Short Communication

Splanchnic inflammatory syndrome and the not-so-silent risk of cancer

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For many years, and in many (all) organ systems, one of the primary risks for developing cancer is the presence of chronic inflammation.[1-5] We have recently reported on the condition we term Splanchnic Inflammatory Syndrome (SIS), which we describe as the imaging findings of inflammation of the organs within the splanchnic system, with the two critical components being upper digestive tract inflammation and down-stream hepatic inflammation.[6] Our theory is based on the observation that individuals with hepatosteatosis, virtually always have inflammation of some combination of the distal esophagus, stomach (usually antrum), duodenum (usually proximal), pan jejunum and pan ileum (not with the primary focus of the distal ileum, as this is where commonly Crohn's Disease appears). The majority of individuals are obese, and abdominal pain is extremely common, probably universally present, and can be generalized, in the right upper quadrant or left upper quadrant. The digestive tract component of the condition relates directly to the clinical conditions of leaky gut, irritable bowel syndrome, and the bowel component of the Metabolic Syndrome (our preferred designation: Splanchnic Metabolic Syndrome), and these may represent progressive states of inflammation, consecutively, but not necessarily with universal progression.

Often, these findings are present for years in sufferers, presumably principally because individuals generally do not alter their dietary regimen. So, the upper digestive tract, liver, pancreas, and gallbladder/biliary tree remain in constant chronic inflammation. Based on our work on the Splanchnic Inflammatory Syndrome, and the resultant chronic inflammation, our theory is that this chronic inflammation may be responsible for malignant disease in the digestive system. The below describes our theory of the effects of malignancy induction, in the upper digestive tract segments individually:

Upper digestive tract: Esophageal cancer has been directly related to reflux disease for decades,[7-9] and our contention is that many of these individuals have chronic inflammation as the principal cause of SIS. The same observation has been made for gastric cancer. Duodenal and jejunal cancers are rarer than esophageal and stomach cancers, but a principal cause is likely chronic inflammation.

Liver: Over the last decade, multiple publications have suggested that Metabolic dysfunction-associated steatotic liver disease (MASLD, formerly nonalcoholic fatty liver disease, NAFLD) and primarily the inflammatory state of Metabolic dysfunction-associated steatohepatitis (MASH, formerly Nonalcoholic steatohepatitis [NASH])) is associated with the risk for the development of hepatocellular carcinoma (HCC), and may now be overtaking both alcohol-related and Hepatitis viral disease-related causes for HCC.[10-15]

Pancreas: Over recent years, it has been recognized that the (Splanchnic) Metabolic Syndrome is often associated with pancreatic steatosis. This has been our experience interpreting MRI studies. Additionally, our current theory is that the now common observation of small pancreatic cysts may reflect a pancreatic response to inflammation tracking from the jejunum through the mesentery to the pancreas. These pancreatic cysts are not related to known acute or chronic pancreatitis. They range in number and size from tiny individual or few cysts (the most common appearance) to numerous varying -sized cysts, with or without intraductal papillary mucinous neoplasms (IPMN). Our working theory is that they arise due to the pancreas being exposed to sustained chronic inflammation of SIS, and reflecting direct inflammatory spread from the duodenum, jejunum, and possibly the stomach. It is common practice to serially image patients with pancreatic cysts, and IPMNs, especially when they exceed 2.5 cm in diameter, because of the risk of cancer. Our current contention is that the risk of cancer does not stem from cysts, per se, rather due to chronic sustained inflammation of the pancreas in SIS. Therefore, pancreatic steatosis, pancreatic cysts/IPMNs, many cases of acute and chronic pancreatitis, and a number of cases of pancreatic cancer, all represent sequela of the chronic inflammation of SIS, as many published data indicate.[16-21]

Gallbladder and biliary tree: Our theory is that most cases of acalculous cholecystitis, and the various forms of biliary dyskinesia and ampullary dysfunctions are secondary/ sympathetic inflammation due to duodenal inflammation. Gallbladder cancer is most often observed in the setting of chronic inflammation associated with/induced by chronic cholecystitis. Although we have not at present conjectured this, it is not unreasonable to consider that the impetus to develop gallstones may be due to the chronic inflammation of SIS. Cholangiocarcinoma and ampullary carcinoma seem more likely to arise secondary to SIS and duodenal inflammation that progresses in a retrograde fashion in the Common Bile Duct (CBD). Prior studies are reporting the connection between chronic inflammation and the development of cancers in the gallbladder and biliary tree.[22-28]

Treatment: The primary management for SIS and the downstream various chronic inflammation-related malignancies starts with prevention. The critical recognition of a healthy diet for essentially all diseases, from heart disease and neurocognitive disease to COVID-19 infection, was most recently emphasized. We would term such a diet as the umbrella term the Wholesome Diet (we will describe it in a

future publication). Regarding choices in diet, for most individuals, the commonly recognized strategies are: cut down sugar, limit gluten, limit dairy, and stop smoking tobacco and other substances. It is also clear that it is paramount to avoid ultra-processed food altogether, due to the increased risk of cancer and cardiometabolic diseases.[29-33] In a few subjects, more in-depth dietary evaluation is necessary to manage food allergies and intolerance, such as limiting nightshade vegetables (e.g., tomatoes, white potatoes), some nuts, strawberries, etc. Development of, or ameliorating, symptoms is the most straightforward finding to pay attention to in creating an optimal diet for those individuals with a complex history of chemical sensitivities.

Conclusion

Chronic inflammation of the Splanchnic Inflammatory Syndrome is likely a common cause of many cancers of the splanchnic system. Prevention is the most obvious and practical approach. The principal management, which is the safest, most effective, and most cost-efficient approach, is attention to diet.

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None.

Conflicts of interest

None.

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