E-CADHERIN AND CD44V6 EXPRESSION IN HUMAN HEPATOCELLULAR CARCINOMAS

ZHENG Jian-ming, ZHENG Wei-qiang, GONG Zhi-jin, ZHU Ming-hua, DAI Yi-min, ZHANG Zhao-huan

1Department of Pathology, Changhai Hospital, Secondary Military Medical University, Shanghai, 200433; 2Grade 98, Department of Military Surgeon, Secondary Military Medical University, Shanghai 200433

ABSTRACT

Objective: To investigate the significance of E-cadherin (E-cad) and CD44v6 expression in human hepatocellular carcinomas (HCCs). Methods: An immunohistochemical method was used to detect E-cad and CD44v6 expression in 66 cases of HCCs. Results: The positive rates of E-cad and CD44v6 expression in human HCCs were 42.4%(28/66) and 39.4%(26/66), respectively. There was an inverse correlation between E-cad expression and invasive and metastatic potential of HCCs (P<0.01), and a positive correlation between the CD44v6 expression and invasive and metastatic potential of HCCs (P<0.01). Moreover, the 5-year survival rate in the E-cad-positive group was higher than in E-cad-negative group (P<0.01), and that in the CD44v6-positive group was lower than in the CD44v6-negative expression group (P<0.05). Conclusion: these data show a possible association between E-cad and CD44v6 expression and the potential of invasion and metastasis in HCCs. E-cad and CD44v6 expression may be used as an auxiliary prognostic indicator in HCCs.

Key words: E-cadherin, Carcinoma, Liver neoplasms, Metastasis

Received date: August 23, 2001; Accepted date: October 15, 2001.
Foundation item: This work was supported by the National Natural Science Foundation of China (No. 3880388).
*Author to whom correspondence should be addressed.
Phone: (0086-21)-25070660; Fax: (0086-21)-25070278; E-mail: jmzheng@smmu.edu.cn
Biography: Zheng Jian-ming(1962-), master of medicine, attending physician, Secondary Military Medical University, majors in pathology.

MATERIALS AND METHODS

Materials

A total of 66 patients with HCCs who underwent surgical resection in Changhai hospital from 1992 to 1994 were involved in this study. There were 52 males and 14 females, and the mean age of the patients was 49.2 years (27-68). The tissues were fixed in 10% buffered formalin and paraffined by routine methods. 4 μm-thick sections were cut. All cases had been confirmed by the specialist in the pathological department. The HCCs were classified according to Edmonson grade standard and 13 of which were Edmonson grade I, 27 were grade II, 20 were grade III, 6 were grade IV. The HCCs were classified as three subgroups by the tumor size, of which 17 were ≤5 cm, 39 were 5 cm–10 cm, and 10 were ≥10 cm. With the intent to reflect the tendency of invasion and metastasis of tumors better, the tumors were classified as high potential of invasion and metastasis group or low potential group by the following standard the clinic-pathological data. Those conformed to whichever condition laid behind belonged to the high potential group, otherwise to low potential group. 1) Lymph node metastasis; 2) Formation of cancer embolus in the portal; 3) The number of tumors around the area of carcinoma in the same lobule of liver was not smaller than 2, or with many satellite nodes or with capsule
invaded or damaged. Of the 66 cases of HCCs, 22 cases belonged in high potential group and 44 cases in low potential group.

Reagents

E-cad mouse monoclonal antibody (santa Crux Co.), diluted 1: 10; CD44v6 antibody (Wuhan Boshide Co.), diluted 1: 50; LSAB kit (Dako Co.)

Methods

Using the immunohistochemistry LSAB method: the slides were routinely dewaxed, dehydrated and disposed as follows, 3%H2O2, 20 min→0.1% trypsin, 15 min→1: 10 E-cad antibody or 1: 50 CD44v6 antibody at 4°C overnight→1: 100 b-SAM Ig 37°C 40min→1:100-SHRP 37°C 30min→0.05% DAB, then the sections were counterstained with hematoxylin.

Determination of Results

Referring to Bankfalri A standard[3]. In E-cad staining, cells with obvious brown stain on cytomembrane were considered positive for staining. The slides were scored on the basis of the number of the positive cells. -: none of tumor cells were stained; +: less than 5% were stained; ++: the percentage of stained cells was between 5% and 75%; +++: more than 75% were stained. CD44v6 staining was based on determination standard in literature[4]: Positive staining of CD44v6 was also localized in cytomembrane, +: ≥5% of tumor cells were stained; -: no detectable expression or <5% of tumor cells were stained.

RESULTS

Expression of E-cad in HCCs

The expression of E-cad were located on cytomembrane. Of the 66 specimens of HCCs, positive rates of E-cad expression were 42.4%(28/66), mostly ranging from + to ++ (Figure 1A), though all the corresponding paracancerous tissues showed strong expression.

Expression of CD44v6 in HCCs

The products of CD44v6 expression were also located on the cytomembrane (Figure 1B). Of the 66 cases of HCCs tissues, the positive rates of CD44v6 expression were 39.4% (26/66), though all the corresponding paracancerous tissues showed negative or poor expression.

Relationship between the Expression of E-cad and CD44v6 and the Clinicopathological Parameters of HCCs

The results of E-cad and CD44v6 expression in all subgroups were showed in Table 1. Statistical analysis that the difference of positive rates of E-cad and CD44v6 expression was significant between the high potential of invasion and metastasis groups and low potential groups.

![Fig. 1. E-cadherin and CD44v6 Expression in HCCs (H.E× 400).](image)

(A) E-cadherin expression showed as membrane weak positive staining. (B) Strong positive expression in the cell membrane of CD44v6.

Relationship between the Expression of E-cad and CD44v6 and Survival of Patients who Underwent Curative Resection for HCCs

Positive staining of E-cad was seen in 28 of 66 cases of HCCs and negative staining in 38, and their 5-year survival rates were 71.4% (20/28) and 28.9% (11/38), respectively. the difference was significant (P<0.01). Positive staining of CD44v6 was seen in 26 of 66 cases of HCCs and negative