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Incidental Finding of Lynch Syndrome Role of Genetic Counselling

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ABSTRACT The most common familial colorectal cancer (CRC) known is Lynch syndrome (LS) which is caused by mutations in DNA mismatch repair (MMR) genes. LS accounts for three to five percent of CRC and increases the risk of several types of cancers such as CRC, endometrial cancer in women, and to a lesser extent in other cancers like small intestine, ovary, stomach, urinary and hepatobiliary. The syndrome follows an autosomal dominant inheritance pattern and the cancers are characterized by their occurrence at an early age, familial involvement and development of metachronous cancers in the same individual. Here, the researchers report two CRC cases diagnosed with strong family history of CRC and various cancers. For one case, microsatellite instability (MSI-H) was confirmed by polymerase chain reaction (PCR) but immunohistochemistry (IHC) showed abnormal staining. Inherited cancer testing using germline multigene mutation analysis using Next Generation Sequencing (NGS) detected heterozygous likely pathogenic (p.Glu102Asp) and pathogenic (p.Ala681Thr) missense mutations in MLH1 gene in both the probands respectively. Post-test genetic counselling recommended other family members for screening and testing for the presence of the same mutation. A pre symptomatic diagnosis was made leading to an adapted surveillance strategy. The case reports illustrated in this paper have also highlighted the importance of genetic counselling and screening to detect an inherited cancer syndrome.