BACKGROUND: Crohn’s disease (CD) patients present characteristic abnormalities in the mesenteric adipose tissue (MAT) near the affected intestinal area. The MAT is thickened and wraps around the bowel circumference (1). Recent evidence indicates that this tissue plays a role in storing memory immune cells and potentially supporting antigen-driven immune responses (2). Therefore, the goal of the present study was to identify the microRNAs (miR) expression profile of the MAT of CD patients and means of an RNA sequencing (RNAseq) analysis (2) and to perform a biological validation of the results comparing to controls (CTR).

METHODS: For this purpose, 25 patients with active Crohn disease who underwent surgery were included in the study. The study group consisted of 15 patients operated on for other diseases, except inflammatory bowel diseases. The in silico analysis of the modulated miR was performed by Targetscan and the enrichment of the metabolic pathways through the DAVID platform. The biological validation of the transcripts was performed by RT-qPCR analysis. The data were analyzed using the nonparametric Mann-Whitney Test. Univariate and multivariate analysis were performed based on the Cox regression model for correlations between gene expressions and the disease recurrence after surgery. The level of significance was set at P < 0.05. The study was approved by the Research Ethics Committee.

RESULTS: RNAseq identified a significant increase in miR-650 expression in the MAT of the CD group compared to the CTR (P = 0.05; P < 0.01). Among the 227 downregulated genes, 25 were validated by in silico analysis as a predicted target for miR-650. The enrichment analysis of metabolic pathways containing the miR-650 target genes identified the metabolism pathway of alanine, aspartate and glutamate. GFPT2 and ALDH4A1 were identified as miR-650 target genes of this enriched pathway. The biological validation by RT-qPCR confirmed significant increased miR-650 expression in the MAT of CD compared to the CTR (P = 0.008, besides decreased levels of GPFT2 (P = 0.026) and ALDH4A1 (P = 0.006)) target genes. Moreover, Cox regression analysis showed that the miR-650 levels in the MAT of CD patients strongly correlated with the post-operative disease recurrence in the first 26 postoperative months (Hazard Ratio = 6.85; Confidence Interval 95%, P = 0.006).

CONCLUSION: For the first time, the modulation of miR-650 and its target genes (ALDH4A1 and GPFT2) were validated in the MAT of CD patients. Indeed, the miR-650 levels correlated to a higher risk of post-operative disease recurrence. Although a larger multicenter prospective study is needed, these findings may constitute a potential tool to guide the clinical management after surgical resection.


REFERENCES

P063

Prophylaxis of Hepatitis B Reactivation and Inflammatory Bowel Disease: A case report

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BACKGROUND: The risk of opportunistic infections is increasing with the progressive use of immunosuppressants and biological therapy in IBD treatment. In this scenario, screening for Hepatitis B virus (HBV) is important in order to prevent viral reactivation.

METHODS: CASE REPORT. A 48 year old female with longstanding ulcerative proctitis (diagnosed in 2008) was evaluated and prescribed with 3 bowel movements a day with mucus and blood, diffuse abdominal pain, tenesmus, and urgent evacuation. Laboratory tests showed leukocytosis without left shift, normal platelets and liver tests. Flexible sigmoidoscopy showed a severe disease activity (Mayo score 3) in the rectum and sigmoid. The patient was admitted to our hospital and received IV corticosteroids without response. Then he was treated with infliximab and ifosfamide. He developed anti-HIV, anti-HBc, IgG were positive. At admission, HBV DNA was detected (225 IU/mL). Other labs were consistent with chronic hepatitis B (Anti-HBeAg positive, HBsAg negative, Anti-HBcAg positive). Abdominal ultrasonography and ultrasound were normal. Considering the serological profile and the use of high-dose corticosteroids, infliximab, and azathioprine, Entecavir 0,5 mg/day was initiated.

RESULTS: HBV produces stable cccDNA mini-chromosome in infected hepatocytes, that can be present even after the loss of the HBs antigen and seroconversion to anti-HBs. cccDNA serves as a matrix for HBV replication and is resistant to antiviral treatment, unlike what occurs with the sole use of interferon. Inflammatary prophylaxis should be done with nucleotide analogs (NA) with high potency (Entecavir, Telbivudine Disoproxil Fumarate or Telbivudine Alademinude). Lamivudine and other NAs are not recommended because of the risk of selection of resistant strains, but it can be used if it is the only option. Prophylaxis should be maintained for 6–12 months after the suspension of the immunosuppressant. Pre-emptive therapy with an anti-HBV can be performed in moderate risk patients with easy access to serial viral load dosage, transaminases and serology.

CONCLUSION: Screening for HBV infection should be a routine in IBD patients mainly at diagnosis, as HBV reactivation can occur in the context of immunosuppressive therapy. As this risk depends on host factors, virological factors, and type and degree of immunosuppression, therapeutic prophylactic strategies must be individualized.

P064

Clinical Aspects of Pediatric Inflammatory Bowel Disease – A Multicentric Study From Brazil

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Inflammatory Bowel Disease or Bowel Endometriosis? Two Cases of Large Bowel Obstruction

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CASE: Endometriosis, endometrial glands and stroma outside of the uterus, may occur in "extra-genital" locations and can present with symptoms of inflammatory bowel disease (IBD). We report 2 cases of reproductive-aged women with inflammatory and/or obstructive symptoms secondary to presumed IBD who were found to have endometriosis on surgical pathology. The first patient presented with weight loss, generalised abdominal pain, and vomiting, and was found to have an inflammatory cecal mass during endoscopic evaluation for IBD. At operation, an inverted appendix was identified and removed. Surgical pathology revealed appendiceal endometriosis. The second patient was diagnosed with fibrostenotic and inflammatory Crohn's disease of the sigmoid colon. Despite treatment with biologics, she suffered obstructive symptoms from a sigmoid stricture that could not be traversed endoscopically. She was taken to the operating room for sigmoid colectomy. Final pathological revealed endometriosis involving the sigmoid colon. Reproductive age women with gastrointestinal manifestations that are unusual for IBD or that do not respond predictably to medical therapy, endometriosis should be considered in the differential diagnosis.

Hospitalization and Surgery Rates in Patients With Inflammatory Bowel Disease in Brazil: A Time-Trend Analysis

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BACKGROUND: Inflammatory bowel diseases (IBD) are chronic diseases of the gastrointestinal tract with increasing incidence worldwide and prevalence in the last few decades. Surgical risks related to IBD are usually under-acknowledged. Furthermore, there is a growing interest in the management of these diseases with a goal of understanding the changes in their behavior and relation to demographic factors affecting IBD population distribution, with the objective of proposing earlier and more effective interventions. Objective: The aim of this study is to evaluate IBD-related hospitalization and surgery rates in Brazil, geographical distribution, time trends, and mortality associated with surgical procedures.

METHODS: Data from hospital admission registries, available in the Brazilian health system national bank (DATASUS), were retrospectively collected, regarding IBD-related hospitalizations (identified using ICD-10), frequency of hospitalisations, surgeries, and deaths related to surgical procedures, as well as sociodemographic data, from January 2005 to December 2015. RESULTS: Hospitalization rates in Brazil decreased by 24% in the analyzed period, and proportion of surgeries related to IBD decreased by 35.2%. The largest proportion of surgeries occurred in Crohn's disease (CD) patients, mostly young adults (age 20–39 years followed by 40–59 years) and female patients. Enterectomy was the most performed surgery. Surgical mortality decreased by 46% (19.8% in 2005 to 10.6% in 2015). The most economically developed regions of the country and metropolitan integrated municipalities presented the highest hospitalization and surgical rates. The poorest municipalities and non-integrated metropolitan municipalities presented the highest mortality rate related to surgery.

CONCLUSION: Brazil follows the global decrease in surgical procedures, mortality and hospitalizations related to IBD. Moreover, the observed distribution of hospitalizations and surgeries was unequal, prevailing in the wealthiest and most developed regions. Early diagnosis and referral to a specialized gastroenterologist for a structured management plan may contribute to a reduction of surgical hospitalization and mortality rates related to IBD. Brazil, a continental country, with distinct geographic areas and socioeconomic disparities, needs a more integrated health system, with better distribution of IBD referral services.