Risk of cutaneous malignancy with vedolizumab

Finally, the use of vedolizumab has not been linked to malignancy (215). A recent analysis of clinical trials and real-world evidence did not demonstrate a rate of malignancy that was higher than expected based on the general population.

In summary, the presence of chronic immunosuppression has been linked to an increased risk for the development of squamous cell carcinomas (SCC) and to a lesser degree also basal cell carcinomas (BCC) (216–220). Most studies regarding NMSC in patients on immunosuppression have been reported in solid organ transplant patients with substantially less published regarding the incidence of NMSC in patients with IBD.

Key concept

11. All patients with CD and UC should be screened for depression and anxiety at baseline and annually. Patients who screen positive for anxiety and/or depression should be referred for counseling/therapy.

Summary of evidence

Pathophysiology The etiology of IBD and disease activity after periods of remission is complex and likely involves an interaction between multiple factors. Psychological stress has been reported by both caregivers and patients to exacerbate disease, but the published literature is conflicting, in part because of the inherent difficulty in studying this area and diversity of measurement tools used. However, newer studies and animal data suggest that depression and anxiety play a role in disease course. Recent research has highlighted an important role for the enteric nervous system in mediating intestinal inflammation in the presence of chronic stress (221). It has been found that chronically elevated levels of glucocorticoids drive the generation of an inflammatory subset of enteric glia that promotes monocyte-mediated and TNF-mediated inflammation through CSF. After being triggered by glucocorticoids, some glial cells release molecules that stimulate immune cells. In turn, those immune cells release molecules that would normally be used to fight off pathogens but in this case end up promoting bowel inflammation. In addition, glucocorticoids cause transcriptional immaturity in enteric neurons, acetylcholine deficiency, and dysmotility through TGF-β. The authors of this recent research verified the connection between the psychological state, intestinal inflammation, and dysmotility in 3 cohorts of patients with IBD. Together, these findings offer a mechanistic explanation for the impact of the brain on peripheral inflammation, define the enteric nervous system as a relay between psychological stress and gut inflammation, and suggest that stress management could serve as a valuable component of IBD care.

Epidemiology Current evidence suggests that mood disorders, in particular depression and anxiety, are more prevalent in patients with IBD than the background population. The literature is somewhat confusing as studies vary with regard to inclusion of which IBD diagnosis patients have, the state of disease activity (active vs in remission), the mood disorder studied, and the measurement tool used. A recent systematic review and meta-analysis to study the prevalence of anxiety and depression in patients with IBD included 77 studies. The authors found that anxiety symptoms were present in 32.1% of patients with IBD vs 10.4% of the background population in 58 studies, and depression was found in 25.2% with IBD vs 17.9% in non-IBD controls in 75 studies. In those studies that reported on patients with CD and UC, patients with CD were 20% more likely to report anxiety (OR 1.2, 95% CI 1.1–1.4) as well as depression compared with those with UC (OR 1.2, 95% CI 1.1–1.4). It was also reported that patients with active IBD were more than twice as likely to have anxiety (OR 2.5, 95% CI 1.5–4.1) and 3 times more likely to have depression (OR 3.1, 1.9–4.9) than those with IBD in remission (222). In a more recent population based cohort study\, Umar et al examined the incidence of mental illnesses in their IBD population from the United Kingdom (223). They found that either diagnosis was associated with a higher incidence rate of depression (IRR 1.36, 95% CI 1.31–1.42) and anxiety (IRR 1.17, 95% CI 1.11–1.24) than healthy controls.

Effect on disease course In 2004, Mittermaier et al studied the impact of depression on relapse of IBD (224). This was a prospective longitudinal study of 60 patients with IBD (both CD and UC) in remission. Patients were evaluated every 3 months for 18 months with the Beck Depression inventory (BDI), Spielberger Anxiety inventory, IBD Quality of Life Questionnaire (IBDQ), Perceived Stress Questionnaire, and the Rating for IBD Patient Concerns. At baseline, 28% of patients had depression. A higher BDI score at baseline predicted total number of relapses after 12 and 18 months.

In another study in patients receiving infliximab therapy for their CD, the impact of depression on disease course was measured. One hundred consecutive patients underwent assessment of clinical and psychological variables at baseline and at 4 weeks after infliximab initiation. The presence of major depression at baseline predicted a lower clinical remission rate. Depression was found to be an independent determinant of active disease both at baseline and re-evaluation (HR 2.27, 1.36–3.79) (225). In a case–control study of patients with active CD, anxiety and depression were measured in quiescent vs active disease (226). Anxiety and depression scores were significantly worse in those not being treated with any immune modulating therapy, and treatment with a thiopurine to achieve remission was associated with improved psychiatric survey scores. However, a later study of 139 patients with IBD, IBS, and hepatitis C enrolled in a 1-year observational cohort prospective study of patient outcomes in relation to psychological comorbidity (227), there was no relationship between depression and anxiety and total number relapses in the IBD group specifically as compared with the IBS and hepatitis C groups. In a study of patients with IBD in several Boston area hospitals, surgery seemed to increase the risk for depression and anxiety for both UC and CD, with a risk of 16% in CD and 11% in UC within 5 years of surgery (228).

Psychological stress has also been studied in IBD populations. In a Canadian study, 101 patients with CD in remission were followed prospectively for up to a year to examine clinical, biological, and psychosocial parameters as predictors of clinical relapse (229). Monthly measurements of psychological distress and perceived stress were measured. The interaction of perceived stress and avoidance coping (a coping strategy defined as taking time away from a situation) were predictors of earlier relapse (HR 7.0, 95% CI 2.3–21.8) in the 37 patients that experienced a relapse. A cohort of 75 patients in remission with UC was followed for a year, with endoscopy and long-term perceived stress measured at baseline (230). The Hospital Anxiety and Depression Scale was