

Progress Of Gastrointestinal Neoplasms and Therapeutic Advances

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Abstract. In recent times, there has been a notable rise in the incidence of gastrointestinal neoplasms due to changes in diet and lifestyle. When it comes to cancer-related deaths in males under 50, colorectal cancer ranks first, and in women, it is second. Gastric cancer and colorectal cancer are the two main types of intestinal neoplasms. Among East Asian populations, gastric cancer has the highest incidence rates. Studies reveal a critical role for gastrointestinal microecology in the development and course of gastrointestinal tumors. In addition to providing a brief overview of the pathophysiology and standard treatments for stomach tumors, this paper addresses the state of research regarding the connection between gastrointestinal microecology and immunological treatment of stomach tumors. The process by which gastric cancer develops is complex and involves variations in growth patterns, mucus separation, cellular structure, and genetic makeup. Microecological imbalances, genetic factors, and poor dietary practices are major causes of gastric cancer. Chemotherapy, surgery, radiation therapy, and targeted therapies are among the current treatment options. Immune checkpoint antagonists, combination immunotherapy, and adoptive immune-mediated cell therapy have all shown notable effectiveness in clinical practice. However, immunotherapy still faces obstacles from immune-related side effects and treatment resistance. Subsequent investigations will probe further into the correlation between gastrointestinal microecology and gastrointestinal tumors, presenting novel approaches to the management and avoidance of gastrointestinal neoplasms.

Keywords: Gastrointestinal Neoplasms; Gastric Cancer; Colorectal Cancer; Immunotherapy; Microecology; Genetic Factors; Chemotherapy; Surgical Treatment; Dietary Habits; Immune Checkpoint Inhibitors.

1. Introduction

The prevalence of gastrointestinal neoplasms has significantly grown over the past several decades due to changes in dietary practices and lifestyles. Gastrointestinal neoplasms mainly include gastric cancer and colorectal cancer. Currently, colorectal cancer ranks second in women aged 50 and younger and first in men for cancer-related deaths [1]. The death rates from stomach cancers are twice as high in Black and Native American populations as in White people [1]. Gastric cancer has the highest incidence rate among populations in East Asia [2]. Compared to countries with medium and low HDI levels, countries with high Human Development Index experience a relatively lower share of deaths [2]. Research has shown that the origin and progression of gastrointestinal cancers are significantly influenced by gastrointestinal microecology [3]. In addition to providing a short overview of the pathophysiology and conventional management of gastric tumors, this article addresses the state of the field on the connection between gastrointestinal microecology and immunology-based gastric tumor therapy.

2. Pathogenesis of Gastric Neoplasms

The pathogenesis and progression of stomach cancer are complex and multifaceted [4]. Gastric cancer is divided into "intestinal cancer" and "diffuse cancer" based on differences in genetic structure, cell structure, mucus separation, and growth patterns. Proto-oncogene stimulation, tumor suppressor gene inactivation and mutation, apoptotic gene imbalance, and metastasis-related gene activity may

cause unchecked cell proliferation, which can result in malignant transformation and metastasis. Different pathological types of gastric cancer involve different tumor genes and related molecules. Abnormal expression of cell adhesion proteins caused by gene mutations promotes cancer cell metastasis. Malignant cells elude immune surveillance, impede the body's reaction to infection, as well as facilitate their own growth by using immunomodulatory cells and the self-recognition system [5]. Bad eating habits, irregular living habits environment, heredity, and infection may affect stomach health [6].

2.1. Bad Eating Habits

Bad eating habits is the most important factor leading to gastric cancer. Unhealthy eating habits include intake of carcinogens and their precursors, overeating, eating foods that are high in sugar, fat, and salt, erratic eating, and insufficient intake of fruits and vegetables. Benzo (a) pyrene and other polycyclic aromatic hydrocarbons. Nitrites of preserved foods may be converted into nitrosamines with strong carcinogenic properties in the body. Excessive intake of salt increases osmotic pressure, which may cause damage to the gastric mucosa and promote gastritis. The high salt environment also promotes the growth and reproduction of *H. pylori*. It should not be ignored that the large number of people infected with *H. pylori* is caused by not using public chopsticks in public places. Alcohol, which has a strong stimulating effect on the stomach, is also one of the common foods that induce stomach tumors. Insufficient intake of fruits and vegetables will directly lead to insufficient intake of essential nutrients including dietary fiber, vitamins, and minerals, which can decrease the immune ability to suppress cancer.

2.2. Genetic Factors

The development of stomach cancer is linked to congenital variables such as inheritance and race [7]. Individuals who have inherited CDH1 mutations from their family are at a significantly greater chance of developing gastric signet ring tumor as well as invasive lobular breast cancer [8].

3. Traditional Treatment of Gastric Neoplasms

3.1. Surgical Resection

There was no disparity in the survival rate over a five-year period or postoperative mortality comparing elective total gastrectomy and subtotal gastrectomy for adenocarcinoma of the gastric antrum when the surgery was performed with the intention of curing the disease [9]. For people suffering from clinical first-stage stomach cancer, laparoscopy-assisted distal gastrectomy is a safer option than traditional open distal gastrointestinal surgery. It gives the advantage of reducing the occurrence of wound problems.

3.2. Chemotherapy

Chemotherapy drugs with reduced toxicity and targeted treatments using molecules have shown to be very effective in improving the prognosis for individuals suffering gastric and gastro-esophageal carcinoma via sequential methods of therapy. The TOGA (Trastuzumab for Gastric Cancer) study demonstrated that the addition of trastuzumab to conventional treatment resulted in a modest although statistically significant improvement in survival among individuals who had advanced HER2-positive stomach carcinoma [10]. Adding trastuzumab/pertuzumab to postoperative FLOT (fluorouracil, leucovorin, oxaliplatin, and docetaxel) significantly improved the rates of pathological complete response (PCR) and nodal adverse. However, this improvement come at the cost of a greater incidence of diarrhea and leukopenia.

3.3. Radiation Therapy

Radiation therapy, used as an adjuvant, can enhance survival and local control. It shows a low local recurrence rate, despite having significant heterogeneity [11]. For patients suffering from bleeding gastric cancer who experienced mild side effects, palliative radiation therapy is an effective hemostasis method. The use of radiotherapy in patients with advanced gastric cancer who have been stabilized by chemotherapy can prolong disease control and help prolong survival. The future direction of radiotherapy is how to minimize the damage of radiation to the normal physiological functions of the body. Adjuvant therapy combining radiation and chemotherapy is often used for advanced stomach cancer.

4. Immunotherapy

The autoimmune system in humans is capable of eliminating cancer cells and stopping tumor growth. To become resistant to apoptosis, the tumor cells continuously modify their genetic, epigenetic, and metabolic makeup. In addition, it induces the buildup of immunosuppressive cells like as suppressor cells derived from myeloid cells and regulatory T cells, and alters all components of the host's immune system, enabling it to avoid immune surveillance. Currently, tumor immunotherapy used in clinical settings primarily include immune checkpoint antagonists, adoptive immune-mediated treatment, and combination immunotherapy [12].

4.1. Immune Checkpoint Inhibitors (ICI)

Specific antigens present on the outer layer of cancer cells form a connection with immunological checkpoint particles, rendering the antigens indiscernible to T cells. Consequently, this hinders the activation of T cells. When an immune checkpoint inhibitor is added, the T cells are able to identify the unique antigens on the cancer cells' surface. This process successfully stimulates the activation of T cells and prevents cancer cells from escaping the body's defenses. Immune checkpoint antagonists include both antibodies and small compounds [13]. The use of this therapy has resulted in enduring positive changes in patients' health conditions, as well as in a minority of cases, extended periods of complete absence of cancer symptoms, extending for a long time [14].

The function of T cell's costimulatory receptor CTLA-4 is to prevent self-reactive activation and proliferation of T cells [15]. One of the most promising cancer treatment approaches is the use of checkpoint antagonists such as anti-PD-1 or anti-PD-L1, which produce strong antitumor responses with minimal side effects. Nevertheless, the limited and uneven presence of PD-1 in the cancerous cell's microenvironment hinders their effectiveness, limiting their use to certain cancer types [16]. An assay with high sensitivity is necessary to determine the levels of biomarkers in a group of patients, for the purpose of deciding the feasibility of PD-1 or PD-L1 treatment.

B7-H3 promotes tumor cell immune escape by inhibiting the function of $\gamma\delta$ T cells, an important immune cell with a key role in fighting tumors, thus providing a survival advantage for cancer cells in the tumor immune microenvironment [17]. The proliferation of MC38 cancerous colon cells was successfully inhibited with the use of B7-H5 inhibition, employing a B7-H5 monoclonal antibody (B7-H5 mAb) [18]. Therefore, B7-H5 might serve as a valuable prognostic indicator of colorectal cancer as well as a potential target for immune therapy against the illness. Two drawbacks of ICI therapy include immune-related negative effects and resistance to treatment [19].

4.2. Adoptive Immune Cell Treatment

An immunological technique called adoptive immune cell treatment (ACT) involves growing, modifying, and reintroducing ex vivo autologous cancer-cognate cells that kill tumors. Individuals suffering from advanced carcinoma of the stomach may have a longer survival time with adoptive immune cell treatment. Furthermore, individuals diagnosed with stage IV stomach cancer saw a significant increase in their lifespan when they underwent chemotherapy and adoptive immune cell treatment using tumor-associated cells. One significant advantage of ACT treatment is its capacity to

cultivate a substantial quantity of anti-tumor T cells in a controlled laboratory environment, allowing for the selection of T cells with a strong affinity for the target antigen [20].

Furthermore, apart from chimeric antigen receptor T cell treatment, NK cells and a specific kind of T cells known as $\gamma\delta$ T cells may also be used. The main obstacle to the continued advancement of adoptive immune cell treatment for cancer remedy will be identifying antigenic targets which successfully mitigate "off-tumor, on-target" effects [20].

4.3. Combination Immunotherapy

Except for individuals with microsatellite-instability high (MSI-H), the use of immune checkpoint inhibitors as a single treatment has failed to demonstrate any effectiveness in treating advanced recalcitrant colorectal carcinoma. The use of durvalumab and tremelimumab, together with an immune checkpoint inhibitor, may extend the overall lifespan of individuals with advanced recalcitrant colorectal carcinoma. In addition, the use of Pembrolizumab, an antibody that targets the PD-1 protein, in conjunction with Lenvatinib, a drug that inhibits several kinases including vascular endothelial growth factor receptors and other receptor tyrosine kinases, has shown significant cancer-fighting effects and a satisfactory safety profile in individuals suffering from advanced stomach carcinoma [21].

4.4. Additional analysis of ICI

Since immunotherapy may not be able to strengthen an immune system that has been compromised, treatment with immunosuppressive anticancer medications, such as chemotherapy and radiation therapy, must come before immunotherapy. Treatments aimed at eliciting adaptive immune responses against a tumor mass might not be able to successfully target the small subset of cancer stem cells that promote tumor growth and recurrence because those progenitor cells might express different antigens. Anticipating the adverse consequences that immune tolerance mechanisms might impose on patients is imperative.

5. Conclusion

The increasing prevalence of gastrointestinal (GI) neoplasms, notably gastric and colorectal cancers, has become a pressing health concern globally, attributed significantly to shifts in dietary habits and lifestyle changes. This paper provides a critical examination of the underlying mechanisms of these cancers and assesses the advancements in therapeutic approaches, with a notable emphasis on the burgeoning field of immunotherapy and the pivotal role of gastrointestinal microecology.

Gastric cancer, distinguished into intestinal and diffuse types, unfolds through a complex interplay of genetic, environmental, and dietary factors. This review highlights the multifaceted genesis of GI tumors, underscoring the significance of carcinogenic diets, the transformational impact of poor dietary practices, and the genetic predispositions that collectively contribute to cancer development. Environmental influences, alongside genetic vulnerabilities, set the stage for the malignancies, with unhealthy dietary habits acting as a catalyst in this deleterious process.

The treatment landscape for GI neoplasms has traditionally been dominated by chemotherapy, surgical interventions, and radiation therapy, each carrying its own set of benefits and limitations. Chemotherapy, while effective, often presents a high toxicity burden on patients. Surgical options and radiation therapy offer potential curative outcomes but are limited by their invasiveness and the stage of cancer at diagnosis. Recent years have seen a pivot towards targeted therapies, aiming to minimize side effects while maximizing therapeutic efficacy. These treatments target specific cancer cell mechanisms, offering a beacon of hope for improved patient outcomes.

Immunotherapy is being recognized as a groundbreaking method in the therapy of carcinoma. Utilizing the body's immune system to combat carcinoma, therapies including immune checkpoint inhibitors, adoptive immune cell therapy, and combination immunotherapy have shown encouraging outcomes. In contrast to conventional treatments, these medicines have a possibility to provide

prolonged remission for a specific group of patients. However, the use of immunotherapy is not without difficulties, as problems like immune-associated side effects and the emergence of resistance present significant obstacles to its widespread use.

The research examines the crucial significance of gastrointestinal microecology in the growth and advancement of gastrointestinal malignancies, offering a fresh viewpoint on the therapy of cancer. Because of the intricate relationship between the immune system and the gut microbiota, modifying this microecology may enhance the efficacy of immunotherapies and lead to important breakthroughs in the treatment of cancer.

Despite the promise of these advanced therapeutic approaches, the paper acknowledges the complexity of cancer treatment. The heterogeneity of GI tumors, combined with the individual variability in patient response, underscores the necessity for personalized treatment modalities. Future research is poised to explore the integration of microecological insights with immunotherapy, aiming to unlock new pathways for the management and prevention of GI neoplasms.

In conclusion, while traditional treatments continue to be a cornerstone in the management of GI cancers, the integration of microecological research and the advancements in immunotherapy are paving the way for more personalized and effective treatment strategies. The investigation into the interdependent connection between the gut microbiota and the immune system has promising possibilities for the advancement of cancer therapy, perhaps revolutionizing the field of cancer treatment.

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