MOLECULAR ANALYSIS BY REAL TIME PCR: DNA was extracted using the QIAmp DNA minikit, and quantified using a NanoDrop 2000 UV-Vis Spectrophotometer. The *RAS* genes were analyzed with PCR based mutation detection panels using allele-specific probes. The *KRAS* assay detects mutations in KRAS exons 2, 3, and 4, as well as the *BRAF* V600E. The *NRAS* assay detects mutations in exons 2, 3, and 4. The presence of mutations is detected with an analytical specificity of 100%, and the limit of detection for each assay is less than 1%. We detected the amplification signal using the Applied Biosystems 7500 Fast Dx real-time PCR instrument with SDS Software.

The patient tested positive for *KRAS* c.38G>A (G13D) mutation in exon 2. No mutations were amplified within exon 3, and 4 of this gene. Surprisingly, the patient also tested positive for NRAS c.34G>T (G12C) mutation, with this gene's other codons testing wildtype.

FINAL DIAGNOSIS:

A case of colorectal cancer (CRC) indicative of HNPCC/Lynch Syndrome with loss in MSH2 and MSH6 proteins, and concurrent mutations in *KRAS* and *NRAS* genes.

DISCUSSION

Colorectal cancer (CRC) is the third most common cancer in terms of incidence (1.36 million new cases) and cancer-related deaths (723,000 deaths).[1] Roughly, one-fourth of these new cases present with synchronous metastases, and half progress to metastases. Its incidence in Asia is lower; the rate in India for males and females is 4.3, and 3.4 per 1,00,000 population respectively.[2] Ongoing research, and therapeutic advances have led to improvement in overall survival (OS) of about 30 months, and resort to at least two treatment regimens in patients with metastatic disease (mCRC). HNPCC/Lynch syndrome accounts for approximately 2-4% of CRC and 1-4% of endometrial cancers.[3,4]

The MMR system guards against base-base mismatches, and insertion/deletion mispairs that occur during DNA replication, recombination, and repair. Mutations in MMR genes including *MSH2, MSH3, MSH6, MLH1, PMS1,* and *PMS2* may be associated with HNPCC, sporadic cancers, resistance to chemotherapeutics, and alterations in meiosis.[5] The inheritance of MMR genes is autosomal dominant, and their