Breast cancer and contralateral risk in TP53 carriers and Radiotherapy results in decreased time to second cancer in children with Li Fraumeni Syndrome

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Abstract

Li Fraumeni Syndrome (LFS) arising from germline *TP53* mutation results in defective DNA repair and increased risk of multiple primary cancers beginning in childhood with a high risk of breast cancer in women. *TP53* pathogenic variants were present in 21/379 (5.5%) women with breast cancer aged <31 and 7/57 (12.3%) <26 with high rates in DCIS and HER2+ disease. Contralateral rates were higher in women with TP53 aged <35 than in BRCA1/2 at 3% annually.

Curative intent radiotherapy is often used to treat childhood cancer but its impact in children in LFS has not been reviewed. We undertook a retrospective case-series review of 43 children with a solid cancer diagnosed ≤16years to assess time and survival following second cancer diagnosis. Following radiotherapy for the first cancer diagnosis, median time to second primary cancer diagnosis was 13.3years and median survival 9.7years. Where no radiotherapy was received median time to second primary cancer diagnosis was 25.1years [Chi^2=14.8,P<0.0001;HR=7.9 (95% CI:2.8-22.6)], and median survival of 29.2years [Chi^2=12.5,P=0.004,HR=3.2 (95% CI:1.5-6.6)]. Radiotherapy for first cancer in children with LFS is associated with adverse outcomes and ought be considered only in the absence of other potentially curative options. Where unavoidable, second cancer risks must be minimised. This may also have implications for women with breast cancer as second primary sarcomas have been reported at higher rates after radiotherapy.