MISMATCH REPAIR GENES IN COLORECTAL CARCINOMA

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Received: 12 February 2015 / Accepted: 24 April 2015

Microsatellite instability (MSI) results from defective DNA produced as an end result of mismatch. Approximately 12 to 18% of colorectal carcinomas show MSI. Microsatellite instability is the result of defects in genes hMLH1, hMSH2, hPMS1, hPMS2, GTBP/hMSH6 (1). Tumours which have MSI are called MSI-H. MSI-H tumours are significant predictors of disseminated disease in colorectal cancer (2). Tumours on right side of colon (caecum / ascending colon), those in patients younger than 50 years, and those with medullary or signet ring morphology are suggestive of mismatch repair (MMR) loss and should be screened for MMR proteins by immunohistochemistry (IHC). The results of IHC should be interpreted and subsequently followed up as follows:

1) All four proteins are present and there is no family history (80% of total cases): Stop further testing
2) MLH 1 and PMS 2 are absent (15% of total cases): Check for BRAF mutation analysis: If present, stop testing: If negative, sequence for gene rearrangement.
3) MSH 2 and or MSH 6 absent (5% of total cases): Sequence for gene rearrangement.

The figure shows adenocarcinoma of rectum, moderately differentiated, hematoxylin and eosin stained slide at 40X magnification. Immunohistochemical stain MLH 1 (inset) shows positive staining in the tumour cells as well as benign epithelial cells (acting as positive internal control).

Positive staining demonstrates that the tumour is negative for microsatellite instability. A negative staining would mean tumour is MSI high or microsatellite unstable.

References:
