Patoloji Bülteni 2002; 19(2): 63-65
Turkish Bulletin of Pathology 2002; 19(2): 63-65

Evaluation of the incidence of HBsAg And HBcAg expressions by immunohistochemically in adult forensic autopsy livers

Erişkin adli otopsi karaciğerlerinde immünhistokimyasal HBsAg ve HBcAg ekspresyonları insidansının değerlendirilmesi

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There are more than 350 million HBV (Hepatitis B Virus) carriers all over the world. In Turkey there are more than 4-5 million HBV carriers [1-3] Thus, viral hepatitis takes an important place among all infectious diseases seen in Turkey. We reexamined the liver slides of 42 autopsies performed in years 1999-2000, in the Hospital of Inonu University, so we had the opportunity to investigate the frequency of HBsAg and HBcAg immunohistochemically, in the liver tissues of the normal population. Among the investigated liver tissues of 42 autopsies, we found HBsAg positivity in 4 (9.52%) of them immunohistochemically, and no positivity for HBcAg was detected in these 4 autopsy livers.

Key Words: Autopsy, Hepatitis, HBsAg, HbcAg

Dünyada 350 milyondan fazla HBV (Hepatit B Virüs) taşıyıcısı vardır. Bu sayı Türkiye' de 4-5 milyondan fazladır [1-3]. Bu durumda viral hepatitler Türkiye' de gözlenen tüm infeksiyöz hastalıklar arasında önemli bir yere sahip olmaktadır. İnönü Üniversitesi Tıp fakültesi Hastanesinde 1999-2000 yıllarında yapılmış olan 42 otopsiye ait preperatları yeniden incelemek suretiyle normal populasyona ait karaciğer dokularında immunohistokimyasal olarak HbsAg ve HbcAg sıklığını araştırma fırsatı bulduk. Karaciğer dokularını incelediğimiz 42 otopsi vakasından 4 tanesinde (% 9.52) HbsAg immunohistokimyasal olarak pozitif bulunurken, bu 4 vakadan hiçbirinin karaciğerinde HbcAg pozitifliği gözlenmedi.

Anahtar Kelimeler: Otopsi, Hepatit, HbsAg, HBcAg

Nowadays it is suggested that, there are more than 350 million HBV(Hepatitis B virus) carriers in the world, and over 4-5 million HBV carriers in Turkey [1-2]. So, HBV still remains to be one of the most curious public health problems. The only reservoir of HBV is the human and the most important spread factors are the carriers[4]. Taking this subject as our starting point we reexamined the liver slides of 42 forensic autopsies performed in years 1999-2000, in the Hospital of Inonu University, thus we had the opportunity to investigate the frequency of HBsAg and HBcAg immunohistochemically, in the liver tissues of the normal population. In these selected cases; none of them died because of a liver pathology, there was no autolysis in the liver tissues and all of the cases were over 20 years of age. We have no information about the health condition of the cases, before their death.

MATERIALS AND METHODS

Hematoxylin&eosin stained slides of the 42 forensic autopsy cases were rewieved. We took new 5 μm sections from each of the archived blocks and stained them histochemically with PAS, reticulin and Masson's Trichrome, to evaluate the arrengement of reticulin fibers, the amount of fibrosis and the amount of intracellular glycogen content. We also stained tissue sections immunohistochemically with HBsAg and HBcAg by using both positive and negative controls.

For the evaluation of the activity of hepatitis and amount of fibrosis in the liver tissues we used modified Ishak- Knodell grading system; hepatitis activity index (HAI), which mainly depends on the necroinflamatory scores[5-6] (table1). The hepatic lesions, which are not mentioned in the criteria of this grading system, such as cholestasis, steatosis, ballooning degeneration, were also noted (tables 2-3).

RESULTS

Among the investigated livers of 42 autopsies, we found HBsAg positivity in four of them (9.52%) immunohistochemically, and no positivity for HBcAg was deteceted in these four autopsy livers. There was severe confluent necrosis in one case, while all four cases had mild piece-meal necrosis and moderate portal inflammation. Apopitosis was moderate in two of four and mild in two cases.

When modified HAI grading is applied to all 42 autopsy livers, four of them were found to be over 6/18, which means intermediate activity for chronic hepatitis. Two cases of intermediate activity, showed no positivity for neither HbsAg, nor HbcAg immunohistochemically. Among those four cases of intermediate activity for hepatitis, two cases were immunohistochemically positive for HBsAg and had the criteria for chronic hepatitis B infection.

In the other two cases positive for HBsAg immuno-

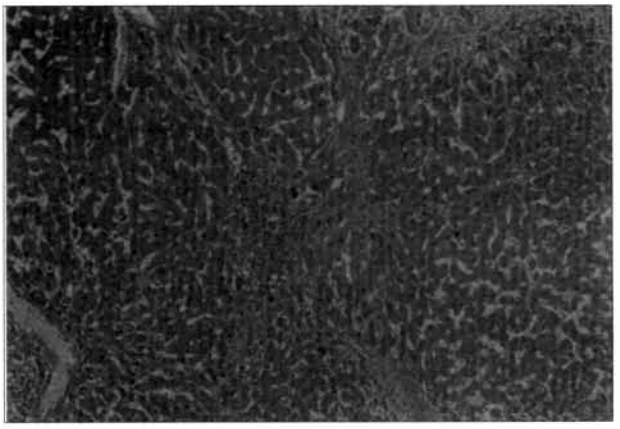


Figure 1: Positivity for HBsAg immunohistochemically in an autopsy liver, with an activity of 6/18 and fibrosis of 1/6 (Case 40, x100)

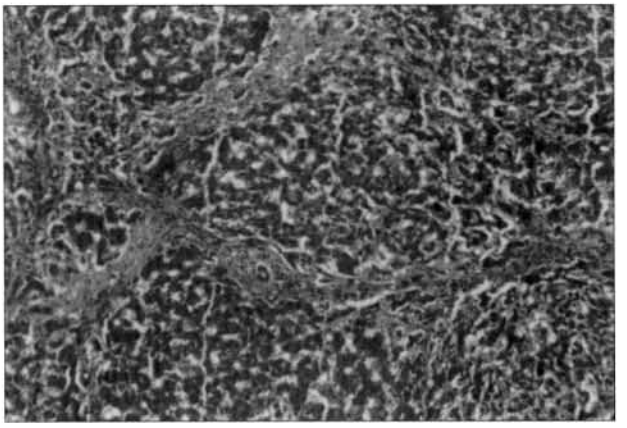


Figure 2: Prominent fibrosis in an autopsy liver which is negative for H BsAg immunohistochemically (Case 36, Masson's Trichrome, x400)

histochemically, HAI was evaluated as 5/18 and 4/18 respectively and they were accepted as cases with mild activity.

There was no serious fibrosis in all four cases positive for HBsAg. However, in one case, negative for HBsAg immunohistochemically, fibrosis was found to be 5/6 and had micronodular pattern of cirrhosis.

DISCUSSION

HBV can produce several forms of hepatitis, such as; acute hepatitis, nonprogressive chronic hepatitis, progressive chronic hepatitis ending in cirrhosis, fulminant hepatitis with massive liver necrosis, an asymptomatic carrier state, with or without progressive subclinical disease, and the backdrop for hepatitis D virus[3]. HBV (Hepatitis B virus) is the most important etiologic agent of hepatocellular carcinoma, and the risk of hepatocellular carcinoma is 200 times greater in the people positive for HBsAg, than the negative ones. [5,9]. After the disease, with cessation of viral replication and the appearance of antiviral antibodies, infectivity ends and liver damage subsides, however the risk of hepatocellular carcinoma persists[3].

Acute viral hepatitis is characterised by hepatocellular necrosis, a portal and lobular lymphocytic infiltrate, and regenerative activity. The infiltrate of viral hepatitis is predominantly composed of lymphocytes, and is most prominent in the portal tracts, and may spill over into the periportal parenchyma[9].

Taking into consideration all these criteria, we applied the modified HAI grading to all 42 autopsy livers. None of the autopsy livers had hepatocellular carcinoma, even an occult one. Two of the four HBsAg positive cases were proved to be chronic hepatitis of intermediate grade (10/18 and 6/18 respectively), caused by HBV.The lowest activity for hepatitis among the HBsAg positive cases was 4/18, which means chronic hepatitis of low grade(Table1). Two cases, which were HbsAg and HbcAg negative, also had an intermediate grade HAI, thus we could not prove their cause to be of viral etiology. One of these two showed severe fibrosis (cirrhosis), and did not show any clue about the etiology for fibrosis. This cirrhosis could have been developed secondary to chronic alcohol administration, HCV hepatitis, toxic hepatitis or it might be a cryptogenic one .

When HAI grading is applied to all 42 cases, it can easily be seen that, the highest values belonged to the ones positive for HbsAg, except for a case among HBsAg negative ones, which had HAI of 8/18. There was no evidence about the etiology of intermediate grade activity for hepatitis in this case. The case with severe fibrosis and HAI of 8/18, was another exception for intermediate HAI among the cases negative for HBsAg.

When the proportion of HBV indicators and HBV cariers is taken into consideration, world is divided into low, medium and high endemic regions. The percentage of cariers in medium endemic regions vary between 2% and 10%[1-3]. The seroprevalance of HBsAg in the normal population in Turkey was found to be between 1.3% and 11.5% in different studies and these results led Turkey to be in the medium endemic region for HBV infection. [1,2,4,7]. In an autopsy study performed in Sydney, the positivity for HBsAg was found 29%, very high when compared with the HBsAg investigations in the serum (4%) of the ordinary people living in Sydney[8].

One of the results of our study is about public health, if we think that one of every ten people is an HBV carrier. In Turkey, as HBV infection risk is highest in people working in health and medicine, our results seem to be more important for doctors and technicians, especially working in forensic medicine and pathology. This means that they need to protect themselves against this severe desease.

An other result is about the activity of these occasional HBV(+) livers of our autopsy cases. In our study, there were four HbsAg (+) cases and 2 of them had chronic active hepatitis, which means; though they had

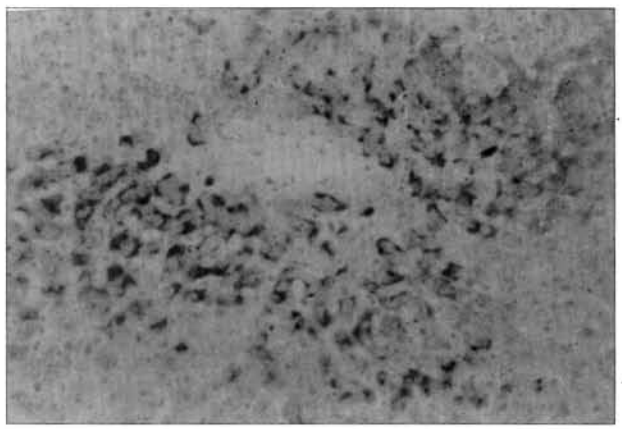


Figure 3: Intermedrate activity (8/18) and prominent fibrosis in an autopsy liver, which is negative for HBsAg (x400).

	Hepatitis in Periportal or periseptal spaces (piecemeal necrosis)	*Confluent necrosis*	*Focal lytic necrosis, apopitosis and focal inflamation*	*Portal inflamation*	***HAI***	***Fibrosis***
Case6	1/4	5/6	2/4	2/4	10/18	0/6
Case7	1/4	1/6	2/4	2/4	6/18	1/6
Case16	1/4	0/6	1/4	2/4	4/18	1/6
Case40	1/4	1/6	1/4	2/4	5/18	2/6

Table 1: Modified HAI Grading (necroinflamatuary scores), and fibrosis index applied to the HBsAg (+) autopsy livers (4,5)

Cases	***Modified HAI grading***	***fibrosis***	***HBcAg***	***HBsAg***	***Other lesions***
Case6	10/18	0/6	(-)	(+)	Prominent ballooning degeneration
Case7	6/18	1/6	(-)	(+)	Kolestasis
Case16	4/18	1/6	(-)	(+)	Slight kolestasis
Case25	8/18	1/6	(-)	(-)	Kolestasis
Case36	8/18	5/6	(-)	(-)	----
Case40	5/18	2/6	(-)	(+)	----

Table 2: Autopsy cases showing HBsAg positivity, fibrosis and HAI grading greater than 6/18

Steatosis (macro and micro vesicular)	7 cases
Kolestasis (perisantral, intracanalicular)	11 cases
Ballooning degeneration	3 cases

Table 3: Number of cases showing noninflammatory hepatic lesions

such a severe active desease, they were not aware of their disease. This is a real health and social problem, if we think that they were married and had children.

As a conclusion, in our study, the incidence of HBsAg in the autopsy livers, with a value of 9.52 %, is a real threat for public health in Turkey. When this study is compared with seroprevalance studies previously performed in different parts of Turkey we can say that our results showed correlationn with these studies. This means that, the severity of the endemicity of HBV infection still persists in Turkey.

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