CASE REPORT

DOES HIV INFECTION ACCELERATE THE DEVELOPMENT OF HEPATOCELLULAR CARCINOMA? A CASE REPORT IN A YOUNG MAN

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Abstract. Hepatocellular carcinoma (HCC) is an important cancer. It occurs more often in men than women, and occurs mostly in people 50 to 60 years old. HCC has not been previously reported in a young HIV-seropositive patient in Thailand. We documented a very rare case of HCC in a 33 year old man. He was diagnosed and treated as *Salmonella* septicemia and tuberculosis. However, additional diagnosis based on pathological study disclosed a moderately differentiated HCC. Immunohistochemical study of the liver tissue was positive for hepatitis B surface antigen (HBsAg).

Hepatocellular carcinoma is a very important liver cancer. It accounts for 80 to 90% of all liver cancers. The disease is more prevalent in parts of Africa and Asia than in North and South America and Europe. In Thailand, the overall incidence rate ranged between 6.4 and 87.5 per 100,000 in males and 1.4 to 37.2 in females (Deerasamee, 1999). Khon Kaen, a province of the northeastern part of Thailand continues to have the highest incidence in the world in both males and females or both sexes combined (Parkin *et al,* 1997). The cause of liver cancer is unknown, but contributing factors include chronic liver disease, viral hepatitis, hemochromatosis, hepatic carcinogens and toxins. Hepatitis B surface antigen could be detected in 61-63.8% of HCC patients (Petchlai *et al,* 1992). We report here an interesting case of HCC in a young man who was co-infected with human immunodeficiency virus (HIV) infection.

A 33 year old male, a resident of Bangkok, Thailand presented with fever and cough for 2 months. Pertinent physical examination at the first consultation showed decrease breath sound at the right side of the chest wall, oral trash and cervical lymphadenopathy. He was an intravenous drug user for 5 years. Test for Anti HIV was seropositive. He was not aware of HIV infection prior to this illness. Chest X-ray revealed infiltration at the right upper lung field. Though sputum examination for acid-fast bacillus was negative, he was given anti-tuberculous drugs (isoniazid, rifampicin, pyrazenamide and ethambutol). For oral trash, cotrimazole was prescribed. One month later, he came back with the chief complaint of blunt injury at his eye and head. A cabinet fell down to him and injured his right parietal area and right eye. He also admitted not taking the medications previously prescribed. Physical examination showed oral candidiasis, swelling and tenderness of the right upper eyelid with hematoma 1.5 cm in diameter, tender scalp and hematoma at the right parietal area 7 cm in diameter, generalized cervical lymphadenopathy and palpable liver edge at 1 cm below the right costal margin. He was subsequently admitted. Aspiration of the cystic hematoma at the parietal area revealed 50 ml of yellow pus. Hemoculture and culture from the pus was positive for *Salmonella* sp. He was given

ceftrazone (1 g IV q 12 hr), aside from anti-tuberculous drugs and cotrimazole for his oral candidiasis. He was generally weak. His condition gradually deteriorated. Ten days after admission, he developed neck stiffness. Lumbar puncture was performed. Cerebrospinal fluid showed normal open and close pressure, few lymphocytes, with the low sugar (CSF sugar 41 mg%, blood sugar 154 mg%) and high protein (516 mg%) profile. Even though, acid-fast bacillus could not be detected, he was diagnosed as tuberculous meningitis and anti-tuberculous drugs were continued. He expired 12 days after admission with clinical diagnosis of salmonella septicemia and tuberculosis. Pertinent laboratory data revealed Hct 16.2%, WBC 3,600/mm^3, neutrophils 96%, lymphocytes 2%, monocytes 2%, platelets 217,000/ml, TB 1.0 mg%, DB 0.6 mg%, AP 148 mg%, Chol 39 mg/dl, AST 47 IU/l, ALT 55 IU/l, TP 7 g/l, Alb 1.8 g/l, BUN 11 mg/dl, Cr 0.5 mg/dl and normal electrolytes. Liver biopsy was performed to study the pathology of the liver in AIDS patients but unexpectedly revealed hepatocellular carcinoma. Other histologic findings included congestion, intact lobular architecture, normal hepatocytes, reactive Kupffer cells and chronic inflammation at the portal tracts. Further immunohistochemistry study for hepatitis B surface antigen (HBsAg) was positive.

Hepatocellular carcinoma had never been considered of in this case. Firstly, the patient was young, the age of which cancer is rarely included in the differential diagnosis. Secondly, his presentation was fever with cough, which was more likely to be an infectious process. Furthermore with HIV co-infection, opportunistic infection was of interest to search for. Thirdly, physical examination and laboratory data were not suggestive to liver cancer except mild liver enlargement, which is often a non specific findings. Hence, HCC was only detected after death.

Human immunodeficiency virus infected patients are very frequently complicated with malignancies (Biggar *et al,* 1989; Rabkin and Blattner, 1991) and in general they are rapidly progressive because of the immunodeficient state. The most common malignancies are Kaposi's sarcoma (Niedt and Schinella,1985; Tanaka *et al,* 1996a) and malignant lymphoma (Harnly *et al,*1988; Herndier *et al,*1994). Cappell (1991) reported hepatic malignancy and syndrome associated with AIDS, and found Kaposi's sarcoma as the most common malignancy, followed by non-Hodgkin's lymphoma infiltration and peliosis hepatis. Liver cancers are rarely reported in association with HIV infection. A study in Zimbabwe presented younger HCC patients to have high prevalences of HBsAg and anti-HIV and a low prevalence of anti-HCV; while older patients had a high prevalence of anti-HCV and low prevalences of HBsAg and anti-HIV. This suggested that HCV infection is probably an important etiological agent of HCC, however, the role of HIV infection as a cause of HCC either singly or as a co-factor with hepatitis B virus infection remains speculative and warrants further study (Weinig *et al,*1997). HCC usually occurs in patients with hepatitis virus infection. However, Tanaka *et al* (1996b) reported a very rare case of HCC developed in a normal liver without HBV and HCV infection in a 51 year old man. Occurrence below the age of 40 is rare and intriguing factor should be search for. In this presented case, it is interesting to note the occurrence of HCC in a young patient with HIV infection. Based on the evidence of the case, we can speculate that HIV infection may speed up the progression time of HBV induced HCC and/or HIV infection may trigger the proliferation of HCC in this young male.

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REFERENCES

Biggar RJ, Burnett W, Mikl J, Nasca P. Cancer among New York men at risk of acquired immunodefi-

ciency syndrome. *Int J Cancer* 1989; 43: 979-85.

Cappell MS. Hepatobiliary manifestations of the acquired immune deficiency syndrome. *Am J Gastroenterol* 1991; 86: 1-15.

Deerasamee S. A monograph on cancer in Thailand, Vol II, 1992-1994. International Agency for Research on Cancer (IARC) Technical Report No. 34. Lyon: World Health Organization, 1999: 45-8.

Harnly ME, Swan SH, Holly EA, Kelter EA, Padian N. Temporal trends in the incidence of non-Hodgkin's lymphoma and selected malignancies in a population with a high incidence of acquired immunodeficiency syndrome. *Am J Epidemiol* 1988; 128: 261-7.

Herndier BG, Kaplan LD, McGrath MS. Pathogenesis of AIDS lymphoma . *AIDS* 1994; 8: 1025-49.

Niedt GW, Schinella RA. Acquired immunodeficiency syndrome. *Arch Patholol Lab Med* 1985; 109: 727-34.

Parkin DM, Whelan SL, Ferlay J, Raymond R, Young J. Cancer incidence in five continents, Vol VII. Scientific Publication No. 143. International Agency for Research on Cancer (IARC), Lyon 1997.

Petchlai B, Srivatanakul P, Puntanee K, *et al*. Antibodies to hepatitis C virus among patients with hepatocellular carcinoma and blood donors in Thailand. *J Med Assoc Thai* 1992; 75 (suppl): 168-171.

Rabkin CS, Blattner WA. HIV infection and cancer other than non-Hodgkin's lymphoma and Kaposi's sarcoma. *Cancer Surv* 1991; 10: 151-60.

Tanaka T, Hoshino Y, Hayashi S, *et al.* A case of hepatocellular carcinoma in normal liver with no evidence of HBV or HCV infection. *Hepatogastroenterol* 1996a; 43: 1390-4.

Tanaka T, Imamura A, Masuda G, *et al*. A case of hepatocellular carcinoma in HIV-infected patient. *Hepatogastroenterol* 1996b; 43:1067-72.

Weinig M, Hakim JG, Gudza I, Tobaiwa O. Hepatitis C virus and HIV antibodies in patients with hepatocellular carcinoma in Zimbabwe: a pilot study. *Trans R Soc Trop Med Hyg* 1997; 91: 570-2.