Abdominal Radiology

Published online: 22 December 2015

Abdom Radiol (2016) 41:207–214
DOI: 10.1007/s00261-015-0560-3

Isolated recto-sigmoid colitis: a new imaging pattern of ipilimumab-associated colitis

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Abstract

Purpose: The purpose of this study is to describe typical CT findings and distinct imaging patterns of ipilimumab-associated colitis in immunotherapeutic treatment of melanoma.
Materials and methods: This HIPAA-compliant retrospective study included 86 patients with melanoma imaged with CT or PET/CT of the abdomen and pelvis during or shortly after administration of ipilimumab. Twelve of 86 patients (14%) developed symptoms of colitis and underwent CT imaging of the abdomen and pelvis while symptomatic. Two radiologists reviewed CT images to evaluate for the presence of CT findings of colitis including mesenteric vessel engorgement, pericolonic inflammatory change, hyperenhancement of colonic mucosa, colonic wall thickening, fluid-filled colonic distension, pneumoperitoneum, pneumatosis, and diverticulosis in the inflamed segment of colon. One nuclear medicine radiologist reviewed PET images for abnormally increased FDG uptake in the colon. The diagnosis of ipilimumab-associated colitis was made based on clinical presentation, imaging findings, and laboratory data.
Results: Common CT findings of ipilimumab-associated colitis included colonic mucosal hyperenhancement (10/12 [83%]), mesenteric vessel engorgement (9/12 [75.0%]), colonic wall thickening (9/12 [75%]), and pericolonic fat stranding (2/12 [16%]). No patient developed pneumatosis or pneumoperitoneum. Diffuse colitis was present in 4/12 (33%) patients. Segmental colitis with associated diverticulosis (was present in 2/12 (17%) patients). A third pattern, isolated recto-sigmoid colitis without diverticulosis, was observed in 6/12 (50%) patients. All patients with colitis demonstrated recto-sigmoid involvement.
Conclusions: A third radiologic pattern of ipilimumab-associated colitis was observed in this study: isolated recto-sigmoid colitis without diverticulosis. All patterns of ipilimumab-associated colitis include recto-sigmoid involvement.

Key words: Ipilimumab—Immunotherapy—Melanoma—CT—Colitis

Immunologic therapy is an evolving approach to cancer treatment and advances in the understanding of the biologic pathways that regulate immune responses have delivered new molecular targets for oncologic therapies [1]. Cytotoxic T-lymphocyte antigen-4 (CTLA-4), one such target, is a receptor protein found on the surface of activated T-cells. Stimulation of CTLA-4 results in inhibition and apoptosis of activated T-cells. Thus, CTLA-4 is a key immune checkpoint molecule which negatively regulates T-cell activation [1]. Ipilimumab (Yervoy, Bristol-Myers Squibb, New York City, NY) is a fully human monoclonal antibody (IgG1) directed against CTLA-4. By inhibiting the effects of CTLA-4, ipilimumab promotes anti-tumor T-cell immunity [2–5]. Phase II and phase III clinical trials have demonstrated that ipilimumab therapy results in a statistically significant survival benefit for patients with metastatic melanoma [6–9]. In March 2011, the United States Food and Drug Administration approved ipilimumab as monotherapy for metastatic melanoma.

Clinical experience with ipilimumab immunotherapy has demonstrated that suppression of CTLA-4 also results in a variety of dose-dependent, immune-related side effects resulting from tissue damage caused by activated T-cells. These side effects have been termed "immune

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related adverse events" (irAEs) and include dermatitis, colitis, hepatitis, endocrinopathies, hypophysitis, iridocylitis, neuropathy, and nephritis [10]. While the skin is the organ affected most frequently by ipilimumab-associated irAEs across clinical trials, colitis has the potential to be life threatening, and severe diarrhea necessitates cessation of immunotherapy in some patients [11]. Histologic assessment of bowel biopsies in patients treated with ipilimumab suggests that dysregulation of mucosal immunity, evidenced by altered antibody levels to enteric flora and inflammatory cell infiltration into the gastrointestinal mucosa, results in the clinical syndrome of diarrhea and colitis [12].

To our knowledge, there are relatively few reports in the literature describing the imaging findings of ipilimumab-associated colitis. O'Regan et al. illustrated two cases of ipilimumab-associated colitis, one of which demonstrated mural thickening of the sigmoid colon, mesenteric hypervascularity, and pericolonic fat stranding, and another of which presented with colonic distention and pneumoperitoneum [13]. Lyall et al. reported a case of ipilimumab-associated colitis which presented as diffuse colonic wall thickening with increased FDG-avidity on PET/CT and resolved with systemic corticosteroid therapy [14]. Bronstein et al. described five cases of diffuse colonic wall thickening and one case of segmental colonic wall thickening in the setting of colitis related to anti-CTLA-4 antibody therapy [15]. Finally, Kim et al. described numerous CT findings in a retrospective review of 16 patients with ipilimumab-associated colitis and concluded that there are two different radiologic and clinical manifestations of ipilimumab-associated colitis: diffuse colitis and segmental colitis with associated diverticulosis (SCAD) [16].

The purpose of this study is to further describe and characterize the typical CT findings and distinct imaging patterns of ipilimumab-associated colitis.

Materials and methods

Patient selection

This was a HIPAA-compliant retrospective study which was approved by the institutional review board at our institution. The requirement for informed consent was waived. Eighty-six patients with melanoma who were treated with ipilimumab and underwent CT or PET/CT imaging of the abdomen and pelvis during or within two weeks after administration of ipilimumab were identified through a search of the electronic medical record. Thirteen of those 86 patients (15%) treated with ipilimumab developed symptoms of colitis (diarrhea, nausea, abdominal pain) and all underwent CT imaging of the abdomen and pelvis at the time of their symptoms. One patient was excluded because of a prior history of ulcerative colitis. Twelve patients comprise the cohort of patients included in this study. An evaluation of each of these patients by the oncologist did not reveal an alternative etiology for the gastrointestinal symptoms, and the diagnosis of ipilimumab-associated colitis was made on the basis of clinical presentation, imaging findings, and laboratory data. In addition to imaging performed at the time for presentation for patients who developed clinical signs and symptoms of colitis, all patients underwent baseline CT imaging at the time of initiation of ipilimumab therapy and restaging CT imaging at 3–4 month intervals while receiving ipilimumab therapy.

CT acquisition

CT examinations of the abdomen and pelvis were performed using either a 16-detector (LightSpeed 16, VCT 750 HD, or GE Discovery STE PET/CT, GE Healthcare, Milwaukee, Wisconsin), a 64-detector (GE Discovery 690 PET/CT), or a 128-detector (Somatom Definition Flash; Siemens Healthcare, Malvern, Pennsylvania) CT system. Technical acquisition parameters for abdominopelvic CT imaging in these patients include helical mode, 120 kVp, beam pitch 0.8–1.35, automated tube current modulation, minimum tube current 100–150 mAs, and reconstructed section thickness and interval of 5 mm. For PET/CT systems, the noise index was 18 with other acquisition parameters the same as for abdominopelvic CT. Administered intravenous contrast material was 150 mL (Isovue-300, 300 mg I/mL) injected at a rate of 3 mL/s. Imaging was performed during the portal venous phase of enhancement (70–90 s post-contrast media administration), and coronal reformatted images were reconstructed from 0.6–0.625 mm thick axial sections. Per institution protocol, patients did not receive oral contrast. The study included 5 CTs and 7 PET/CTs.

PET/CT acquisition

Patients received nothing by mouth for at least 4 h preceding the PET/CT scan. Blood glucose was measured to assure that it was within the normal range, and if patients had received insulin, the scan was delayed for 4 h. Patients were then injected intravenously with 0.14–0.18 mCi/kg 2-deoxy-2-(^{18}F)fluoro-D-glucose (FDG) and placed in a darkened quiet room for a minimum uptake period of 1 h. PET images were then acquired in 3D mode from skull vertex to mid thighs using either a GE Discovery STE or GE Discovery 690 scanner. Time per bed position varied depending upon patient weight as follows: 2:00 min for 70–80 kg, 2:30 min for 81–90 kg, 3:00 min for 91–113 kg, 3:30 min for 114–136 kg, and 4:00 min for >136 kg.

Images were reconstructed with two iterations of the ordered subsets expectation maximization algorithm, incorporating corrections for detector sensitivity, dead time, scattered events, random events, and attenuation,

based on CT. Time-of-flight information was incorporated from images on Discovery 690 system. Attenuation-corrected PET images were reviewed along with the CT images. Maximum standardized uptake value (SUVmax) was computed using a spherical ROI and the formula [mCi/mL in region of interest]/[injected activity in mCi/ bodyweight (g)].

Image assessment

CT examinations of the abdomen and pelvis were interpreted retrospectively on a dedicated PACS workstation by two radiologists, one of whom is faculty radiologist with 13 years of experience and another of whom is abdominal imaging fellow. Radiologists were blinded to clinical and laboratory data, with the exceptions that the patients had clinical symptoms of colitis and were receiving ipilimumab therapy. The CT examinations were evaluated for the presence and extent of mesenteric vessel engorgement, pericolonic inflammatory change, hyperenhancement of the colonic mucosa, colonic wall thickening, a fluid-filled distended colon, pneumoperitoneum, pneumatosis, and diverticulosis in the inflamed segment of colon. Disagreements between the two radiologists were minor and were resolved by consensus. Imaging examinations obtained at the time the patients presented with clinical signs and symptoms of colitis were compared with CT scans obtained prior to treatment with ipilimumab to establish that the findings described above had developed in the interval, concurrent with ipilimumab therapy, and the clinical presentation of colitis.

Mesenteric vessel engorgement was defined as a subjective increase in caliber or tortuosity of the vasa recta vessels on the CT obtained at the time of clinical symptoms of colitis in comparison with the pre-therapy CT. Hyperenhancement of the colonic mucosa was defined as focal or diffuse enhancement of the colonic mucosa which was subjectively increased in comparison with the mucosal enhancement of other segments of colon, the small bowel, and/or the stomach. Colonic wall thickening was defined as a mean colonic wall thickness greater than 4 mm when measured in two representative locations [17]. The extent of colonic wall thickening was categorized as focal (<10 cm), segmental (10–30 cm), or diffuse (>30 cm) [18]. Colonic dilation was defined as a colonic luminal diameter greater than 8 cm for the cecum or greater than 6 cm for the rest of the colon [19, 20].

PET examinations were reviewed by a nuclear medicine radiologist with 2 years of experience for evidence of increased FDG uptake in the affected colonic segments. Uptake was considered significant if bowel SUVmax was greater than the liver SUVmax and not obviously related to physiologic peristalsis. None of the patients had been on metformin at the time of PET imaging, which is known to result in diffuse bowel FDG uptake [21].

Clinical analysis

Chart analysis using the institutional electronic medical record system (EPIC, Verona, Wisconsin) was performed for patient demographics including age and gender, presentation of gastrointestinal symptoms, other immune-related adverse events, and therapeutic course. Clinical markers for causes of infectious colitis (fecal leukocytes, clostridium difficile toxin, parasite screen, stool culture) were also recorded. Grading for colitis was based on severity: grade 1 is defined as an increase of <4 stools per day; grade 2 as mild to moderate abdominal pain and/or an increase of 4–6 stools per day; grade 3 as severe abdominal pain and an increase of ≥ 7 stools per day over baseline and/or incontinence or hospitalization; and grade 4 as symptoms creating life-threatening consequences or when urgent intervention indicated [22].

Statistical analysis

Statistical analysis was performed using SSPS Software (IBM, Armonk, New York). In order to test for differences in mean clinical colitis scores for the various radiological patterns, a one-way analysis of variance (ANOVA) was performed. Then, the Mann–Whitney U test was used to test for differences in mean clinical colitis score between the pattern with the highest mean score and all other patterns, as well as between the pattern with the lowest mean score and all others.

Results

Patient demographics, imaging findings, clinical presentation, and treatment are summarized in Table I. Five patients were enrolled in a phase III randomized trial for dosing of ipilimumab (3 vs. 10 mg/kg); of these patients, 2 received 3 mg/kg and 3 received 10 mg/kg. The standard dosing for ipilimumab intravenously was 3 mg/kg over 90 min. At the time of symptoms, seven patients had undergone contrast enhanced CT as part of a PET/CT and five patients were imaged with contrast enhanced CT alone.

Imaging findings

The frequency of CT findings of ipilimumab-associated colitis in this study included: colonic mucosal hyperenhancement (10/12 [83%]), mesenteric vessel engorgement (9/12 [75%]), colonic wall thickening 8/12 [75%]), and pericolonic fat stranding (2/12 [16%]). All twelve patients had hyperenhancement of the rectum and distal sigmoid colon on CT. Of the eight patients who developed colonic wall thickening, two patients demonstrated diffuse colonic wall thickening and six patients demonstrated segmental wall thickening. The colon was dilated and fluid-filled in 3/12 (25%) patients. None of the patients in this study developed colonic pneumatosis or pneu-

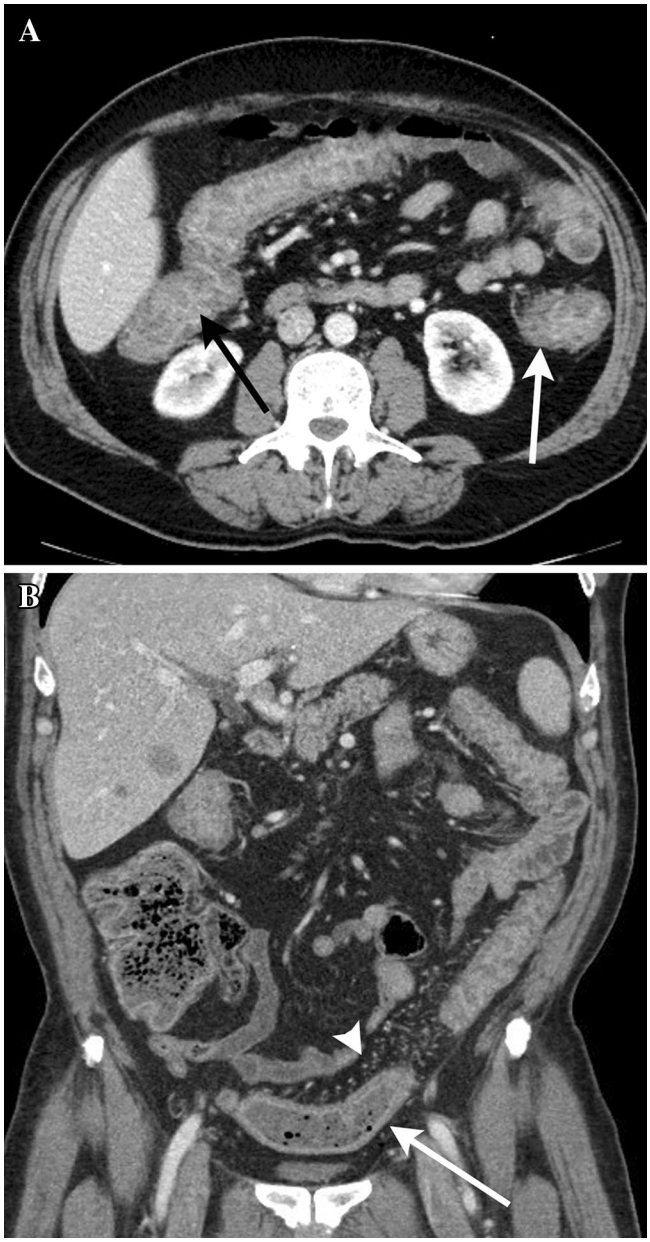

Fig. 1. Transverse (**A**) and coronal reformation (**B**) CT images in a 64-year-old male with diffuse colitis pattern. There is diffuse bowel wall thickening (*white arrow*), mucosal hyperenhancement (*black arrow*), and mesenteric vessel engorgement (*white arrow head*) extending from the rectum through the cecum in a patient with ipilimumab-associated colitis.

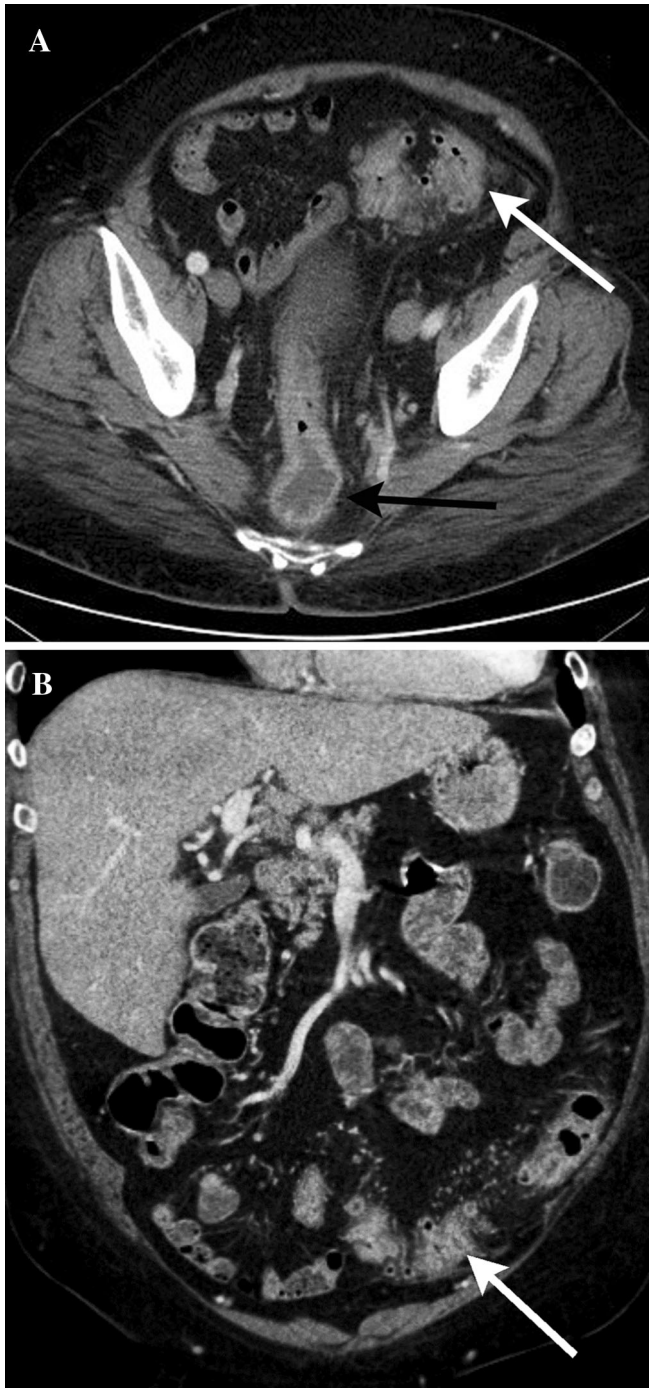

Fig. 2. Transverse (**A**) and coronal reformation (**B**) CT images in a 71-year-old male with segmental colitis with associated diverticulosis pattern. There is colonic wall thickening (*white arrow*), pericolonic fat stranding, mesenteric vessel engorgement, and mucosal hyperenhancement involving the recto-sigmoid colon, a segment of colon with diverticulosis.

moperitoneum secondary to ipilimumab-associated colitis. Of the seven patients who had concomitant PET imaging, 6 (86%) demonstrated increased FDG uptake which correlated directly with the CT findings of colitis. The seventh patient had no abnormal FDG uptake.

Three distinct patterns of ipilimumab-associated colitis were observed. Two of these patterns, the diffuse colitis pattern and the SCAD pattern, have been described previously [16]. The diffuse colitis pattern, characterized by findings of mild colonic inflammation extending from the rectum through the cecum, was present in 4/12 (33%) patients. Three of the patients with the diffuse colitis pattern (Fig. 1 A and B) demonstrated diffuse colonic

mucosal hyperenhancement, wall thickening, and mesenteric vessel engorgement, and one patient had more segmental involvement of the right colon and recto-sigmoid. Three of the four patients (75%) with the diffuse colitis pattern had correlating increased FDG uptake throughout the colon, and 1 of these 3 (33%) patients had relatively greater uptake in the recto-sigmoid colon. The SCAD pattern, characterized by findings of inflammation limited to a segment of the colon which contains diverticulosis, was present in 2/12 (17%) patients (Fig. 2 A and B). These patients had segmental wall thickening and diverticulosis of the sigmoid colon with associated mesenteric vessel engorgement, and colonic mucosal hyperenhancement involving the sigmoid and rectum. One patient with SCAD also had pericolonic fat stranding on CT. Neither of the patients with SCAD pattern had PET imaging. A third pattern of ipilimumab-associated colitis, isolated recto-sigmoid colitis without diverticulosis, was observed in 6/12 (50%) patients (Fig. 3 A and B, Fig. 4). All six patients with isolated recto-sigmoid colitis demonstrated mucosal hyperenhancement, and two had associated wall thickening of the sigmoid colon. Pericolonic fat stranding was not a feature of the isolated recto-sigmoid colitis pattern. Four of the six patients with isolated recto-sigmoid colitis pattern underwent PET imaging, and of these 4, 1 patient (25%) had corresponding increased FDG uptake throughout the recto-sigmoid colon, 2 (50%) had FDG uptake either in the rectum or sigmoid, but not both and 1 patient (25%) had no appreciable increased FDG uptake in the rectosigmoid.

Clinical features

The most common clinical symptom of ipilimumab-associated colitis was loose stool with an increase in number of bowel movements. None of the patients presented with fever or chills. Two patients presented with clinically evident hematochezia and underwent either colonoscopy or flexible sigmoidoscopy. Given the presentations and closely related timing to ipilimumab therapy, clinical markers for causes of infectious colitis (fecal leukocytes, clostridium difficile toxin, parasite screen, stool culture) were drawn in only two patients and were negative in both patients. Eight patients (67%) were treated with a high dose oral steroid taper, three patients (25%) also received intravenous steroids, two patients (17%) were treated with infliximab after failure of symptom reduction with steroids, and one patient (8%) underwent total colectomy after failure of medical therapy. There was no statistically significant difference in ipilimumab dose (3 vs. 10 mg/kg) and either presentation of symptoms, severity of colitis, or radiologic manifestation of colitis. Four patients (33%) also demonstrated other evidence of irAEs. There was no statistically significant relationship between clinical presentation and severity of symptoms with presence of additional irAEs.

Statistical analysis

The one-way ANOVA demonstrated a trend toward differences in clinical severity of colitis based on radiographic pattern, which did not reach statistical significance ($p = 0.07$). The SCAD pattern was associated with the highest mean clinical score (3.5 vs. 2.0 for all others, $p = 0.12$), and the recto-sigmoid pattern was associated with the lowest mean score (1.7 vs. 2.8 for all others, $p = 0.07$). Overall, there was a trend toward more severe colitis for the SCAD pattern and less severe colitis with the recto-sigmoid pattern.

Discussion

Ipilimumab-associated colitis is a significant complication of immunotherapy for patients with metastatic melanoma and may necessitate cessation of treatment [11]. Although the clinical presentation and imaging appearance of ipilimumab-associated colitis is nonspecific compared with other causes of colitis, timely diagnosis and treatment of patients who develop this complication is critical. It is therefore important for radiologists to be familiar with the common clinical presentation, CT findings, and distinct imaging patterns seen in patients with ipilimumab-associated colitis.

Prior reports describing the clinical presentation of ipilimumab-associated colitis indicate that diarrhea is the hallmark symptom [11, 16, 23, 24]. This diarrhea can range from three loose stools daily to twenty watery stools daily and some patients report hematochezia. Associated presenting symptoms may include abdominal pain, nausea, vomiting, fever, and anal pain in a minority of patients. GI related symptoms often occur in the first 16 weeks of treatment and reported incidence of colitis after ipilimumab therapy is between 20% and 35% [11, 23, 25–28]. Symptoms of colitis can be mild and self-limiting; however, grade 3/4 colitis may require high dose corticosteroids and infliximab, a monoclonal antibody against tumor necrosis factor alpha [11, 25]. Although ipilimumab-associated colitis is typically responsive to medical therapy, intestinal perforation secondary to ipilimumab treatment has been reported [6, 29–31]. The predominant colonoscopic finding of ipilimumab-induced colitis is a distal and often diffuse inflammatory colitis with neutrophilic and/or lymphocytic cryptitis and neutrophilic infiltration with ulceration of the mucosal surface [26]. Given the high overall incidence of colitis after ipilimumab therapy, most patients no longer require diagnosis with colonoscopy and therapy is based on the recognition of symptoms [32, 33].

Prior studies have reported imaging findings of ipilimumab-associated colitis, including segmental or diffuse colonic wall thickening, mesenteric vascular engorgement, pericolonic inflammatory change, mucosal hyperenhancement, and a fluid-filled, distended colon

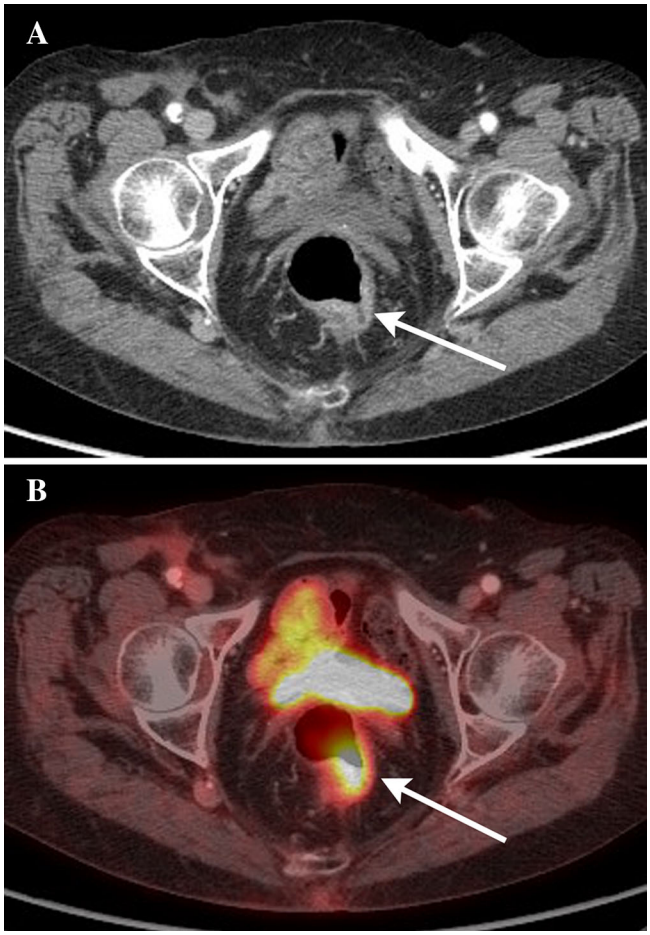

Fig. 3. Transverse CT (**A**) and PET (**B**) images in a 60-year-old male with isolated recto-sigmoid colitis without associated diverticulosis. There is colonic wall thickening, mucosal hyperenhancement, and pericolonic inflammatory change isolated to the recto-sigmoid colon (*white arrow*). There is no associated colonic diverticulosis.

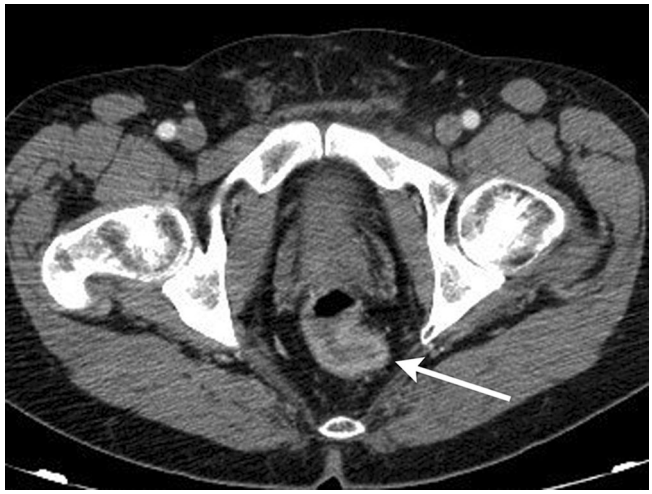

Fig. 4. Transverse CT images in a 55-year-old male with isolated recto-sigmoid colitis without associated diverticulosis. There is colonic wall thickening and mucosal hyperenhancement isolated to the recto-sigmoid colon (*white arrow*). There is no associated colonic diverticulosis.

suggestive of active diarrhea [13–16]. In the most comprehensive description of these findings, Kim et al. [16] reported that mesenteric vessel engorgement was the most common imaging finding of ipilimumab-associated colitis, followed by colonic wall thickening. Although the most common imaging finding in our patient population was mucosal hyperenhancement, colonic wall thickening and mesenteric vessel engorgement were prevalent as well. Additionally, the absence of any cases of colonic pneumatosis in our cohort is consistent with prior reports and serves as further supporting evidence that the presence of colonic pneumatosis makes ipilimumab-associated colitis a less likely diagnostic consideration.

In addition to a description of the common CT findings of ipilimumab-associated colitis, Kim et al. reported two distinct radiological and clinical presentations in this patient population: diffuse colitis and SCAD [16]. Twelve of the sixteen patients in that cohort demonstrate the diffuse colitis pattern on CT, characterized by mild diffuse bowel wall thickening and mesenteric vessel engorgement. Four of the sixteen patients manifested colitis in the SCAD pattern, characterized by moderate segmental wall thickening associated with diverticulosis. One half of the patients in our study with ipilimumab-associated colitis presented with CT findings that were consistent with the one of the two previously described radiologic patterns of disease. However, one half of our patients presented with isolated recto-sigmoid colitis without associated diverticulosis. Given the frequency of manifestation of this form of colitis, we believe it is important to recognize isolated recto-sigmoid colitis without diverticulosis as a third distinct imaging pattern in patients with ipilimumab-associated colitis.

Although the presentation of clinical symptoms of ipilimumab-associated colitis is similar to those of inflammatory bowel disease, the histologic distribution is different from Crohn's disease and ulcerative colitis. Although ipilimumab-associated colitis manifests in a distal colonic distribution, most reports note that the inflammation spares the rectum [11, 12, 23]. We found evidence of recto-sigmoid inflammation on CT in all of the patients included in our study, and both patients who underwent endoscopic evaluation had histopathologically-proven rectal involvement. We propose that the presence of rectal inflammation is, in fact, an expected manifestation of ipilimumab-associated colitis.

To date, there is only one case report in the literature on the PET appearance of ipilimumab-associated colitis [14]. In our study, more than half of the patients had concomitant PET imaging and most of the PET studies (85%) demonstrated abnormally increased FDG uptake

in the segments of colon that appeared inflamed on CT. As utilization of intravenous contrast in PET/CT imaging is variable and separate reporting for CT findings in PET/CT is not standardized [34, 35], familiarity with the PET manifestations of ipilimumab-associated colitis is essential to identification of this treatable disease.

Despite this study's small sample size, we found trends toward more clinically severe colitis with the SCAD pattern of ipilimumab-associated colitis and less severe colitis with the isolated recto-sigmoid pattern. Berman et al. previously found no association between any endoscopic finding and the development of grade 2 or greater colitis [12]. However, the key difference between the SCAD and recto-sigmoid patterns of colitis is the presence of diverticula. Segmental colitis associated with diverticula, SCAD, is a known variant of chronic colitis that is limited to areas of diverticula [36]. The prevalence of SCAD is unknown but is estimated to be between 0.3% and 1.3% [37]. Histologically, the disease mimics chronic idiopathic inflammatory bowel disease with inflammatory reaction restricted to the mucosa [38]. It is characterized by luminal mucosal inflammation with or without involving the diverticula themselves. Neither of the patients included in this study with SCAD pattern of colitis after ipilimumab had any evidence of the SCAD prior to treatment. It is unclear whether the ipilimumab-associated form of SCAD and the chronic colitis of diverticular disease-associated colitis are one and the same entity. Further investigation of the relationship between ipilimumab-associated colitis and SCAD is warranted. Since all of the patients included in the current study as well as those of Kim et al. demonstrated recto-sigmoid involvement on CT, recto-sigmoid inflammation likely represents an early manifestation of ipilimumab-associated colitis and should be sought prospectively to allow for early treatment with steroids [16].

The success of ipilimumab in improving survival in patients with melanoma has re-invigorated the field of immuno-oncology, with numerous novel checkpoint inhibitors at various stages of development. Agents designed to interrupt the action of programmed cell death 1 (PD-1) and its ligand PD-LI which is expressed in peripheral tissues and cancers are currently approved for the treatment of melanoma and most recently non-small cell lung cancer [39–41]. Although colitis is less frequent with anti-PD1 monotherapy, future strategies include combinations of immune modulators and these will likely be associated with higher incidence of immune-mediated adverse events [42]. To date, the use of concurrent ipilimumab and nivolumab is associated with a higher frequency of severe colitis than monotherapy with either agent [43].

With promising clinical activity seen with checkpoint inhibitors across a number of tumor types, including non-small-cell lung, prostate, renal cell, bladder, breast, colorectal, pancreatic, hepatocellular, and gastroesophageal cancers, as well as acute leukemia and non-Hodgkins lymphoma, these agents will likely become a mainstay of oncologic therapy [44, 45]. Available data suggest that rate and severity of irAEs for non-melanoma indications mirror those seen in the treatment of melanoma [11]. At the same time, additional immune modulators have entered the therapeutic world for oncologic and non-oncologic indications and reports of immune-mediated colitis are growing [25, 46–48]. Becoming familiar with the imaging signs of colitis in patients being treated with immunotherapies will become more important for radiologists as these patients may present with symptoms of abdominal pain and undergo emergent imaging.

There are several limitations to our study, particularly the relatively small size of our cohort and its retrospective, observational nature. As there is now increased awareness of and vigilance for irAEs, CT is now performed sporadically in this patient population. The retrospective nature of our study raises the issue of observational bias in determining the presence or absence and extent of colitis-related findings.

In summary, in addition to the two distinct radiologic patterns of ipilimumab-associated colitis described previously, the diffuse colitis pattern and the SCAD pattern, we present a third distinct radiologic pattern of ipilimumab-associated colitis: isolated recto-sigmoid colitis without diverticulosis. Ipilimumab-associated colitis always involves the distal colon with recto-sigmoid involvement in all three patterns. There is a tendency toward more clinically severe colitis when the SCAD pattern is observed on CT.

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