Background

Lynch Syndrome (LS) is a genetic disorder that accounts for 2-4% of all colorectal cancers (CRC) and is caused by germline mutations in the DNA mismatch repair (MMR) genes (Figure 1). Germline mutations cause more rapid carcinogenesis increasing polyp progression to 1-3 years instead of the usual 8-17 years in the general population (Figure 2). Increased colonoscopy surveillance is recommended every 1-2 years beginning at age 20-25 as it has been shown to reduce CRC mortality and incidence in individuals with LS.

Materials and Methods

A 59-year-old Caucasian female presented to cancer genetics secondary to a personal history of endometrial cancer diagnosed at age 41 and a known familial MLH1 mutation (Figure 3), Q328X (982C>T), discovered in a first-degree relative. Treatment included total abdominal hysterectomy, bilateral salpingo-oophorectomy, and radiation therapy. Family history included a brother with CRC at age 49, father CRC at age 53, three paternal uncles with CRC, paternal aunt CRC at age 35, paternal first cousin CRC in his 30s. Following genetic counseling and with informed consent peripheral blood was sent for MLH1 single site analysis. Molecular analysis identified a deleterious mutation, Q328X (982C>T), in the MLH1 gene (Figure 4) confirming the diagnosis of LS. The patient began annual high risk colonoscopy screening for colorectal cancer.

Results

First screening colonoscopy was negative. Within 11 months the patient presented with a colonic obstruction. Colonoscopy revealed a completely obstructing mass in the distal sigmoid colon (Figure 5). The patient was treated with a total abdominal colectomy and adjuvant chemotherapy. Pathology revealed an invasive colonic adenocarcinoma with mucinous and signet-ring features.

Conclusions

This case demonstrates the very rapid development of colon cancer in a patient with LS who was undergoing annual high risk colonoscopy surveillance. Research has shown a more rapid carcinogenesis in LS cancers, which is illustrated in this case where the transition from normal mucosa to obstruction occurred in under a year. This case highlights the need for heightened awareness of rapid polyp progression, the possibility of missed cancers on screening colonoscopies, and incorporation of family history when determining the best screening and prevention plan for patient’s with LS.

References