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Gene expression analysis of oncogene transcript in aberrant crypt foci, in comparison to the normal colonic mucosa and colorectal carcinoma, from formalin fixed paraffin embedded tissue samples

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Background and aims

Aberrant Crypt Foci (ACF) are early microscopic mucosal lesions in the colon which can be detected by magnified chromoendoscopy. The main purpose of this study was to develop an ex-vivo model of identifying the ACF-like lesions on grossly normal looking colonic mucosa so that the model resembles the chromoendoscopic procedure. We investigated the comprehensive gene expression analysis in ACF to understand them better. Further, correlation between genetic alterations amongst various topographic ACF-groups were also analysed.

Methods

A total of 35 positive cases with numerous ACF (more than 4 per 2 sq mm mucosal fragment) and corresponding tumour cases were selected out of 302 colectomy specimens received in the department. Another 20 cases were selected retrospectively as controls from colectomies performed for causes with no malignant potential. Gene expression analysis by Real Time polymerase chain reaction (RT-PCR) was performed on ACF in relation to control and tumour, and immunohistochemical test was performed to correlate the gene expression and protein expression for some of the transcripts. Gene expression data was correlated with the clinical parameters, as site and size of the tumours, tumour stage and lymph node metastasis, histological and topographical types of ACF etc.

Results

In comparison to the controls, ACF positive samples showed significant alterations in KRAS, CDKN1A, CDKN2A, MLH1, VEGFA, and CCL5 genes. Similarly, alteration in CDKN2A, PTEN, and SMAD4 genes were noted in ACF positive samples compared to tumour. No correlation between gene expression and ACF characteristics were noted.

Conclusion

Irrespective of morphological characteristics any ACF-like lesions needs to be addressed seriously with regular screening and follow up. Pathogenesis of such early neoplastic lesions in human colon is multifactorial and complex. Further studies may throw light on identifying prospective pathways which can be targeted to prevent the progression of these lesions.