Synchronous Gastric Epithelioid Gastrointestinal Stromal Tumor and Mesenteric Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma: A case report.
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Introduction:
Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors of the gastrointestinal tract, and approximately 60% of the cases arise in the stomach. Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) is a mature B-cell neoplasia, which is the most common leukemia of adults in the western countries, but rare in the eastern countries. Both of these tumors are of relatively low incidence (approximately 10 per 100,000 per year each) but a high frequency of a secondary malignancy has been increasingly reported in both tumors, separately. GISTs have been known to occur as part of tumor syndrome and slightly above 30 cases of synchronous occurrence of GISTs and other gastrointestinal malignancies have been reported, including adenosarcoma, lymphomas, leukemia and carcinoids. Although multiple cases of synchronous GIST and lymphomas have been reported in the literature, most of them have been low-grade lymphomas of the mucosa-associated lymphoid tissue (MAIT) type or diffuse large B-cell lymphomas (DLBCL). We present the case of a GIST occurring synchronously with CLL/SLL. No previous case of synchronous CLL/SLL and GIST was found in a review of the literature.

Case Report:
This is the case of a 63 year old female with history of abdominal discomfort and gastroparesis who was found with a submucosal gastric tumor on endoscopy. A mucosal biopsy done at endoscopy was found negative for neoplasia, but no submucosa was present in biopsy. Endoscopic Ultrasound (EUS) evaluation and Computed Tomography (CT) of the abdomen confirmed the submucosal mass emerging from the inferior gastric corpus wall and measuring 3.6 x 3.1 cm. On ultrasound the mass was suggestive of spina. In both radiologic studies, an incidental finding of multiple large hypoechoic mesenteric masses suggestive of intraabdominal lymphadenopathy was observed, the largest measuring 7.5 x 2.2 cm. Ultrasound guided fine needle aspiration of both masses was performed during endoscopic ultrasound, and evaluated at another institution. The submucosal gastric mass was diagnosed as an epithelioid gastrointestinal tumor (GIST) and the mesenteric mass as “Aberrant B-lymphocytes consistent with chronic lymphocytic leukemia/small lymphocytic lymphoma”. At the “Administración de Servicios Médicos” (ASEM), the gastric tumor was completely resected and a biopsy of the mesenteric mass suspected to be a lymphoma was done. The biopsy of the synchronous mesenteric masses (lymph nodes) presented effacement of the normal architecture by a monomorphic population of small lymphoid cells. The immunohistochemistry was positive for B-cell markers (CD20, CD79a) as well as CDS, CD23, CD43 and bcl-2, but negative for cyclinD1 and bcl-6 (Figs. 5-7). Based on these findings the diagnosis of chronic lymphocytic leukemia/ small lymphocytic lymphoma (CLL/SLL) in the mesentery was made. Peripheral blood showed a white blood cell count within normal limits, but with relative lymphocytosis (63%: 4.3x10⁹cells/L). A Bone marrow biopsy and aspiration showed 50% of lymphoid cells. Cytogenetics done by FISH show 11q- abnormality in 6% of nuclei examined which is associated with poor prognosis. Other unfavorable data included CD38 expression in more than 30% of cells, but favorable prognostic data is a low expression of ZAP-70 by flow cytometry. ZAP-70 has been developed as a surrogate for CLL mutational status of IGHV gene. Elevated ZAP-70 as well as 11q deletion correlates with unmuted IGHV, which confers a decreased survival (6-9 years compared to 13-24 years in hypermutated IGHV). PCR hypermutation analysis could not be completed to evaluate IGHV mutational status, and prognosis in this patient has to be evaluated with clinical status and other markers of tumor burden. Of these markers, only β2-microglobulin is mildly elevated. Since CL/L usually has an indolent course, this patient is being followed without chemotherapeutic treatment.

Discussion:
Although it is not possible to answer if the presence of two synchronous tumors may be due to a common genetic mechanism or random coincidence, some theories suggest a genetic instability or defect in DNA repair mechanism as possible hypothesis for predisposition for multiple neoplasia. Others believe that this might be regarded as a failure of the general immunological defense mechanism in malignant disorders (Bloodland the pattern of excess cancers in CLL survivors suggests an influence of immunodeficiency known to be associated to CLL. Given the prolonged survival of patients with CLL, the high incidence of multiple neoplasia is an important factor for evaluation of these patients.

The biopsy of the synchronous mesenteric masses (lymph nodes) presented effacement of the normal architecture by a monomorphic population of small lymphoid cells (Fig.4). Immunohistochemistry was positive for B-cell markers (CD20, CD79a) as well as CDS, CD23, CD43 and bcl-2, but negative for cyclinD1 and bcl-6 (Figs. 5-7). Based on these findings the diagnosis of chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) in the mesentery was made. Peripheral blood showed a white blood cell count within normal limits, but with relative lymphocytosis (63%: 4.3x10⁹cells/L). A Bone marrow biopsy and aspiration showed 50% of lymphoid cells. Cytogenetics done by FISH show 11q- abnormality in 6% of nuclei examined which is associated with poor prognosis. Other unfavorable data included CD38 expression in more than 30% of cells, but favorable prognostic data is a low expression of ZAP-70 by flow cytometry. ZAP-70 has been developed as a surrogate for CLL mutational status of IGHV gene. Elevated ZAP-70 as well as 11q deletion correlates with unmuted IGHV, which confers a decreased survival (6-9 years compared to 13-24 years in hypermutated IGHV). PCR hypermutation analysis could not be completed to evaluate IGHV mutational status, and prognosis in this patient has to be evaluated with clinical status and other markers of tumor burden. Of these markers, only β2-microglobulin is mildly elevated. Since CL/L usually has an indolent course, this patient is being followed without chemotherapeutic treatment.

References:
6. Scotts MA, Pagron GD. (September 1978) Three additional malignancies occurring within one year in a patient with chronic lymphatic leukaemia. Postgraduate Medical 54; 613-614.