

PROLIFERATION ACTIVITY AND EPITHELIAL-MESENCHYMAL TRANSITION IN HEPATOCELLULAR CARCINOMA: A PILOT STUDY

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BACKGROUND

Liver cancer is the fifth most frequently diagnosed cancer and the second leading oncologic death cause worldwide. The high mortality from hepatocellular carcinoma (HCC) is mainly attributed to the invasion pattern and intrahepatic and/or extrahepatic metastases, but the exact mechanism remains unclear (*Hao et al.*, 2014). Yet, the escape of neoplastic cells from the solid tumour might be due to dedifferentiation which occurs by loss of cell-to-cell contacts and the concomitant gain of migratory and invasive abilities. This phenotypical conversion of cells, collectively designated as epithelial-mesenchymal transition (EMT), has been described in different types of carcinoma including HCC (*Mikulitis et al.*, 2009).

AIM

To evaluate the proliferation activity (by Ki-67) and EMT (by vimentin and E-cadherin) in HCC.

MATERIALS AND METHODS

In a retrospective study, 50 consecutive, morphologically confirmed cases of HCC were enrolled. The expression of Ki-67, vimentin and E-cadherin was detected by immunohistochemistry. The proliferation fraction was scored quantitatively (%) in the neoplastic nuclei. Expression of vimentin and E-cadherin was evaluated semi-quantitatively by intensity (scale, 0–3) and the fraction (%) of positive neoplastic cells.

RESULTS

There were 36 (72.0%; 95% confidence interval (CI): 58.2–82.6) males and 14 (28%; 95% CI: 17.4–41.8) females among the patients. The age ranged from 22 years (a single case of fibrolamellar HCC) to 82 years. After exclusion of the outlier, the mean age was 63.8 years \pm standard deviation (SD) 9.4 (95% CI: 61.1–66.5; residual range 42–82).

Fig.1. Hepatocellular carcinoma, showing trabecular architecture (A), Mallory's hyaline (B) and inflammation (C)

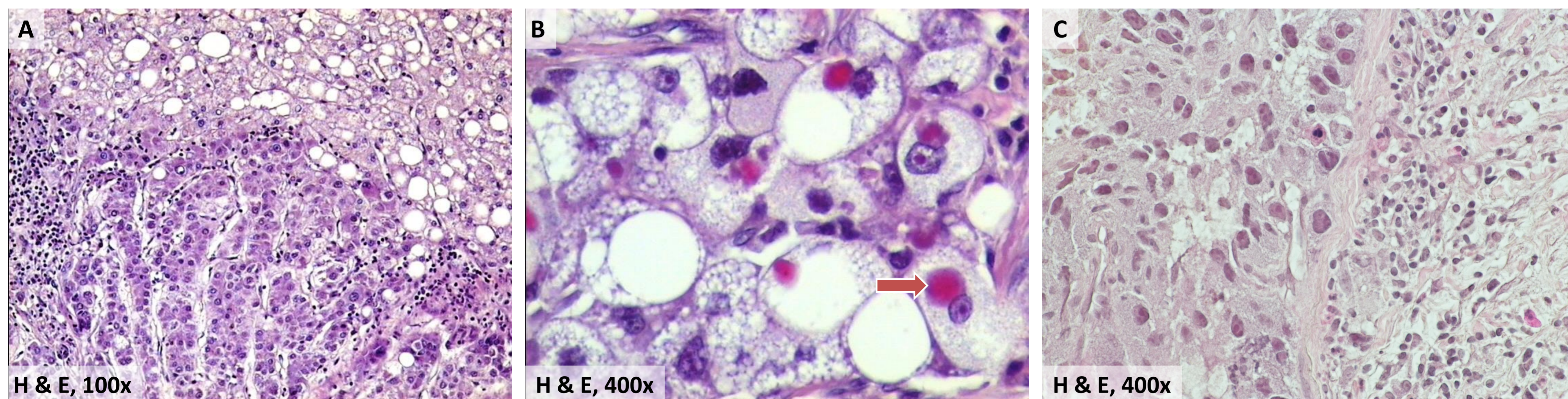
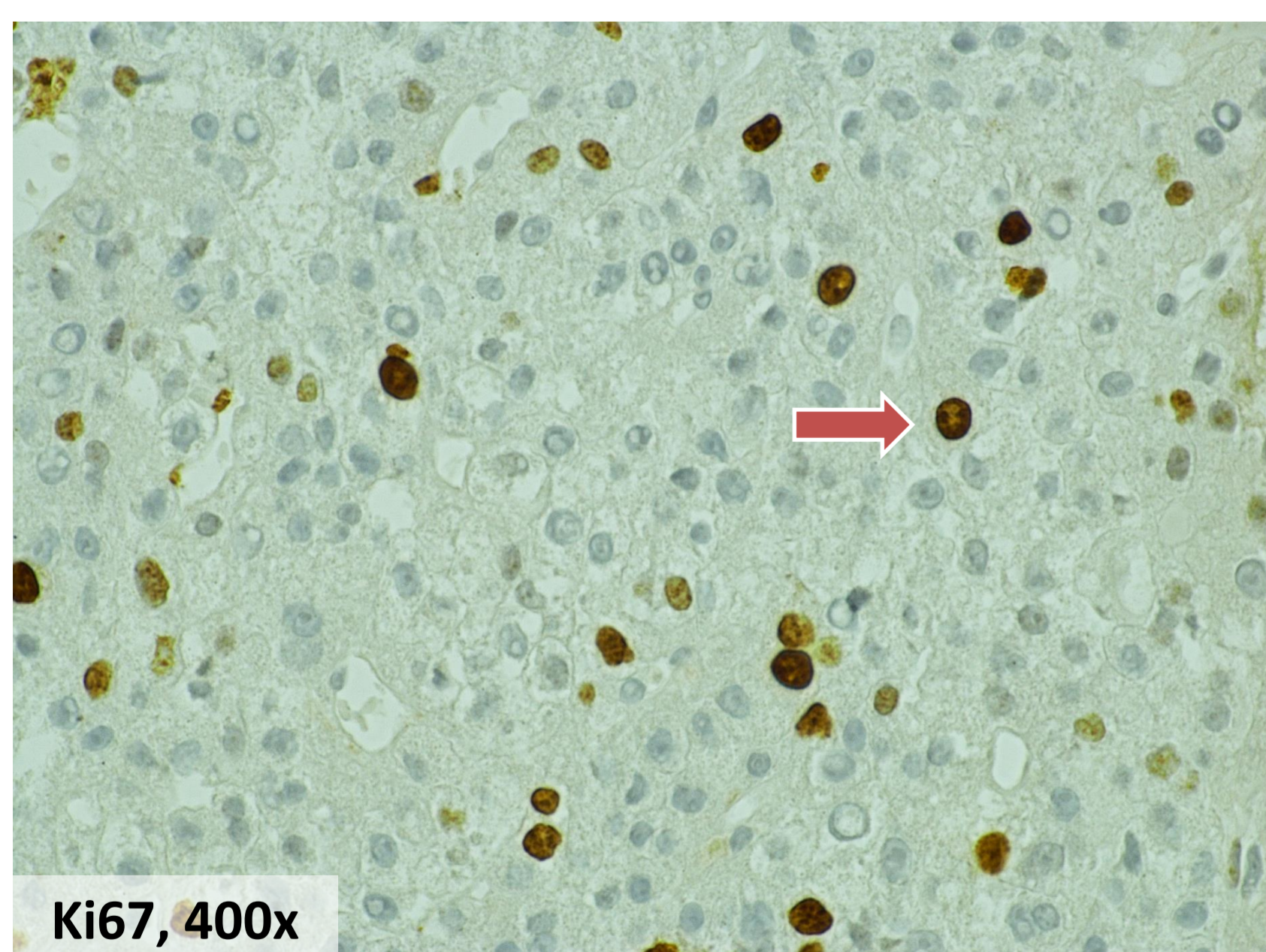
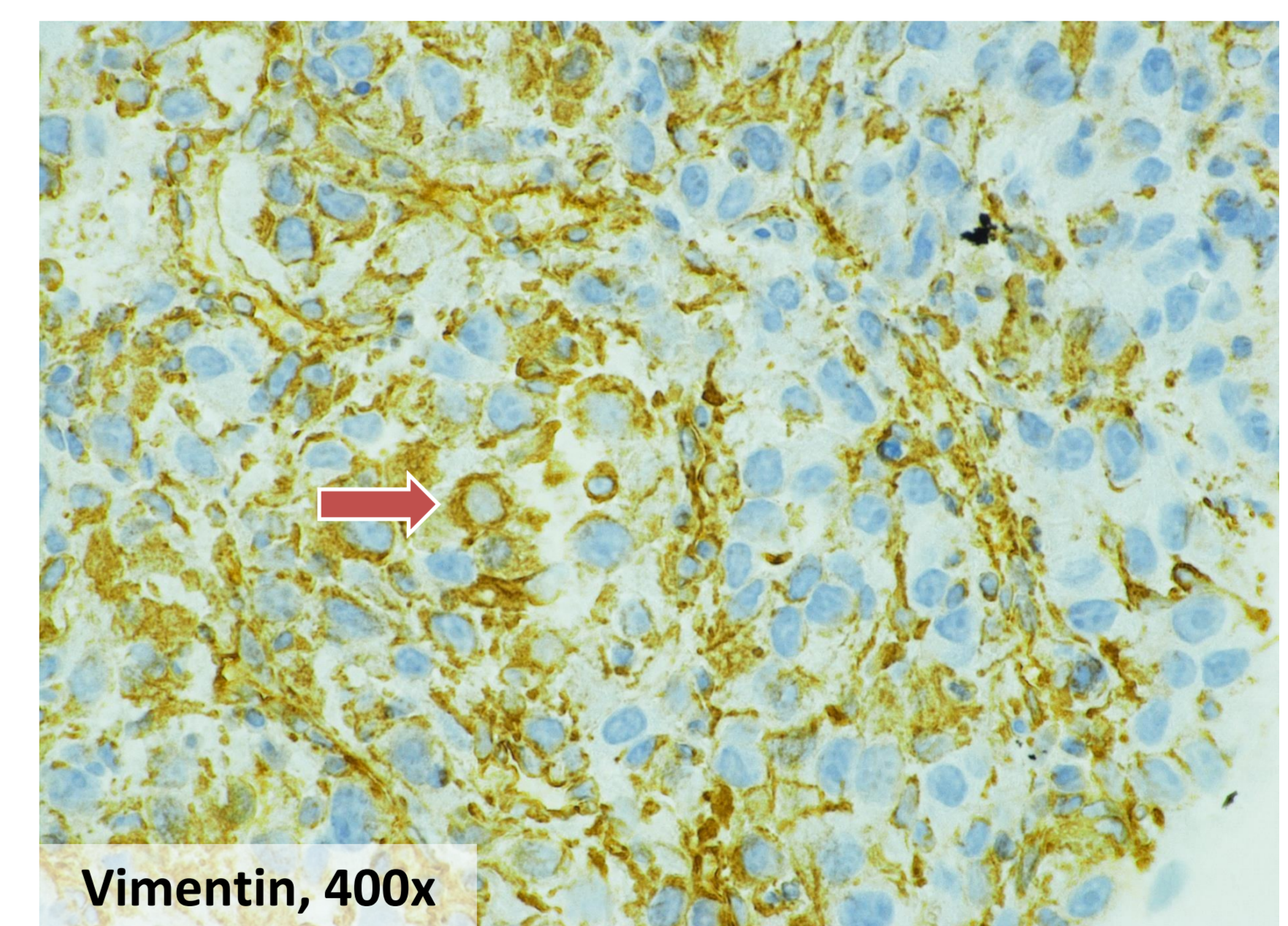


Fig.2. Ki67 expression in HCC



The mean proliferation fraction was 26.1% \pm SD 18.2 (95% CI: 17.6–34.6; range 2.0–73.0). The mean expression of E-cadherin was 1.5 \pm SD 1.0, comparable with the moderate intensity of peritumoural benign hepatocytes (1.7 \pm SD 1.0) but being less than in reactive bile ducts (2.7 \pm SD 0.4). HCCs were mostly negative (85.0% of cases; 95% CI: 63.1–95.6) for vimentin. The mean expression of vimentin was 0.2 \pm SD 0.6. The hepatocytes were invariably negative while reactive bile ducts showed higher expression: 1.3 \pm SD 1.2.

Fig.3. Vimentin expression in HCC



CONCLUSIONS AND DISCUSSION

1. Expression of EMT marker vimentin was a rare event in the present group.
2. Our data match with other studies, suggesting that HCC is a discohesive malignancy with low E-cadherin expression. Reduced E-cadherin expression correlates with lower overall survival for HCC patients, metastasis and vascular invasion (*Chen et al.*, 2014), thus, in our opinion, upregulation of E-cadherin has a potential of novel therapeutic treatment.
3. Our data suggest that HCC is tumour with low proliferative activity indirectly indicating low efficacy of chemotherapy.