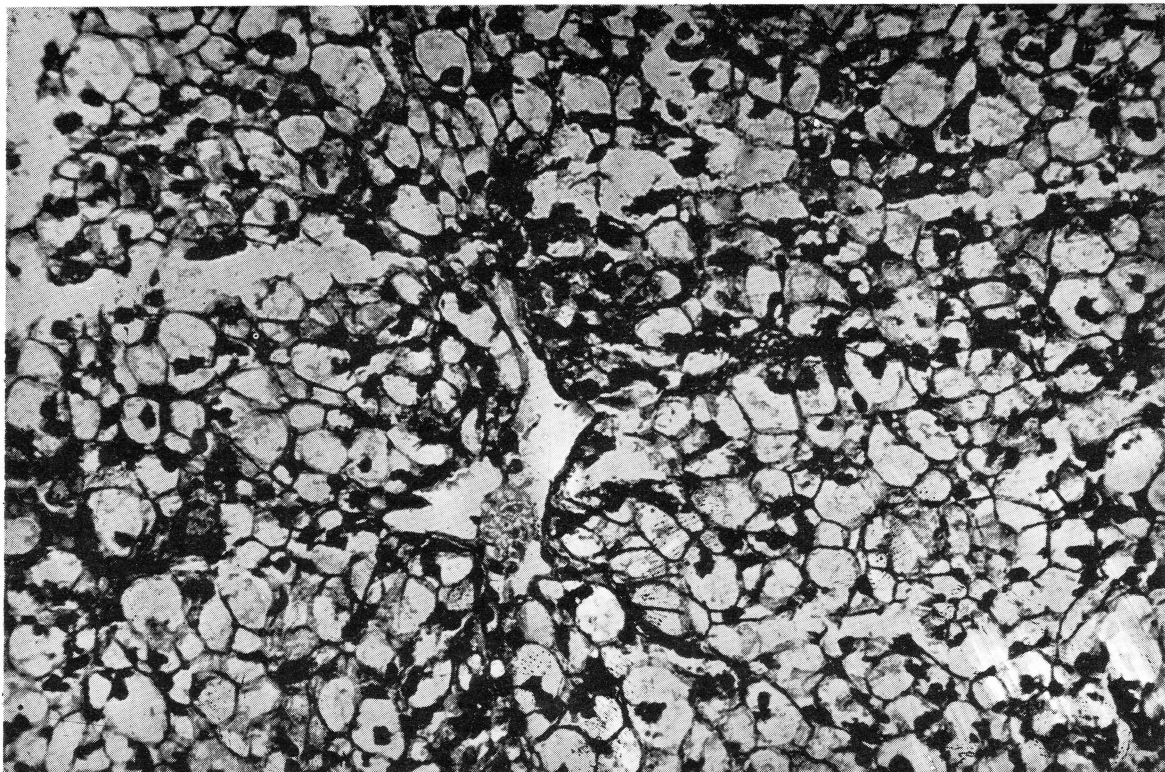
Poorly differentiated trabecular carcinoma showing trabecular pattern with greater degree of anaplasia. H&E x 296.

FIG. III



Pleomorphic type carcinoma showing marked cellular pleomorphism and bizarre giant cells. HE x 296.

FIG. IV



Showing clear cell type hepatocellular carcinoma. H&E X 296.

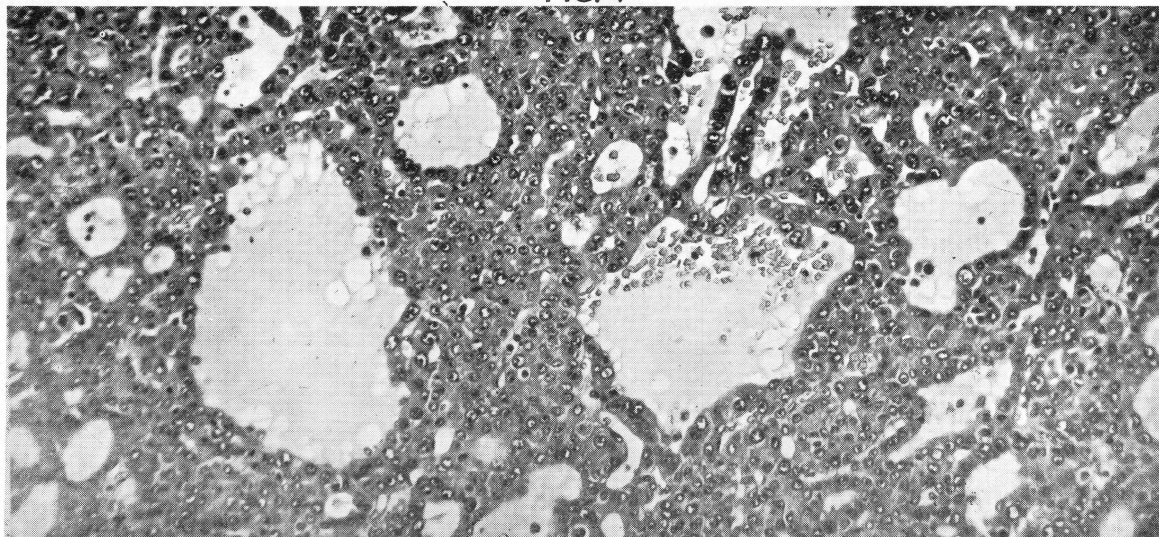
Clear Cell Type

Seven cases (4.2%) were classified as clear cell carcinoma (Fig. 4) showing a slight increase over Anthony's figure of 4 cases (4.5%).

Tubular or Adenoid Type

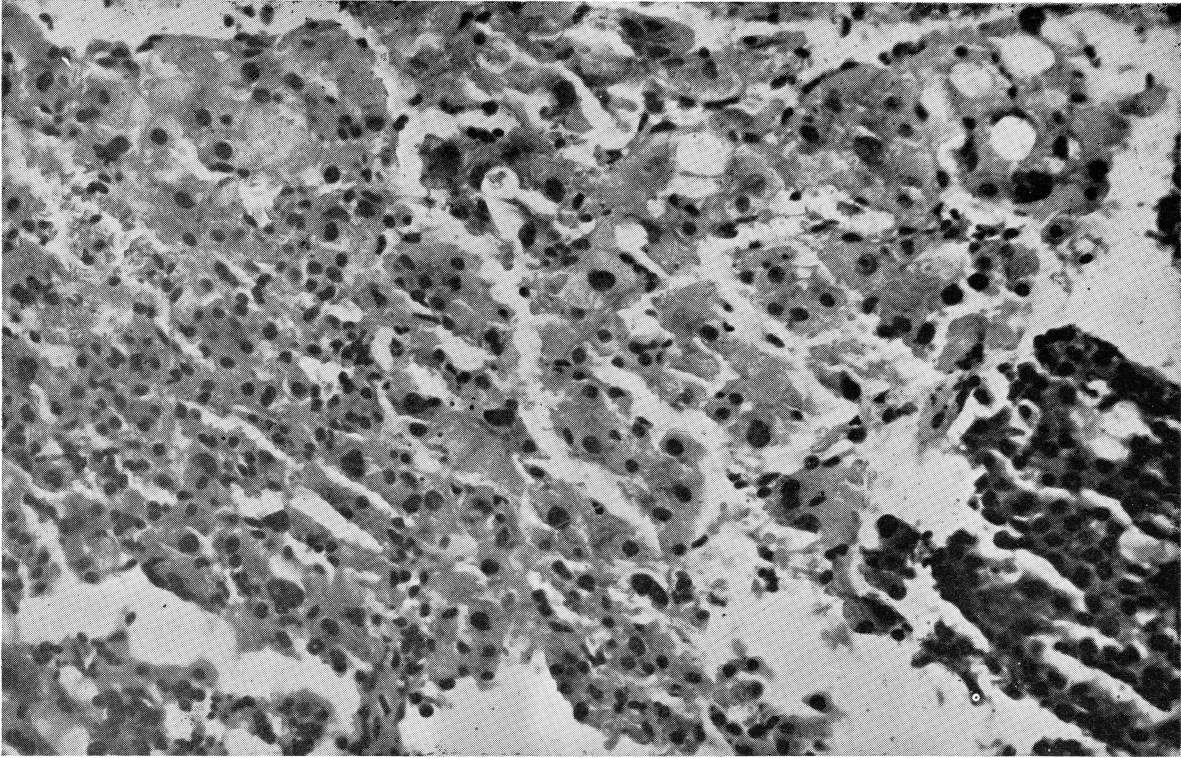
Six cases (3.6%) were seen with tubular carcinoma pattern (Fig. 5). The present figure is lower than a figure of 7.2 per cent in Uganda (Anthony, 1973).

FIG. V



Adenoid type carcinoma showing canaliculi, ducts, acini and cystic spaces of variable sizes. Lumens show homogenous material. H&E 296.

FIG. VI



Showing liver cell dysplasia with well differentiated trabecular carcinoma on the right hand lower corner. H&E 296.

Other Unclassifiable Tumours: 6 (3.6%) Cases

A few cases were difficult to classify in the above variants either due to inadequate biopsy material or a typical appearances.

Some had an appearance of scirrhous carcinoma with polygonal cells having prominent nucleoli and granular eosinophilic cytoplasm. Others had either small cell carcinoma or spindle-cell sarcoma-like appearances. The hepatic origin of these tumours became evident by the cytology of the tumour cells in certain areas.

Associated Conditions

Cirrhosis

Cirrhosis was present 97 (58.4%) cases. Macronodular (postnecrotic and posthepatic) cirrhosis (68.1%) was commonly associated with liver cell carcinoma. Micronodular (nutritional) cirrhosis (4.1%) was found infrequently. Cirrhosis was unclassifiable in 27 (27.8%) cases due to inadequate biopsy material.

The association between hepatocellular carcinoma and cirrhosis varies from 65% to 95% in various studies (Berman, 1951; Edmondson, 1958; Pavlica and Samuel, 1970; Anthony 1973). The apparently low incidence of cirrhosis in the present study may be due to the inclusion chiefly of biopsy material. This is evident by the fact that hepatocellular carcinomas

were associated with cirrhosis in 90% of our autopsy cases.

Liver Cell Dysplasia

This is characterized by the presence of groups of liver cells or a nodule of liver cells which showed nuclear and cytoplasmic enlargement, nuclear pleomorphism, often double nuclei and occasional mitotic figures (Anthony 1973, Fig. 6). These features were noted in only 15(9%) cases. Anthony (1973) found dysplasia in a greater proportion of cases but this may be due to the large sampling of his tumours which came from autopsies. He regarded dysplasia as pre-malignant change. This requires further confirmation by more autopsy studies.

Aetiology

The liver of the Zambian is exposed to a wide variety of harmful stimuli such as malaria, malnutrition, schistosomiasis, siderosis, tuberculosis, bacterial and viral infections from early childhood. A review of liver biopsies during the present study revealed that chronic liver diseases like toxic hepatitis, viral hepatitis, siderosis, schistosomiasis and cirrhosis were frequently encountered. These diseases have been incriminated as possible causes of liver cell carcinoma (Oettle, 1965; Vogel et al, 1970). Toxic hepatitis may

be associated with pneumonia, ingestion of African herbal medicines (Bhagwandeem et al., 1975) and mycotoxins contaminating staple diets.

Epidemic form of viral hepatitis is uncommon in Zambia (Bhagwandeem et al, 1975). However, sporadic cases of viral hepatitis is fairly common and tend to be due to Hepatitis B-antigen (also called hepatitis – associated antigen – HAA). A high frequency of HB-Ag was found in sera of patients with hepatitis, cirrhosis and hepatocellular carcinoma in Africa (Maynard et al., 1970; Vogel et al, 1970 and 1972; Anthony et al., 1972). A high frequency of HB-Ag (50%) and alpha – fetoprotein has been noted with hepatocellular carcinoma in Zambia (Bayley, 1976). Liver cell carcinoma was most commonly associated with macronodular cirrhosis in our autopsy and biopsy material. These findings suggest that an antecedent viral hepatitis due to HB-Ag may play an important role in the aetiology and pathogenesis of hepatocellular carcinoma.

Alcoholic fatty liver and alcoholic cirrhosis were uncommon in Zambian Africans. Micronodular cirrhosis was infrequently associated with liver cell carcinoma in this series. Oettle (1965) suggested siderosis and schistosomiasis as possible causes of liver carcinoma. Both conditions were frequently seen in Zambia. However, hepatic schistosomiasis was not associated with hepatocellular carcinoma and siderosis was minimal or mild in 20% cases of hepatoma. Both of them do not seem to have a casual role for liver cancer in Zambia.

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