Reviewer’s report

Title: Tumor Biology of Rectal Cancers in Young Patients

Authors:
Eva Fernebro (Eva.Fernebro@onk.lu.se)
Britta Halvarsson (Britta.Halvarsson@skane.se)
Bo Baldetorp (Bo.Baldetorp@onk.lu.se)
Mef Nilbert (Mef.Nilbert@onk.lu.se)

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Reviewer: Annika Lindblom

Level of interest: A paper whose findings are important to those with closely related research interests

Advice on publication: Unable to decide on acceptance or rejection until the authors have responded to the compulsory revisions

The report Tumour Biology of Rectal Cancers in Young Patients by Eva Fernebro et al.

This report evaluate 30 CRC cases below 50 years of age considering MSI-status, DNA-ploidy, KRAS and CTNNB1 mutations, p53 -, SZ-catenin and MSH2, MLH1 immunohistochemistry.

All but three tumours were MSI negative and expressed both MSH2 and MLH1. All three MSI positive tumours lacked expression of MSH2. Most of the tumours were aneuploid, six had KRAS mutations, no CTNNB1 mutations, but 23 showed an increased staining and 18 tumours had detectable p53 staining.

Comments:

This study shows that few rectal tumours in cases before age 50 are MSI positive, and, importantly, demonstrates that MSI positive rectal cancer before this age should be considered HNPCC and imply a genetic counselling. The rest of the findings are similar to what has previously been reported from rectal cancer in general.

Discretionary revisions:

Table 1, tumor location could be changed to more commonly used terms of proximal - distal tumors

Compulsory revisions:

Family history of cancer is at present limited to HNPCC or no HNPCC or zero, which might mean that information, could be missing (table 1). It would be of interest to know if there is any family history of CRC in the 27 MSI early onset CRC cases. Since early age of onset predicts familial cases many of them might be hereditary with another predisposing gene than the tested two MMR genes. It would be of value to have some more information on family history to support a genetic predisposition. This new data should be added to results and discussion, and table 1 could use more codes do explain this new
information under family history.

Competing interests:

None declared.