

Title: Should BRAF ^{V600E}mutation and NIS expression affect the response to radioactive iodine therapy in papillary thyroid carcinoma patients?

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This study aims to (1) evaluate the immunohistochemical expression of mutant form of BRAF ($BRAF^{V600E)}$ and Na^{+}/I^{-} symporter (NIS) in 81 formalin-fixed paraffin-embedded blocks of papillary thyroid carcinoma (PTC) (2) correlate their expression with clinicopathological features, American Thyroid Association (ATA) risk stratification, prognosis of PTC patients and cumulative I^{131} dose (RAIT). Seventy-nine percent of specimens showed positive cytoplasmic expression of $BRAF^{V600E}$ .Statistically significant relation was detected between positive $BRAF^{V600E}$ expression and larger tumor size (P <0.001), presence of lymphovascular invasion (P= 0.002), lymph node metastasis (P= 0.01), classic type of PTC (p<0.001), increased cumulative dose of RAIT (p=0.036) and high risk and intermediate risk patients (p=0.001). Sixty specimens showed positive aberrant expression of NIS (27cytoplasmic and 33 nuclear staining patterns) while only 9 specimens showed active membranous expression. NIS expression did not show statistically significant difference with any of clinicopathological variables. However, the cumulative dose of ^{131}I treatment decreased with increased NIS expression. Statistically significant positive correlation was detected between $BRAF^{V600E}$ positive expression and increased NIS expression (p=0.018).Furthermore, patients

with high risk category and those with positive$BRAF^{V600E}$ expression experienced shorter disease-free survival with (P=0.002 & P=0.075) respectively. In conclusion, $BRAF^{V600E}$ mutation was associated with high risk characteristics of PTC patients. Not only membranous but also aberrant NIS expression is associated with decreased cumulative dose of RAIT. Our cases with mutant BRAF were-associated with increased NIS expression but showed increased cumulative dose of RAIT. This implies that $BRAF^{V600E}$ mutation may affect response RAIT by mechanisms other than NIS expression.

Biography

The presenting author; Heba E.M. El-Deek has completed her PhD at a year 2014 from Faculty of Medicine, Assiut University, Assiut, Egypt. She has good experience in diagnosis of surgical pathology cases, immunohistochemistry and tissue microarray construction. She has many international publications.

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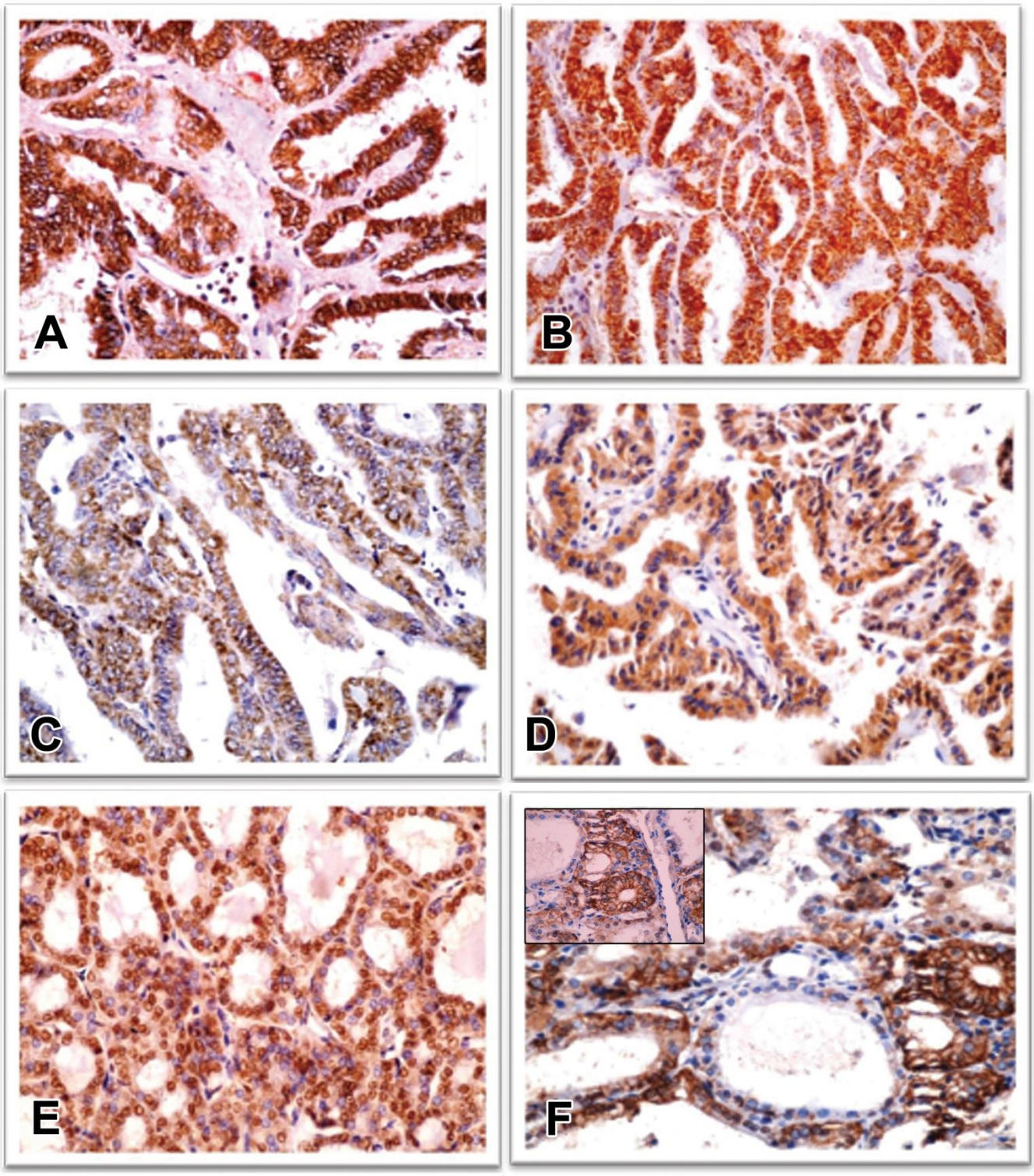


Figure 1: Expression of $BRAF^{V600E}$ and NIS in different types of PTC

Positive expression of $BRAF^{V600E}$ score 3 (A), score 2 (B) (x400), equivocal expression of $BRAF^{V600E}$ (C) (x400), Cytoplasmic expression of NIS (D), Nuclear expression of NIS (E) membranous expression of NIS (f) (X400, inset X600)