EBV infection and expression of HER2 and CD34 in gastric cancer, how are they related?

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Introduction: Gastric cancer (GC), as a multifactorial disease, exhibits a complex pathogenesis, having intraand inter-tumor heterogeneity, challenging the efficacy of current treatments[1.2]. GC as a major global health problem, better diagnostic and therapeutic strategies are needed, leading to further biomarkers research associated to innovative targeted therapies [3,4]. Objectives: Our aim was to study human epidermal growth factor receptor 2 (HER2), Epstein-Barr virus (EBV) latent membrane protein 1 (LMP1) and CD34 expression in GC samples to understand the relationship between these markers and relate them with the clinicopathological characteristics. Methods: Thirty samples of primary carcinoma gastrectomy cases performed between February 2017 and December 2021 at the Hospital Distrital da Figueira da Foz, EPE were studied after approval by the ethics committee. Immunohistochemistry assays were performed in sections of the selected tumor representative samples. Results: All samples were negative for LMP1 EBV and only 2 GC samples were positive to HER2. Significant statistical relationship was found between gender and CD34+ stroma cells. Microvessel density (MVD) and stroma CD34⁺ cells presented relations with clinicopathological features, and a positive tendency between them. Conclusions: Our study was able to identify a relation between CD34⁺ stroma cells and females. With this study, we mainly explored the potential role of CD34 as a biomarker in GC and projected possible associations of prognostic and therapeutic value towards other HER2 and LMP1 EBV markers.

Keywords: Stomach Neoplasms; Antigens, CD34; Genes, erbB; Epstein-Barr Virus Infections; Tertiary Lymphoid Structures

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References:

- [1]. Smyth EC, Nilsson M, Grabsch HI, van Grieken NC, Lordick F. Gastric cancer. The Lancet 2020, 396, 635-648.
- [2]. Johnston FM, Beckman M. Updates on Management of Gastric Cancer. Curr Oncol Rep 2019, 21, 67.
- [3]. Li F, Meng G, Tan B, Chen Z, Ji Q, Wang X, et al. Relationship between HER2 expression and tumor interstitial angiogenesis in primary gastric cancer and its effect on prognosis. Pathol Res Pract 2021, 217, 153280.
- Stanek L, Gurlich R, Musil Z, Havluj L, Whitley A. Monitoring EBV infection, MSI, PDL-1 expression, Her-2/neu [4]. amplification as a biomarker for PD-1 inhibition in gastric cancer. Bratisl Lek Listy 2022, 123, 83-86.