Extra-intestinal malignancies in inflammatory bowel diseases: An update with emphasis on MDCT and MR imaging features

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Inflammatory bowel diseases (IBD), which include Crohn’s disease (CD) and ulcerative colitis (UC), are characterized by chronic inflammation of the gastrointestinal tract [1—3]. Gastrointestinal cancers are of major concern in the follow-up of IBD patients, so that they have already received a great attention in the gastroenterological and radiological literatures [4—9]. However, although they are somewhat rarer, extra-intestinal malignancies associated with IBD, such as cholangiocarcinoma, lymphoma and skin cancers may occur and the risk is increased by immunosuppressive treatments [10—20]. A meta-analysis found that the relative risk of extra-intestinal cancer and that of lymphoma by comparison with the standard population were 1.27 (95% confidence interval [CI]: 1.1—1.47) and 1.42 (95% CI: 1.16—1.73) [19].

Multidetector row computed tomography (MDCT) and magnetic resonance (MR) imaging are now screening modalities of major importance for diagnosing complications in IBD patients as well as problem-solving tools for IBD patients presenting with unusual symptoms [2—4,8]. Consequently, radiologists are currently on the frontline of management of IBD patients in many occasions. Because of the rarity of extra-intestinal malignancies in IBD patients, knowledge of their imaging features is based on case reports and scarce studies that included a few patients [21—24].

The goal of this review is to illustrate the MDCT and MR imaging features of extra-intestinal malignancies that occur in patients with IBD and provide an update on their specific pathogenesis, clinical features and screening recommendations, if any, that would be useful to the radiologist.

### Cholangiocarcinoma

#### Incidence, prevalence and risk factors

Primary sclerosing cholangitis (PSC), which is considered as an intermediate step in the development of cholangiocarcinoma is associated with IBD in 60 to 80% of patients [25]. UC is present in 48 to 86% of patients and CD in 13 to 25% [25]. Conversely, PSC is the most common hepatobiliary complication observed in IBD patients and seen in approximately 5% of IBD patients [14,25—27]. CD patients have a less marked increased risk of hepatobiliary cancer than those with UC [10].

There is an increased risk for hepatobiliary cancers in patients with UC, including biliary tract and gallbladder cancers [12,28,29] with a standardized incidence rate (SIR) of 2.58 [10]. Of note, severe dysplasia or adenocarcinoma is present in approximately 60% of PSC patients with polypoid lesions of the gallbladder [29].

In IBD patients, the estimated incidence of cholangiocarcinoma is between 0.5% and 1% [30]. The incidence rate of cholangiocarcinoma in IBD patients is four times greater than that in patients without IBD (7.6/100,000 vs. 1.9/100,000, respectively) [14] and the 10-year cumulative risk of cholangiocarcinoma in IBD patients is 0.07%. This increased risk is more prominent in patients with UC than in those with CD, with an incidence rate two times greater for UC patients than for CD patients (8.2/100,000 vs. 4.3/100,000, respectively) [14]. Among IBD patients with cholangiocarcinoma, 65% have definite UC, 25% have definite...
CD and the remaining 10% have an undeterminate diagnosis [14]. Cholangiocarcinoma occurs at a younger age in IBD patients than in the general population without IBD (56 years vs. 71 years, respectively) and in Western countries, cholangiocarcinoma occurring in patients ≤ 40 y.o. is almost always associated with IBD [14]. Of major importance, the risk for cholangiocarcinoma is dramatically more marked in IBD patients with PSC, which is 160-fold that of the general population and estimated to a 5% -10% lifelong risk [25]. The peak incidence of cholangiocarcinoma is observed during the first years following the diagnosis of IBD [14].

Molecular features

The mechanisms of carcinogenesis in PSC are not well elucidated yet. The evolution from PSC to cholangiocarcinoma may result from DNA damage by bile acids in IBD patients with altered DNA repair functions (toxic bile hypothesis) [31], altered functions of a specific cytokine suppressor [32] or altered balance between macrophages and natural killer cells [33].

Clinical and histological features

The majority of IBD patients with PSC are initially asymptomatic with only biological evidence of cholestasis [34]. Symptoms including fatigue, pruritus, right upper quadrant pain, fever and weight loss develop insidiously [34]. Jaundice, pruritus, abdominal pain and fatigue are more frequently observed in PSC patients who will develop cholangiocarcinoma than in those who will not [13]. A high proportion of cholangiocarcinomas are diagnosed within the first year after the diagnosis of PSC is made [13]. The development of PSC-associated cholangiocarcinoma follows a metaplasia-dysplasia-carcinoma sequence.

Clinical implications

In general, UC patients with coexisting PSC have mild, asymptomatic colitis that spares the rectum, so that colon disease may be undetected during rigid sigmoidoscopy [35]. As a consequence, in this group of patients, the radiologist should scrutinize the colon when performing MDCT or MR imaging, to depict, if any, findings that would suggest coexisting IBD [35,36]. However, it is recommended to perform colonoscopy in patients with PSC and UC. In addition, the risk of colon cancer is very high in this population so that the radiologist should also carefully analyze the colon wall.

The major cause of mortality in patients with PSC is the occurrence of cholangiocarcinoma, with a lifetime incidence of 10–15% [35]. To date, no validated screening tool for early detection of cholangiocarcinoma exists so that cholangiocarcinomas are often diagnosed at an advanced stage. The diagnosis of cholangiocarcinoma in association with PSC is difficult and delayed because abnormalities of the biliary tree due to PSC obscure early cholangiocarcinoma.

It is important to note that PSC may display two different presentations. PSC may involve the distal biliary ducts in the absence of visible abnormalities on MDCT and MR imaging. The diagnosis is suggested by the presence of altered liver function tests. This form in association with IBD is observed in 15% of patients, has a better long-term survival rate and carries a low risk for cholangiocarcinoma [25,37]. On the opposite, PSC may involve larger bile ducts, including intrahepatic ones and biliary confluence, and is at high risk of malignant transformation [38].

Early recognition of cholangiocarcinoma can be made by measurement of trypsinogen-2 serum level, which is so far the most accurate means for differentiating PSC from cholangiocarcinoma [39]. Measurement of circulating Angiopoietin-2 in serum may be an additional test for the diagnosis and further clinical management of patients with cholangiocarcinoma [40].

The diagnosis of cholangiocarcinoma in PSC is critical because the tumor has a rapid growth. In addition patients with PSC and cholangiocarcinoma may benefit from orthotopic liver transplantation when the tumor is depicted at a very early stage [41]. However, the question of orthotopic liver transplantation remains debated because best results for orthotopic liver transplantation were obtained in patients with PSC and incidental depiction of cholangiocarcinoma in explanted liver.

Because of the increased risk of biliary cancers including gallbladder cancers, patients with IBD and PSC should be investigated with ultrasonography to depict gallbladder polyps every year and cholecystectomy should be performed even when polyps < 1 cm are present (Fig. 1) [31,42].

Imaging findings

Early diagnosis of cholangiocarcinoma in PSC is difficult because differentiating between benign and malignant ductal strictures is limited with current imaging modalities such as ultrasonography, MDCT, MR imaging, endoscopy, cytology specimens, and serum tumor markers such as carbohydrate antigen (CA) 19–9 [43]. In addition, there are no clear recommendations for surveillance to date but regular MDCT and

![Figure 1. A 52-year-old man with ulcerative colitis and primary sclerosing cholangitis. Ultrasonographic examination of the gallbladder reveals polypoid mass (arrows) with a largest diameter of 18 mm. After cholecystectomy, histopathological analysis confirmed gallbladder polyp with foci of adenocarcinoma.](image)
MR imaging examinations and repeat endoscopic brush cytology of stenotic lesions are recommended [43]. It is assumed that these recommendations should help detect cholangiocarcinoma at an early stage. Of note, metastases are present in up to 50% of patients, supporting the fact that regular surveillance is paramount (Fig. 2) [39,44–46].

The diagnosis of cholangiocarcinoma in PSC is difficult because the tumor has often a longitudinal growth with discrete perineural and perivascular invasion [47] so that the tumor is often not directly visible on imaging at an early stage. In this regard, the diagnosis of cholangiocarcinoma is often unexpected and made during pathological analysis of explanted liver in patients treated by orthotopic liver transplantation [31]. For that reason isolated biliary duct dilatation should be always considered as suspect until the diagnosis of cholangiocarcinoma has been eliminated.

Ultrasoundography has a limited role for the diagnosis of cholangiocarcinoma in IBD patients. The role of ultrasonography is restricted to the depiction of gallbladder polyps in those who have PSC so that cholecystectomy can be performed at an early stage (Fig. 1) [31,42].

MDCT has a sensitivity of 82% and a specificity of 80% for the diagnosis of cholangiocarcinoma [48]. Usually MDCT shows uni- or bilateral intrahepatic bile duct dilatation (Figs. 2 and 3). The tumor itself is well depicted when its presents as a mass-forming cholangiocarcinoma, either intrahepatic or hilar. Cholangiocarcinoma presenting as a stenosis are more difficult to depict because of the underlying PSC. Multiplanar reformatted MDCT images help better localize and delineate small cholangiocarcinoma (Fig. 3). In advanced stage tumors, MDCT may be superior to MR imaging because it better shows abnormal lymph nodes and hepatic parenchymal involvement [45,48,49]. In addition, MDCT is more accurate than MR imaging for the depiction of vascular encasement [50].

MR imaging has a sensitivity of virtually 100% for the detection of mass-forming cholangiocarcinoma [49,50]. This category of cholangiocarcinoma is usually hyperintense on T2-weighted MR imaging and poorly enhancing after gadolinium based contrast agents (Fig. 4). MR cholangiography is equivalent to endoscopic retrograde cholangiography for the diagnosis of PSC [51–53]. MR imaging obtained with

Figure 2. A 55-year-old man with clinically and endoscopically quiescent ulcerative colitis and primary sclerosing cholangitis who developed cholangiocarcinoma; a: MDCT in the axial plane obtained during the portal phase after intravenous administration of iodinated contrast material shows ill-defined, heterogeneous liver lesions (arrows) with intrahepatic bile duct dilatation (arrowheads); b: MDCT of the pelvis shows homogeneous circumferential thickening of the rectal wall (arrow) with en bloc enhancement consistent with chronic changes due to ulcerative colitis.

Figure 3. A 35-year-old man with ulcerative colitis and primary sclerosing cholangitis who developed cholangiocarcinoma; a: MDCT in the axial plane obtained during the arterial phase after intravenous administration of iodinated contrast material shows mildly enhancing, well delineated mass (arrow) at the biliary confluence with intrahepatic bile duct dilatation (arrowhead); b: one month later, MDCT in the axial plane obtained during the arterial phase after intravenous administration of iodinated contrast material shows slight enlargement of the hilar mass (arrow) with more marked intrahepatic bile duct dilatation (arrowheads); c: MDCT in the coronal plane obtained during the portal phase after intravenous administration of iodinated contrast material shows tumor mass (arrow) responsible for bile duct stricture and upstream bile duct dilatation (arrowhead). After orthotopic liver transplantation, histopathological analysis of explanted liver confirmed cholangiocarcinoma.
intradivascular administration of a gadolinium-chelate in combination with MR cholangiography is considered as the best imaging modality for the depiction of cholangiocarcinoma [31,48,52]. However, because it is sometimes difficult to discriminate between benign and malignant stricture, MR cholangiography alone is not recommended [48,54]. Cholangiocarcinoma is best depicted using a combination of T1-weighted image obtained after intravenous administration of a gadolinium-chelate and T2-weighted images [53,55] (Fig. 4). MR cholangiography shows multifocal structures along with dilatations of the biliary tree [54]. Slightly hyperintense foci of hepatic parenchyma adjacent to biliary ducts on T2-weighted images that are hypointense after intravenous administration of gadolinium-chelate suggest the presence of cholangiocarcinoma [55,56]. Recently, diffusion-weighted MR imaging has been shown to improve lesion detection because of markedly restricted diffusion by comparison with adjacent hepatic parenchyma (Fig. 5) [56]. The EASL and the AASLD guidelines recommend MR cholangiography as the first line imaging examination in patients with suspected PSC [34]. However, endoscopic retrograde cholangiography should still be performed when MR cholangiography is doubtful or inconclusive. This is because endoscopic retrograde cholangiography may depict subtle changes that are not visible on MR cholangiography [55]. In addition, MR imaging can depict gallbladder carcinoma, when present, as hyperintense foci of the gallbladder wall on T2-weighted MR images [57].

18Fluoro-deoxy-glucose (FDG) positron emission tomography (PET) CT helps depict cholangiocarcinoma not seen on conventional imaging in 12% of patients with PSC but yields false-positive findings [58,59]. This technique has a sensitivity of 75% and a specificity of 95% [58,59]. However, the role of 18FDG-PET-CT is of limited value because when the tumor is depicted with this technique, it is often beyond the reach of curative treatment [58].

Best results for the diagnosis of cholangiocarcinoma in patients with PSC are obtained with a combination of CA19-9 serum measurement, MR cholangiography, biliary brush cytology and 18FDG-PET-CT [59]. For specific cases, cholangioscopy and intrabiliary ultrasonography can provide additional information by comparison with endoscopic cholangiography alone [60].

Hepatocellular carcinoma

Incidence, prevalence and risk factors

To date, less than 20 cases of hepatocellular carcinoma (HCC) in IBD patients have been reported so that the association between IBD and HCC is not clearly established [22,61–69]. All of them were observed in CD patients and only two cases were found in association with PSC [68,69]. The risk of HCC in patient with PSC is very low [70]. Marginally, one UC patient was reported with a mix tumor (i.e., hepatoccholangiocarcinoma) [71]. By contrast, four cases of the fibrolamellar variant of HCC have been reported and all were found in UC patients [22,72]. Snook et al. have reported one case of well-documented fibrolamellar variant of HCC in one patient with UC and PSC [22].

Prolonged treatment by azathioprine has been advocated as a risk factor for the development of HCC because the majority of patients were receiving this treatment at the time HCC was diagnosed or because they had received azathioprine before [21,62–64,66–69]. However, HCC may develop in patients who did not receive azathioprine [61]. It is acknowledged that the small number of reported cases does not allow drawing firm conclusions and the association may be only fortuitous. Of interest, a majority of HCCs were observed in the absence of any risk factor for the development of this tumor, including the absence of chronic diffuse liver disease [61,65] and only a few developed in the presence of an underlying chronic diffuse disease [68,69].

Molecular features

All but one cases of HCC occurred in CD patients who were receiving azathioprine [61]. It may be thus possible that azathioprine may cause direct toxicity and mutagenic effects and favor the occurrence of HCC. However, the actual role of azathioprine remains debated and other mechanisms, such as focal hepatic glycogenosis, may favor the development of HCC in CD patients [65,66]. In this regard, the association of azathioprine and focal hepatic glycogenosis has been reported in four CD patients with HCC in the absence of cirrhosis or PSC [65,66].

Clinical and histological features

All CD patients with HCC were negative for viral hepatitis test or liver cirrhosis. Only two HCCs developed in CD patients with CD and PSC [68,69]. CD patients with HCC are younger (mean age: 35 years) than the standard population with HCC [21,61]. The majority of HCC were found in patients with quiescent CD that mostly involved the colon.
HCC developed approximately 15.1 years after the onset of CD (range: 6–36 years) [21,65,66].

HCC in IBD patients have a variable histopathological presentation, ranging from well-differentiated tumors with trabecular pattern [61,65] to poorly differentiated HCC with pleomorphic cellular changes [21,64,67]. Some of them were found adjacent to focal hepatocyte glycogenosis [21,67]. The fibrolamellar variant is exceedingly rare [22].

There is no well-defined treatment because of the rarity of the disease. Several options are available, including partial hepatic resection [21,64,65], orthotopic liver transplantation [22], chemoembolization for advanced disease [61] of systemic chemotherapy alone for advanced stages [68].

Imaging findings

On imaging, HCC in IBD patients may present as a single, small, encapsulated hypervascular nodule during the arterial phase of enhancement on MDCT and MR imaging with a typical “wash-out” on the following phases similar to the findings observed in the more common cirrhosis-related HCC (Fig. 6) [61,73–75]. HCC presenting as a single nodule has a diameter ranging from 2.3 to 8 cm and are uniformly located in the right liver [21,67]. A peripheral rim of enhancement has been described in one patient (Fig. 6) [67]. Some authors have reported predominantly necrotic HCC [66]. On MR imaging, the tumor is hyperintense on T2-weighted MR images (Fig. 6) [67]. Rarely, the tumor can be bifocal or may present as multiple nodules of various size and variable degrees of enhancement [61,62,64]. Portal invasion by tumor has been reported in one patient [64]. There is no evidence of underlying liver cirrhosis or PSC on imaging in the majority of cases [21,65].

The imaging features of the fibrolamellar variant of HCC in IBD patient have been reported only once [22]. The authors made a brief description of CT findings and indicated that the tumor that developed in a UC patient presented as an irregular and mildly enhancing centrohepatic mass with multiple accompanying satellite malignant nodules [22].

This presentation is different from the typical findings of this specific tumor (Fig. 7) [76].

Hematological malignancies

Incidence, prevalence and risk factors

Hematological malignancies in IBD patients consist predominantly of non-Hodgkin lymphoma but Hodgkin lymphoma and chronic leukemia have been reported as well [18,19]. Although lymphomas in IBD patients can involve the gastrointestinal tract [77–79] they can also be extra-intestinal [18,19,80–83]. Extra-intestinal lymphoma in IBD patients can be observed UC and CD patients [79]. In CD patients, there is an increased risk for Hodgkin and non-Hodgkin lymphoma, with a standardized incidence rate of 1.42 (95%CI: 1.16–1.73) [19]. In UC patients there is an increased risk for chronic leukemia, with a standardized incidence rate of 2.0 (95%CI: 1.31–3.06) [10].

The risk of lymphoma or acute myeloid leukemia in IBD patients is increased by the use of azathioprine or other purines with an increased risk 3 to 5-fold-higher than in the general population [18,84–86].

It is also very likely that tumor necrosis factor inhibitors may increase the risk of lymphoproliferative disorders in IBD patients [87–89]. There are some studies that suggest an association between Epstein-Barr virus (EBV) infection and hepatosplenic T-cell lymphoma in IBD patients receiving an association of TNF-alpha inhibitors and thiopurine [85,86,90–92].

The association between CD and myeloproliferative disorders has been reported in several case reports [93] and in a cohort study [94] but there is no clearly demonstrated increased risk for IBD patients.

Pathogenesis

It is currently difficult to individualize a specific causative condition for hematological malignancies. Inflammation, immune activation, azathioprine, EBV infection may be
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Figure 6. A 45-year-old man with ulcerative colitis who developed hepatocellular carcinoma in the absence of underlying hepatic disease. a: three-dimensional T1-weighted MR image (3D VIBE; repetition time/echo time = 5.4 ms/1.8 ms; flip angle, 10°) obtained during the arterial phase after intravenous administration of gadoterate meglumine (Dotarem®, Guerbet, Roissy-Charles de Gaulle, France) shows hyperenhancing focal liver lesion (arrow); b: during the portal phase, the lesion shows peripheral rim of enhancement (arrowheads); c: during the late phase, the lesion (arrow) becomes hypointense relative to the adjacent hepatic parenchyma; d: diffusion-weighted MR image (single-shot echo-planar imaging, TR/TE = 3900/91 ms; b = 800 s/mm²) in the axial plane shows hyperintense focal liver lesion with restricted diffusion consistent with malignant lesion. Histopathological analysis revealed well-differentiated hepatocellular carcinoma.

Figure 7. A 32-year-old man with Crohn disease who developed fibrolamellar hepatocellular carcinoma; a: MDCT in the axial plane obtained during the arterial phase after intravenous administration of iodinated contrast material shows large, heterogeneously enhancing mass (arrows) located in the left liver; b: MDCT in the axial plane obtained during the portal phase shows incomplete enhancement of the liver mass (arrows); c: after left hepatectomy, gross examination shows suggestive central scar (arrowheads). The tumor was further confirmed as fibrolamellar hepatocellular carcinoma.

responsible for an increased risk [18,95]. EBV infection may have an intermediate role between immunosuppressive treatment and lymphoma [18]. It has also been suggested that Helicobacter pylori may play a role in the development of lymphoma [18].

Clinical and histological features

The clinical presentation of IBD-related lymphoproliferative disorders do not differ from that of patients without IBD [18].
Regarding lymphoma, three main types have been reported in association with azathioprine treatments. They consist of EBV-related post-transplant like lymphoma, hepatosplenic T-cell lymphoma and post-mononucleosis lymphoproliferation [18,89]. Azathioprine has been particularly implicated in IBD-associated lymphoproliferative disorders risk. Along with immunosuppressive effect, it is assumed that azathioprines may have specific pro-carcinogenic effects. It has been suggested that azathioprine may promote clonal expansion of rare mismatch repair-defective myeloid cells, thus possibly playing a role in the development of some hematological malignancies [17].

IBD patients presenting with mesenteric masses have often a diffuse large B-cell type lymphoma that is more related to EBV virus [18].

Clinical implications

To date, there is no specific test for an early diagnosis of hematological malignancies in IBD patients [18]. Thiopurines should be avoided in young men who are seronegative for EBV [17,18]. Similarly, it is recommended to avoid the association of TNF-alpha inhibitors and thiopurine for more than two years in young men [18].

Imaging findings

No specific imaging findings have been reported for extra-intestinal lymphoproliferative disorders in IBD patients so far. On imaging, lymphoma in IBD patients has the same presentation than that of lymphoma in patients without IBD. Lymphomas can be mesenteric [83], pulmonary [81,96] and hepatosplenic [85,91,97,98]. Percutaneous biopsy is recommended to make a definite diagnosis [96,99].

Extra-intestinal lymphomas usually present as multiple enlarged lymph nodes, mainly in the mesentry (Fig. 8) [100–102] but more rarely they can present as a single enlarged lymph node [83]. On MDCT, enlarged lymph nodes are usually homogeneous and may encape mesenteric vessels [100–102]. On MR imaging, mesenteric masses due to lymphoma are hypointense relative to fat and slightly hyperintense relative to muscle on T1-weighted MR images but isointense or hypointense relative to fat and hyperintense relative to muscle on T2-weighted MR images (Fig. 8) [100,101]. Radiologists should therefore give special attention to enlarged mesenteric lymph nodes in young IBD patients treated with immunosuppressive therapies and warn clinicians of a potential development of an underlying lymphoproliferative disease. Other locations such as the thorax have been reported [81,96]. Thoracic Hodgkin lymphomas in CD patient may present as a single, round, spiculated intrapulmonary nodule on CT [81]. However, Rodriguez et al. have reported one case of thoracic Hodgkin lymphoma presenting as a large (15 × 9 × 9 cm), mediastinal mass that encased the left pulmonary artery [96].

Extra-intestinal lymphoma may also present as hepatic and or splenic nodules, which are predominantly hypoechogenic on ultrasonography [103]. On MR imaging they present as focal hepatic lesions of various dimensions (from 5 mm to 15 cm), which usually have a low signal intensity on T1-weighted MR images and variable signal intensity on T2-weighted MR images [104,105]. A mild rim of enhancement after intravenous administration of gadolinium-chelate is observed in 60% of lesions [105].

Marginally, Winnicki et al. have reported one case of Hodgkin lymphoma that presented as a large vulvar and perineal mass in a 45-year-old woman with CD [106]. Imaging disclosed a large mass (20 × 20 cm) involving the labia majora and the perineum in association with multiple lymph nodes and liver involvement [106].

18FDG-PET-CT has a well-established role in the assessment of diffuse large B-cell and Hodgkin lymphomas [107,108]. It is currently recommended as part of the initial assessment of the disease [107,108].

Miscellaneous malignancies

Skin cancers

The incidence of non-melanoma skin cancer is greater in IBD patients by comparison with patients without IBD (incidence rate ratio: 1.64; 95% CI: 1.51–1.78) [109–111]. The risk is greater for those receiving thiopurines [109,110]. The most common cutaneous malignancies in IBD patients include squamous cell carcinoma and basal cell skin cancer, whereas melanoma is less frequent. The risk for squamous cell carcinoma is greater for CD patients, with a SIR of 2.35 (95% CI: 1.43–3.86) than for UC patients with a SIR of 1.68 (95% CI: 0.90–3.12) [10]. Conversely, the risk for melanoma is slightly less marked for CD patients, with a SIR of 1.35 (95% CI: 0.65–2.82) than for UC patients with a SIR of 1.56 (95% CI: 0.80–3.05) [10].

Thiopurines (including 6-mercaptopurine and azathioprine) are associated with an increased photosensitivity to ultraviolet A light [110]. The risk of skin cancer persists even after discontinuation of the thiopurines, possibly because the damage resulting from the increased ultraviolet light sensitivity has already occurred and cannot be reversed [111]. Use of anti-tumor necrosis factor therapy is also associated with a slightly increased risk of melanoma, but there are no data to determine whether duration of use affects this risk [110]. In addition, the mechanism underlying the increased risk of melanoma requires further study [110].

Imaging, including MDCT at the time of initial diagnosis of T1b–T3b melanoma, clinically N0, M0 melanoma has of low yield with a high false-positive rate, and does not lead to upstaging or change in initial surgical management [112]. It is suggested that imaging of asymptomatic patients at the time of diagnosis may not be warranted [112].

On MR imaging, liver metastases from melanoma are hyperintense on T1-weighted MR images because of melanin content and hypervascular on the early phase after intravenous administration of a gadolinium-chelate [113]. For the initial evaluation, MR imaging has a sensitivity of up to 100% for the detection of hepatic metastases from melanoma on a per lesion basis, which is greater than that of 18FDG-PET-CT, which is 47% [113]. The limitation of 18FDG-PET-CT is the difficulty to depict small metastases [113].

18FDG-PET-CT is not recommended for the initial staging of stage I and stage II melanoma [114] but is recommended in stage III and stage IV [115].
Cervical dysplasia and cervical malignancies

Immunosuppression results in a higher incidence of cervical dysplasia compared with healthy control females [116]. The incidence of abnormal Papanicolaou smear in IBD woman is 42.5% vs. 7% in controls (P < 0.001) [116]. Women with IBD are more likely to have higher-grade lesions than controls (P < 0.001) [116]. In addition, IBD women who had received immunosuppressive treatment are more likely to have an abnormal Papanicolaou smear (P < 0.001) than controls [10].

The risk of cervical cancer in IBD women is 1.15 (95%CI: 0.58–2.29) with no difference between CD and UC women [10].

It is now well admitted that the follow-up of IBD should follow the American College of Obstetrics and Gynecology screening guidelines for immunocompromised individuals [18]. Human papillomavirus vaccine should be performed in all IBD women between 9 and 26 years before starting sexual activity [18].

No specific imaging features have been reported for cervical cancers in IBD women [117]. MR imaging is currently the imaging modality of choice for the initial staging of cervical cancer [118].

Conclusion

Extra-intestinal malignancies in IBD patients are not exceptional. Intrahepatic malignancies such as cholangiocarcinoma and hepatocellular carcinoma are often diagnosed at an advanced stage, resulting in only palliative treatment in a substantial number of patients. Radiologists who at the front line in the investigation of IBD patients must keep in mind that IBD may be associated with extra-intestinal malignancies, especially in IBD patients with PSC and those who have longstanding immunosuppressive therapies, which are likely to favor carcinogenesis. A better knowledge of these specific imaging features should help detect extra-intestinal malignancies at an early stage, thus presumably improving patient prognosis.
Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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