RESEARCH ARTICLE

Relationship between Colonic Polyp Type and the Neutrophil/ Lymphocyte Ratio as a Biomarker

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Abstract

   Aim: We designed this study to investigate the neutrophil lymphocyte ratio as a biomarker in distinguishing colonic polyps which are neoplastic or non-neoplastic. **Materials and Methods:** One hundred and twenty-five patients with colonic polyps were enrolled into the study. The following data were obtained from a computerized patient registry database: mean platelet volume (MPV), uric acid (UA), platelet count (PC), alkaline phosphatase (ALP), gamma-glutamyl transpeptidase (GGT) and the neutrophil to lymphocyte ratio (NLR). Exclusion criteria were active infectious disease, hematological disorders, and malignancies. Colonic polyps divided into two groups as neoplastic polyps (tubular adenoma, villous adenoma, tubulovillous adenoma) and non-neoplastic polyps (hyperplastic polyps, inflammatory pseudopolyps etc). The relationship between colonic polyp type and NLR was evaluated with statistical analysis. **Results:** There were 67 patients (53.6%) with neoplastic and 58 (46.4%) patients with non-neoplastic polyps. Mean NLRs of neoplastic and non-neoplastic groups were respectively 3.32±2.54 and 2.98±3.16 (P<0.05). **Conclusion:** Although sensitivity and specificity are not high, NLR may be used as a biomarker of neoplastic condition of colonic polyps.

Keywords: Colon polyps - neutrophil to lymphocyte ratio - neoplastic polyps

Introduction

   The most common neoplasm of the large intestine are adenomas. It is generally accepted that most colorectal carcinomas arise from adenomas. Presumably, the remainder is overgrown by cancer when the precursor component is not apparent histologically. Adenomas and carcinomas have a similar distribution in the colo-rectum, and adenomas usually precede cancer by about 15 years. Endoscopic removal of polyps decreases the incidence of subsequent colorectal cancer in treated subjects (Fenoglio, 1982; Konishi, 1982).

   The clinical importance of adenomas is almost entirely related to their well-established premalignant nature. In general, the prevalence of adenomas increases dramatically with age. By the fifth decade of life, approximately 12% of individuals have adenomas, of which about 25% are considered high- risk lesions (Morson, 1966; Correa, 1979). Adenomas are morphologically defined as dysplastic clonal proliferations of colonic epithelium. Microscopically, adenomas are categorized architecturally as tubular (Figure 1A), tubulovillous (Figure 1B) and villous (Figure 1C). In general, precise histologic criteria for these separate categories vary widely. However, a reasonable rule is that villous lesions should contain at least 75% villi whereas tubular lesions should contain less than 25% villi. Tubulovillous lesions therefore contain between 25% and 75% villous epithelium (Konishi and Morson, 1982).

   The lifetime prevalence of adenoma is approximately 6%. Therefore, it is easy to deduce that only a small minority of polyps ultimately go on to develop adenocarcinoma. Carcinomas having pushing margins and an inflammatory infiltrate at the interphase between
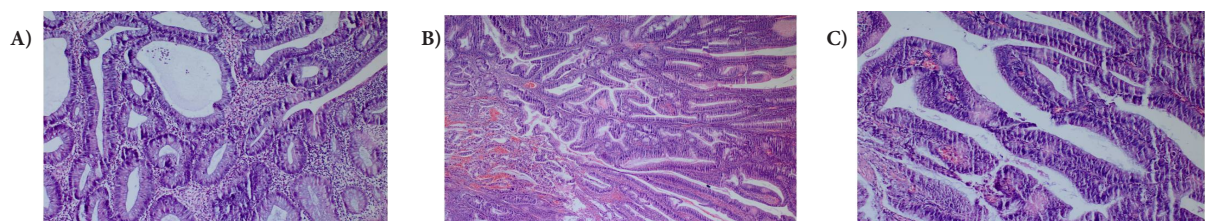

Figure 1. A) Tubular Adenoma, B) Tubulo-Villous Adenoma and, C)Villous Adenoma

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the tumor and the neighboring tissue (made up of plasma cells and lymphocytes and associated with degenerative changes within the tumor) have a better prognosis than those lacking these features.

It is clear that the response of the immune system plays a vital role in the control and progression of many disease states including cancer (Morson, 1966; Correa 1979; Fenoglio,1982). Simple measures of immune responsiveness include simple routine biochemical and haematological markers such as total and differential leukocyte counts and C-reactive protein (CRP), which have been proposed as diagnostic and prognostic factors for a variety of cancers (Fenoglio,1982). This may permit a simple estimate of inflammatory response to cancer which is easily assessed in everyday clinical practice.

Little is known and published about neutrophil lymphocyte ratio and its relationship with prevalent chronic conditions among general population. Therefore, the current study was conducted to investigate the neutrophil lymphocyte ratio as a biomarker in distinguishing colonic polyps are neoplastic or non-neoplastic.

Materials and Methods

One hundred and twenty-five patients with colonic polyp were enrolled into the study. The following data were obtained from a computerized patient registry database: Mean platelet volume (MPV), uric acid (UA), platelet count (PC) , alkaline phosphatase (ALP), Gamma-glutamyl transpeptidase (GGT) and neutrophil to lymphocyte ratio (NLR). Exclusion criteria were active infectious disease, hematological disorders, and malignancies. Colonic polyps divided into two groups as neoplastic polyps (tubuler adenoma, villous adenoma, tubulovillous adenomas) and nonneoplastic polyps (Hyperplastic polyps, inflammatory pseudopolyps etc.).

Statistical analysis
The Shapiro–Wilk test was used to assess the normality of the data. Accordingly, either an independent samples t-test or Mann–Whitney U tests were used to compare the differences between groups. A probability level of P<0.05 was considered statistically significant. MedCalc (Version 9.2.0.1) and SPSS 15.0 (SPSS Inc., Chicago, IL, USA) software were used for all analyses.

Results

There were 67 patients (53.6%) with neoplastic polyp and 58 (46.4%) patients with non-neoplastic polyp. Fourty-six have tubuler, 5 have villous and 7 have tubulo-villous adenoma of neoplastic polyp group. Mean NLR of neoplastic and nonneoplastic groups were respectively 3.32±2.54 and 2.98±3.16. Statistically significant differences in NLR were seen in patients with neoplastic polyp compared to nonneoplastic polyp group (P<0.05). There was no statistically significant difference in the other parameters between groups (Table 1). ROC curve analysis suggested that the optimum NLR cut-off point for neoplastic polyps was 1.97 (sensitivity: 71.93%, specificity: 50.75%).

Table 1. Statistical Analysis of Colonic Polyps

	Nonneoplastic Mean±SD	Neoplastic Mean±SD	P
Age	60.87±14.59	62.43±10.40	>0.05
MPV	8.53±1.55	8.90±1.53	>0.05
Neutrophil	5031.94±2578.51	5505.44±2590.61	>0.05
Lymphocyte	2174.91±799.64	1993.35±823.73	>0.05
PC	251000.00±74139.00	261000.00±85501	>0.05
UA	5.23 ±1.27	5.36±1.92	>0.05
ALP	84.18±41.35	85.48±29.09	>0.05
GGT	47.84±102.27	38.67±27.86	>0.05
NLR	2.98±3.16	3.32±2.54	0.02

Discussion

The relationship between inflammation and cancerous growth has been extensively investigated over the past 150 years. Following Virchow's identification of leukocytes within neoplastic tissue in 1863, the role of inflammatory cells and pathways in the pathogenesis of a variety of tumor groups has become well established. In a variety of malignancies, environmental and infective agents are seen to play critical roles in the production of tissue damage and inflammatory reactions. Furthermore, cytokines, chemokines and angiogenic factors produced in chronic inflammatory states provide a microenvironment favourable for cellular survival and angiogenesis (Coussens et al., 2002; Ueno et al., 2007).

Neutrophilia has been associated with malignancies, although the mechanism of it not completely understood. Studies showed a link between the inflammatory microenvironment of a cancer and systemic responses induced by the tumour. Many cancer survival studies have suggested that NLR is a significant predictor of overall and disease specific survival of patients (Mc Millan et al., 2003; Al et al., 2004; Pages et al., 2005; Walsh et al., 2005; Cho et al., 2008; Halazun et al., 2008; An et al., 2010; Saito et al., 2010; Ubukata et al., 2010; Chua et al., 2011; Ishizuka et al., 2012). Whether the systemic inflammation, which has proven to be a significant predictor of survival of cancer patients, is malignancy associated inflammation or is because of the any co-morbid conditions that cancer patients may have is still unclear. The presence of intra-tumoral T cells was also noted to be correlated with improved survival in epithelial ovarian cancer (Saito et al., 2010), with associated increases in expression of interferon-gamma, IL-2, and with lymphocyte-attracting chemokines within the tumour.

Walsh et al. (2005) have also shown that NLR>5 is to be a marker of survival in colorectal cancer patients (Walsh et al., 2005). The most studied measure of inflammation is CRP , levels of which have been shown to independently predict survival in patients who undergo curative resection for colorectal cancer (Mc Millan et al., 2003). Halazun et al. (2008) demonstrates that the preoperative inflammatory status of patients with liver resections for colorectal liver metastasis, as evidenced by a raised NLR, is associated with poor overall and disease free survival, and an increased risk of recurrence (Halazun et al., 2008). Elevated preoperative NLR increases both risk of death and risk of recurrence in patients who undergo surgery for

colorectal liver metastases (Halazun et al., 2008).

Linton et al. (2012) talked about inflammatory biomarkers can provide valuable prognostic information in patients with malignant pleural mesothelioma (MPM). There is consistent evidence to suggest an association between a systemic inflammatory response , represented by elevated CRP and NLR, and poorer prognosis (Linton et al., 2012).

Imtiaz et al. (2012) found a significant association between NLR and likehood of having hypertension and diabetes mellitus (Imtiaz et al., 2012). But not observed a significant relationship between NLR and asthma or arthritis. Similarly, systemic inflammation reported a significant factor for metabolic syndrom including obesity and diabetes mellitus. Imtiaz et al explained role of inflammation and NLR might have been masked by the intake of anti-inflammatory pain killer drugs (Imtiaz et al., 2012).

In colorectal cancer, the presence of intra-tumoral immune cell infiltrates, markers of T cell migration, activation and differentiation were both associated with reduced early metastatic invasion, early stage disease and improved prognosis (Correa, 1979; Konishi and Morson, 1982).

The clinical importance of adenomas is almost entirely related to their well-established premalignant nature. The abnormal phenotype of the tumour may stimulate an influx of inflammatory lymphocytes around the tumour. The systemic inflammatory response features changes in the relative levels of circulating white blood cells. The well recognized neutrophilia is accompanied by a relative lymhocytopaenia.

The data to support adenomatous polyp–cancer sequence are derived from both epidemiologic and morphologic studies. There are a lots of study about polyp- cancer relationship but there is no study about the relationship between colonic polyp type and NLR. The NLR can be calculated easily from data that are routinely available. NLR could be an important measure of systemic inflammation as it is cost effective, readily available. In this study we demonstrate statistically significant higher NLR in neoplastic polyps when compared non-neoplastics. Also, we demonstrate a cut-off point (1.97; sensitivity: 71.93%, specificity: 50.75%) for neoplastic polyps. Although histopathologic evaluation is gold standard on evaluation for neoplastic potential of polyps, this NLR value may give an opinion and be used a biomarker to differantiate the colonic polyps neoplastic or non-neoplastic.

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