ORIGINAL ARTICLE

The Correlations among Circulating Tumor Cells, Epstein-Barr Virus Status, and Epidemiology in Patients with Nasopharyngeal Carcinoma

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SUMMARY

Background: Studies have shown that circulating tumor cells (CTCs) can be detected in nasopharyngeal carcinoma (NPC). However, the relationship between CTCs and tumor stage is still controversial. This study aims to investigate the correlations among CTCs, Epstein-Barr virus (EBV) status, clinicopathologic features, and epidemiological risk factors in patients with NPC.

Methods: **Three hundred and thirty primary NPC patients with complete clinical data and epidemiology information were collected. Analysis of CTCs was performed using the CTCBIOPSY system. The plasma EBV DNA load was detected by quantitative real-time PCR. Detection of VCA-IgA and EA-IgA antibodies titers was conducted by immunoenzymatic assay. EBNA1-IgA and Zta-IgA were measured using an enzyme-linked immunosorbent assay.**

Results: **The presence of CTCs was associated with high EBV DNA load (p < 0.05). The positive rate of CTCs was correlated with T and M classifications of NPC (T: 13.2% vs. 22.9%; M: 17.9% vs. 34.8%, p < 0.05). Compared with never and former smokers, current smokers exhibited a higher positive rate of EBNA1-IgA (83.3% and 81.0% vs. 92.5%, p < 0.05); the patients with pack-years of smoking ≥ 15 displayed a significantly higher positive rate of EBNA1-IgA than those with pack-years of smoking < 15 (98.0% and 92.5% vs. 81.0%, p < 0.05).**

Conclusions: **CTCs positivity was closely associated with tumor burden and distant metastasis of NPC. Smoking status and smoking cumulative dose of NPC patients might be correlated with EBV activation.**
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Supplementary Data

Supplemental Table S1. Association of CTCs positivity, EBV status and epidemiological factors in NPC patients [M (quartile) or n (%)].

Characteristic and category	n	CTCs positivity	EBV load (IU/mL)	VCA-IgA (titer 1:)	EA-IgA (titer 1:)	EBNA1-IgA	Zta-IgA n (%)
Gender							
Male	246	49 (19.9)	597 (0 - 4,545) *	320 (160 - 640)	80 (40 - 160)	219 (89.0)	161 (65.4) [#]
Female	84	18 (21.4)	0 (0 - 1,453)	160 (160 - 640)	80 (20 - 160)	70 (83.3)	44 (52.4)
Age (years)							
≤ 50	187	39 (20.9)	500 (0 - 3,340)	320 (160 - 640)	80 (40 - 160)	166 (88.8)	128 (68.4) [#]
> 50	143	28 (19.6)	536 (0 - 4,760)	320 (160 - 640)	80 (20 - 160)	123 (86.0)	77 (53.8)
Educational level (years)							
≤ 6	139	29 (20.9)	538 (0 - 3,890)	320 (80 - 640)	80 (20 - 160)	121 (87.1)	83 (59.7)
7 - 9	102	18 (17.6)	500 (0 - 3,713)	320 (160 - 640)	80 (40 - 160)	91 (89.2)	69 (67.6)
10 - 12	59	16 (27.1)	548 (0 - 4,590)	160 (80 - 640)	40 (20 - 160)	49 (83.1)	33 (55.9)
> 12	30	4 (13.3)	584 (0 - 2,915)	320 (80 - 640)	120 (20 - 160)	28 (93.3)	20 (66.7)
Body mass index (kg/m^2)							
< 18.5	37	7 (18.9)	593 (0 - 4,935)	640 (160 - 640)	160 (40 - 160)	36 (97.3)	26 (70.3)
18.5 - 22.9	168	37 (22.0)	500 (0 - 3,133)	320 (100 - 640)	80 (20 - 160)	141 (83.9)	102 (60.7)
≥ 23	125	23 (18.4)	500 (0 - 4,265)	320 (160 - 640)	80 (40 - 160)	112 (89.6)	77 (61.6)
First-degree family history of NPC							
No	306	60 (19.6)	500 (0 - 3,955)	320 (160 - 640)	80 (35 - 160)	267 (87.3)	191 (62.4)
Yes	24	7 (29.2)	500 (0 - 1,080)	320 (100 - 640)	40 (18 - 160)	22 (91.7)	14 (58.3)
Frequency of brushing teeth (times/day)							
≤ 1	215	45 (20.9)	500 (0 - 3,570)	320 (80 - 640)	80 (20 - 160)	190 (88.4)	136 (63.3)
≥ 2	113	21 (18.6)	500 (0 - 4,325)	320 (160 - 640)	80 (40 - 160)	98 (86.7)	68 (60.2)
irregular	2	-	-	-	-	-	-
Smoking status							
Current	159	29 (18.2)	518 (0 - 3,950)	320 (160 - 640)	80 (40 - 160)	147 (92.5) [#]	104 (65.4)
Former	21	7 (33.3)	1,320 (500 -	320 (60 - 640)	80 (10 - 160)	17 (81.0)	11 (52.4)
Never	150	31 (20.7)	500 (0 - 3,062)	160 (80 - 640)	80 (20 - 160)	125 (83.3)	90 (60.0)
No. of cigarettes smoked per day							
< 10	17	4 (23.5)	2,990 (250 -	320 (160 - 640)	80 (40 - 160)	14 (82.4)	11 (64.7)
10 - 19	35	11 (31.4)	538 (0 - 4,010)	320 (160 - 640)	80 (40 - 160)	33 (94.3)	19 (54.3)
≥ 20	121	21 (17.4)	517 (0 - 3,675)	320 (160 - 640)	80 (40 - 160)	111 (91.7)	80 (66.1)
Missing	7	-	-	-	-	-	-
Pack-years of smoking							
< 15	42	14 (33.3)	623 (0 - 3,683)	320 (160 - 320)	80 (40 - 160)	34 (81.0) [#]	23 (54.8)
15 - 29	51	7 (13.7)	795 (0 - 6,660)	320 (160 - 640)	160 (40 - 160)	50 (98.0)	36 (70.6)
≥ 30	80	15 (18.8)	500 (0 - 2,243)	320 (80 - 640)	120 (20 - 160)	74 (92.5)	51 (63.8)
Missing	7	-	-	-	-	-	-
Alcohol drinking							
Yes	112	25 (22.3)	500 (0 - 4,483)	320 (160 - 640)	80 (40 - 160)	99 (88.4)	71 (63.4)
No	218	42 (19.3)	500 (0 - 3,590)	320 (160 - 640)	80 (20 - 160)	190 (87.2)	134 (61.5)
Alcohol consumption (g/day)							
< 10	75	15 (20.0)	500 (0 - 3,170)	320 (160 - 640)	80 (40 - 160)	69 (92.0)	49 (65.3)
10 - 39	22	7 (31.8)	849 (0 - 6,880)	320 (160 - 640)	80 (40 - 160)	20 (90.9)	13 (59.1)
≥ 40	15	3 (20.0)	500 (0 - 4,900)	320 (80 - 640)	160 (40 - 160)	10 (66.7) [#]	9 (60.0)

* - p < 0.05 by Mann-Whitney U test, [#] - p < 0.05 by χ^2 test.