P – 089 Gastric cancer in Lynch Syndrome: Are precancerous conditions co-risk factors?

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Introduction: Gastric cancer (GC) risk in Lynch Syndrome (LS) is up to 13% instead of less than 1% in general population. LS is an autosomal dominant disorder caused by germ-line mutations in one of the mismatch repair (MMR) genes (MSH2, MLH1, MSH6, PMS2) or EpCAM gene determining mainly risk of colorectal and endometrial cancer and a lower risk of small bowel, urothelial and gastric cancer. GCs in this setting are usually intestinal type and show microsatellite instability (MSI-H) and loss of MMR protein expression. There are not clear guidelines for surveillance because the histopathologic transformation pathway is unknown. Since Helicobacter Pylori (HP) infection represents a clinical condition predisposing to gastric cancer its eradication is suggested. In our study we investigate clinical features of GC that develop in patients with this syndrome.

Methods: 139 patients with LS were registered in hereditary tumor register settled in 1994 at our Institution. Thirty-three had mutation in MLH1, 10 in MSH6 and 96 in MSH2 (83 F,56 M; mean age 53).The average follow up time was 10,5 years (2-26 years). Patients were inserted in surveillance program consisting in: colonoscopy starting at 20 years every 2 years until 40 and then annually. Gynecological surveillance for women starting at 30 years, upper GI endoscopy staring at 35 years with an interval of 3 years and abdominal ultrasound and urinal cytology starting at 35 with an interval of 2 years.

Results: Out of 139 Lynch patients 4 (2,8%) (2M; 2F) developed GCs. Three were symptomatic and one was diagnosed for surveillance. MSH2 was mutated in three of them and MLH1 in one. No family history of GC was reported. All GCs displayed MSI-H and loss of related miss match repair (MMR) protein at immunohistochemical analysis. MSH2 mutation patients were a man (62 years) and two women (73 and 50 years). Their GCs were intestinal type linked to HP infection at early stages (T2N0; T2N1; T1N0). MLH1 carrier was a man (53 years). His GC was a diffuse-type adenocarcinoma (T2N0) at fundus without HP infection. Four years before autoimmune gastritis was diagnosed with already atrophic gastritis and deficit of acid secretion and two pyloric gland adenomas were removed at corpus.

Conclusion: Our data suggest that our GCs developed in association to MMR mutation and atrophic gastritis caused by HP infection or autoimmune gastritis. Actually pyloric gland adenomas have been reported as precancerous lesions in autoimmune gastritis. Guidelines suggest gastric surveillance only in selected cases with family history of gastric cancer and suggest testing and treatment of HP infection. Our cases did not display gastric cancer family history. Thus, HP and anti parietal cells antibodies tests should be taken in consideration to select LS patients for gastric surveillance instead of family history.