Desmoid tumours, familial adenomatous polyposis and sporadic infiltrative fibromatosis

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From time to time young adult patients will present with a desmoid tumour, which arouses suspicion of Familial Adenomatous Polyposis (FAP) and the risk of colorectal cancer. Desmoid tumours are unequivocally associated with FAP and many studies have revealed that there is a generalised genotype/phenotype correlation with the likelihood of a FAP patient presenting with such a tumour. In addition, the entity familial infiltrating fibromatosis is considered allelic to FAP since pathogenic variants in *APC* have been identified that are associated with this disorder. Thus patients presenting with desmoid disease should be screened for pathogenic variants in *APC* to either exclude FAP or include it. The majority of patients, however, do not carry a germline pathogenic variant, but rather a somatic mutation in *CTNNB1* (*β-catenin*). Currently, there are only four mutations in *CTNNB1* that have been associated with sporadic desmoid disease, c.121A>G; c.122C>T; c.133T>C and c.134C>T; with the majority of mutations occurring at position c.121A>G. The current literature to date suggests that "sporadic" desmoid tumour patients are a result of mutations within *CTNNB1* and that inherited pathogenic variants in this gene are not compatible with foetal development. At present, the dogma indicates that only *CTNNB1* is associated with sporadic desmoid disease and that *APC* is uniquely associated with inherited forms of disease. Notwithstanding, there remain a percentage to sporadic desmoid tumour patients who do not have a genetic diagnosis. Given that there are FAP families that do not display an overt FAP phenotype but to present with multiple cases of desmoid disease, we reasoned that some of the sporadic desmoid tumour patients who did present with a *CTNNB1* mutation may be the result of an *APC* mutation located within a region of *APC* correlated with desmoid tumour development.