The International Replication Repair Deficiency Consortium

The International Replication Repair Deficiency Consortium (IRRDC) is a collaborative research initiative that aims to better understand and manage rare genetic conditions that result from the loss of DNA replication repair.

Data were collected from patients with confirmed Constitutional Mismatch Repair Deficiency (CMMRD) who were registered in The International Replication Repair Deficiency Consortium. Tumor spectrum, efficacy of the surveillance protocol, and malignant transformation of low-grade lesions were examined for the entire cohort. Survival outcomes were analyzed for patients followed prospectively from the time of surveillance implementation.

A total of 193 malignant tumors in 110 patients were identified. Median age of first cancer diagnosis was 9.2 years (range: 1.7-39.5 years). For patients undergoing surveillance, all GI and other solid tumors, and 75% of brain cancers were detected asymptomatically. By contrast, only 16% of hematologic malignancies were detected asymptomatically ($P < .001$). Eighty-nine patients were followed prospectively and used for survival analysis. Five-year overall survival (OS) was 90% (95% CI, 78.6 to 100) and 50% (95% CI, 39.2 to 63.7) when cancer was detected asymptomatically and symptomatically, respectively ($P = .001$). Patient outcome measured by adherence to the surveillance protocol revealed 4-year OS of 79% (95% CI, 54.8 to 90.9) for patients undergoing full surveillance, 55% (95% CI, 28.5 to 74.5) for partial surveillance, and 15% (95% CI, 5.2 to 28.8) for those not under surveillance ($P < .0001$). Of the 64 low-grade tumors detected, the cumulative likelihood of transformation from low-to high-grade was 81% for GI cancers within 8 years and 100% for gliomas in 6 years.

Surveillance and early cancer detection are associated with improved OS for individuals with CMMRD [1].

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