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652.MULTIPLE MYELOMA: CLINICAL AND EPIDEMIOLOGICAL

Hepatitis B Virus Infection Status and Reactivation Analysis in Multiple Myeloma in China

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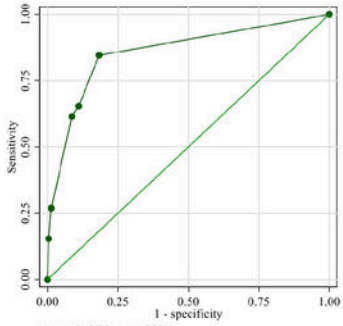
Background:
China is a highly endemic area for Hepatitis B virus (HBV) infection and HBV reactivation is an event of concern in treating patients with hematologic malignancy. However, there were very few reports regarding HBV reactivation in patients with multiple myeloma (MM) in China. Since the approval of novel agents, especially immunotherapy such as monoclonal antibody and chimeric antigen T cell immunotherapy, the risk of HBV reactivation has increased. Therefore, the study aimed to evaluate the HBV infection status in MM and explore the incidence and risk factors of HBV reactivation in MM patients in China.
Methods:
Newly diagnosed MM patients with available serologic assays for HBV infection were retrospectively enrolled between June 30, 2008 and December 30, 2022 in West China Hospital, Sichuan University. Demographic and clinical data were obtained from the "HemaTank" Chinese Multiple Myeloma Database (HCMMD). Meanwhile, patients diagnosed with Waldenstrom Macroglobulinemia (WM) at the same time were enrolled as the control group. HBV reactivation was defined as the occurrence of one of the following: $\geq$ 2 log increase in HBV-DNA levels from baseline level, detection of HBV-DNA with level > 100 IU/ml in a person with undetectable HBV DNA at baseline or HBsAg-negative becoming positive. The penalized maximum likelihood logistic regression for rare events was applied to identify independent risk factors related to HBV reactivation.
Results:
The study recruited 3040 MM patients with a median age of 62 (range 14~98) and 240 WM patients with a median age of 63 (range 25~92). The HBsAg-positive rates were similar between MM and WM (9.4% vs 10.8%, P=0.49), but both the HBcAb-positive rates and HBeAb-positive rates in WM were significantly higher than MM (76.3% vs 60.7%, P<0.001; 37.5% vs 25.1%, P<0.001). The analysis of co-expression of HBV markers shows that the prevalence of HBsAg-/Anti-HBs+/anti-HBC- in MM was significantly higher than WM (16.7% vs 8.3%, P<0.001) and HBsAg-/Anti-HBs-/anti-HBC+ in MM was significantly lower than WM (18.3% vs 27.1%, P<0.001). However, he prevalence of HBsAg+/ HBeAg+/anti-HBC+ and HBsAg+/ anti-HBeAb+/anti-HBC+ were similar between MM and WM (0.5% vs 1.3%, P=0.158; 8.6% vs 8.8%, P=0.503). The baseline characteristics of HBsAg-positive MM and HBsAg-negative MM were summarized in Table 1. The rates of HBsAg-positive MM were significantly increased in young male patients (P<0.05). The level of ALT and AST, and the incidence of HBV reactivation, liver cirrhosis and pulmonary disease were significantly higher in HBsAg-positive MM than in HBsAg-negative MM (P<0.05). Of the 2147 MM patients who have received at least one line of chemotherapy (Table 1), 924 (43%) MM patients received bortezomib-containing or lenalidomide-containing regimens as the frontline therapy, while only 21 (1.0%) received a daratumumab-containing regimen as the frontline therapy. During hospital-documented follow-up visits, 26 (1.21%) MM patients have experienced HBV reactivation. According to the multivariate analysis of risk factors for HBV reactivation in MM, liver cirrhosis (OR 8.63, 95%CI 2.95-25.24, P<0.001), autologous stem cell transplantation (OR 6.03, 95%CI 2.47-14.72, P<0.001) and HBsAg-positive (OR 14.45, 95%CI 6.50-32.14, P<0.001) were independent risk factors associated with high prevalence of HBV reactivation. The ROC curve of the model integrating the three factors is shown in Figure 1, and the AUC was 0.8584.
Conclusions:
Among Chinese MM patients with multiple myeloma, a high proportion of MM patients presented with resolved hepatitis B virus infection, whereas HBV reactivation was pretty rare. However, long-term HBV DNA levels monitoring is still needed for MM patients at high risk for HBV reactivation.

Disclosures No relevant conflicts of interest to declare.

Table 1. The baseline characteristics of HBsAg-positive MM and HBsAg-negative MM.

	HBsAg-postive MM n=287	HBsAg-negative MM n=2753	P-value
Age, mean ± SD	58.87 ± 11.14	61.44 ± 12.04	<0.001
Gender			
Female	103 (35.9%)	1238 (45.0%)	0.003
Male	184 (64.1%)	1515 (55.0%)	
BMI, mean ± SD	22.79 ± 2.90	23.03 ± 3.18	0.50
Smoking history			
No	55 (82.1%)	659 (82.2%)	0.99
Yes	12 (17.9%)	143 (17.8%)	
Alcohol consumption			
No	54 (80.6%)	698 (86.9%)	0.15
Yes	13 (19.4%)	105 (13.1%)	
Hb (g/L), mean ± SD	102.84 ± 31.99	98.44 ± 29.44	0.020
PLT (×10^9/L), mean ± SD	152.44 ± 83.63	171.66 ± 95.20	0.001
WBC (×10^9/L), mean ± SD	6.16 ± 2.65	6.58 ± 4.87	0.15
Lymphocyte (×10^9/L), mean ± SD	1.58 ± 0.79	1.61 ± 1.16	0.65
Neutrophils, mean ± SD	3.94 ± 2.25	4.32 ± 3.87	0.11
CD3+ T cell (%), mean ± SD	69.38 ± 13.80	69.62 ± 12.29	0.88
CD4+ T cell (%), mean ± SD	35.45 ± 11.38	35.41 ± 11.17	0.98
CD8+ T cell (%), mean ± SD	29.42 ± 11.27	30.12 ± 11.72	0.64
Ca, mean ± SD	2.28 ± 0.38	2.27 ± 0.38	0.66
LDH (U/L), median (IQR)	192.00 (152.00, 251.00)	184.50 (147.00, 244.00)	0.23
Cr, median (IQR)	85.00 (65.30, 167.00)	84.95 (65.30, 139.00)	0.55
ALT, median (IQR)	21.00 (14.50, 31.50)	17.00 (12.00, 27.00)	<0.001
AST, median (IQR)	24.50 (18.00, 33.00)	22.00 (17.00, 30.00)	0.001
Albumin, mean ± SD	36.57 ± 7.83	36.06 ± 7.98	0.31
Beta-2 microglobulin, median (IQR)	4.78 (2.67, 11.10)	4.33 (2.77, 8.37)	0.40
IgG, median (IQR)	12.30 (5.50, 33.35)	12.00 (5.96, 33.05)	0.65
IgA, median (IQR)	900.00 (247.00, 2915.00)	715.00 (229.00, 3180.00)	0.34
IgM, median (IQR)	371.00 (168.50, 838.00)	336.00 (161.00, 728.00)	0.11
immunoparesis			
No	56 (22.2%)	448 (18.3%)	0.12
Yes	196 (77.8%)	2006 (81.7%)	
ISS stage			
I	61 (29.8%)	577 (30.4%)	0.068
II	48 (23.4%)	571 (30.1%)	
III	96 (46.8%)	747 (39.4%)	

	HBsAg-postive MM n=287	HBsAg-negative MM n=2753	P-value
HBV reactivation			
No	271 (94.4%)	2743 (99.6%)	<0.001
Yes	16 (5.6%)	10 (0.4%)	
Fatty liver disease			
No	259 (90.2%)	2447 (88.9%)	0.48
Yes	28 (9.8%)	306 (11.1%)	
Liver cirrhosis			
No	268 (93.4%)	2674 (97.1%)	<0.001
Yes	19 (6.6%)	79 (2.9%)	
Tuberculosis			
No	283 (98.6%)	2676 (97.2%)	0.16
Yes	4 (1.4%)	77 (2.8%)	
Hypertension			
No	219 (76.3%)	2045 (74.3%)	0.45
Yes	68 (23.7%)	708 (25.7%)	
Diabetes mellitus			
No	258 (89.9%)	2449 (89.0%)	0.63
Yes	29 (10.1%)	304 (11.0%)	
Renal insufficiency			
No	235 (81.9%)	2214 (80.4%)	0.55
Yes	52 (18.1%)	539 (19.6%)	
Amylosis			
No	271 (94.4%)	2522 (91.6%)	0.097
Yes	16 (5.6%)	231 (8.4%)	
Pulmonary disease			
No	215 (74.9%)	1862 (67.6%)	0.012
Yes	72 (25.1%)	891 (32.4%)	
autologous stem cell transplantation			
No	260 (90.6%)	2561 (93.0%)	0.13
Yes	27 (9.4%)	192 (7.0%)	
Frontline treatment	N=209	N=1938	0.056
Daratumumab-containing regimen	0 (0)	21 (1.1)	
Bortezomib/lenalidomide-containing regimen	7 (3.3)	143 (7.4)	
Bortezomib-containing regimen	58 (27.8)	584 (30.1)	
lenalidomide-containing regimen	16 (7.7)	116 (6.0)	
Thalidomide-containing regimen	95 (45.5)	850 (43.9)	
Others	33 (15.8)	224 (11.6)	



Factors	Odds ratio	Standard error	P value	95% confidence interval	
				lower limit	upper limit
Liver cirrhosis	8.63	4.73	<0.001	2.95	25.24
ASCT	6.03	2.75	<0.001	2.47	14.72
HBsAg-positive	14.45	5.89	<0.001	6.50	32.14

Figure 1. The ROC curves of the penalized maximum likelihood logistic regression model combining factors of liver cirrhosis, autologous stem cell transplantation and HBsAg-positive status used to predict the risk of HBV reactivation in MM receiving chemotherapy.

Figure 1

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