Updates into the potential association between myeloproliferative neoplasms and inflammatory bowel disease

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Inflammatory bowel disease (IBD) and myeloproliferative neoplasms (MPNs) are both chronic disorders in whose pathogenesis low-grade chronic inflammation plays a central contribution. IBD is characterised by chronic inflammation of the digestive tract, while MPNs are characterized by an overproduction of terminally differentiated myeloid cells. IBD may present itself mainly as ulcerative colitis (UC) or Crohn's disease (CD) while the classical Philadelphia-negative MPNs comprise polycythemia vera (PV), essential thrombocythemia (ET) and primary/secondary myelofibrosis (MF). A recent cohort study found that subjects with MPNs have a 2.4-fold increased risk of developing IBD compared to individuals without MPNs. The risk of developing IBD was highest within the first year after the diagnosis of MPN and after five years of being diagnosed with an MPN. However, there was a lower risk of developing IBD between the first year and fifth year of being diagnosed with an MPN. These findings suggest that there may be a common underlying mechanism that drives the pathogenesis of both IBD and MPNs. Moreover, alterations of the gut microbiome have been described both in MPNs and IBD, possibly in direct relationship with the high concentrations of pro-inflammatory cytokines measured in these disorders.

Another common pathogenetic mechanisms linking IBD and MPNs is autoimmunity. In a study conducted to assess the risk of MPNs in patients with a background of autoimmune diseases, a prior history of autoimmune disease was associated with increased risk of MPNs. CD, but not UC, was specifically associated with a 2-to-3-fold elevated risk for subsequent MPNs. This is similar to the findings of Jess et al. who found out that CD patients are at increased risk of lymphoma with no significant risk found in UC. Implicitly, this suggests that individuals living with immune-related diseases are at risk for subsequent MPNs. It has been postulated that a disruption of the JAK2 signalling pathway may be involved in the crosstalk established between CD and MPNs. For example, the detection of the rs10758669 polymorphisms of the JAK2 gene has been demonstrated to elevate the risk of both CD and UC, especially in Caucasian individuals. Moreover, an investigation which aimed to assess the likelihood of cancer in IBD with an onset in the elderly detected no significant risk of colorectal cancer, however, there was an overall increased risk of haematological malignancies, specifically lymphoproliferative and myeloproliferative disorders. Several subjects with UC and CD developed PV, MF, chronic myeloid leukaemia, as well as acute myeloid leukaemia at higher rates versus those predicted for the general population.

Several case reports have documented the coexistence of IBD and MPNs, suggesting a potential link between these two conditions. Literature describes the co-existence of UC and MF, as well as UC and PV complicated by Budd-Chiari syndrome, a thrombotic complication highly suggestive of MPNs. Thrombosis is another common feature of both MPNs and IBD which can occur in the context of the prothrombotic status of the disease itself. While a causal relationship between the use of biologic therapy and MPN development remains unclear, a case report that documented the emergence of ET after two years of biologic therapy initiation has been published. Moreover, JAK inhibitors have been employed for the management of both IBD and MPNs, e.g., filgotinib and upadacitinib for CD, tofacitinib for UC, ruxolitinib and other JAK inhibitors for MPNs. Interestingly, Swei et al. have depicted good results with the administration of ruxolitinib as well in an individual diagnosed with UC. However, the therapeutic potential of this pharmacological agent in IBD is not clear and needs further research.

In conclusion, an association between IBD and MPNs has been hypothesized, underscoring the possibility of shared underlying mechanisms or genetic predispositions. While the exact nature of this intricate relationship remains to be elucidated, the growing body of evidence suggests a potential association. Further research is warranted to understand the pathogenetic crosstalk and explore...
therapeutic strategies that may benefit patients with both IBD and MPNs.

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**References**


