MALT lymphoma of the colon: a clinicopathological review

Norris Hollie,[1] Saja Asakrah [2]

[1]Pathology, Beth Israel Lahey Health, Boston, Massachusetts, USA
[2]Department of Pathology and Laboratory Medicine, Emory University, Atlanta, Georgia

Correspondence to
Dr Saja Asakrah, Emory University, Atlanta 30322-1007, Georgia; saja.asakrah@emory.edu

Received 16 December 2019
Revised 6 January 2020
Accepted 7 January 2020
Published Online First 7 February 2020

ABSTRACT

Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) occurs in approximately 9% of non-Hodgkin B cell lymphoma. However, it occurs only rarely within the colon. The presentation is often asymptomatic, and can have multiple endoscopic appearances, including a single or multinodular polypoid lesion. Furthermore, small biopsies can make histological evaluation challenging. The 2016 WHO classification update includes many molecular features of entities and expands the differential diagnosis of lymphoid lesions of the colon. In addition to immunohistochemistry, molecular methods may be tempting to use for small difficult cases. Furthermore, treatment approaches are varied for this entity, and not well studied. Therefore, an updated review on MALT lymphoma of the colon is needed.

INTRODUCTION

Since being first described by Isaacson in the early 1980s,[1] extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) has been recognised as the third most common non-Hodgkin B cell lymphoma accounting for approximately 9% of cases.[2 3] Though they have a particular predilection to the gastrointestinal (GI) tract, MALT lymphoma of the colon and rectum is the least common GI location.[4 5] Primary colonic lymphoma is rare; however, MALT lymphoma is the second-most occurring non-Hodgkin's lymphoma behind large cell lymphomas.[5]

The pathogenesis of colorectal MALT lymphoma is still not clearly elucidated and does not have evident ties with known MALT lymphoma risk factors such as chronic inflammatory diseases and *Helicobacter pylori*. Histologically, MALT lymphoma is a lowgrade B cell lymphoma lacking pathognomonic morphological and immunophenotypic features. Therefore, distinguishing MALT lymphoma from reactive lymphoid aggregates and low-grade lymphoid mimics can be challenging in small biopsies and in the absence of other ancillary studies.[5 6] In this article, we review the clinical presentation, endoscopic features, histopathology, molecular genetics and management approaches of primary colon MALT lymphoma.

CLINICAL FEATURES

MALT lymphoma of the colon primarily affects individuals in the fifth through seventh decades, though younger presentation may rarely be seen.[7–9] Gender predisposition is from represented equally to a slight female preference.[7 9 10]

Clinically, MALT lymphoma in the colon is often asymptomatic and found on screening colonoscopy.[7 9] However, it can present with abdominal or epigastric pain, weight loss, diarrhoea, constipation, mucoid stool or haematochezia.[7 10] Rarely MALT lymphoma can present as a palpable mass.[7] From a laboratory perspective, mild anaemia and positive stool occult blood in stool are not uncommon.[3 7 10 11] Colonic MALT lymphoma frequently presents without B symptoms and without elevated lactate dehydrogenase (LDH). Congruent with the lack of prominent symptoms or signs, MALT lymphomas are typically low clinical stage (I-II) when discovered, and bone marrow involvement is rare.[7 9 11]

Unknown regional factors may potentially play a role in this lesion. A retrospective study in Canada over a period of 10 years (1999–2009) and including a population of 1.3 million people found only six instances of colon-located MALT lymphomas.[5] Another retrospective study in Spain covering 23 years identified two cases.[12] However, Korean study identified 51 cases in only a 14-year timespan.[9] Exact risk factors are incompletely characterised. One study proposed immunodeficiency as a risk factor (HIV, steroids) in primary colonic lymphoma in general in a small mixed study group that included large cell (n=2) and small non-cleaved cell lymphomas (n=5).[13]

ENDOSCOPIC/COLONOSCOPIC FINDINGS

Colonic MALT lymphoma can have varied appearance endoscopically. The lesions may be single or multiple.[7 14 15] They can be flat, elevated, polypoid or semipedunculated, with a surface that can be smooth, granular or nodular. Ulceration can sometimes be present but is rare compared with gastric MALT lymphoma which is frequently associated with erosion and ulceration. The size can be up to 4–5 cm in a single lesion or multiple centimetre or subcentimetre nodules or polyps.[8 10 16 17] Case reports and series have described redness, angioectasia, irregular vascular patterns and loss of vascularity. Narrow band imaging may reveal a branch-like capillary pattern in patches.[7 10 11]

Within the GI tract, the colon is the least common site of MALT lymphoma, however, the location of lesions ranges from the cecum to rectum.[4 8 17] Within the colorectal tissue, the cecum and rectum occur more often than lesions in the ascending, transverse, descending and sigmoid colon.[7 9] Tumours have also been described as being found in multiple sites within the colorectal.[16 17]

To cite: Hollie N, Asakrah S. *J Clin Pathol* 2020;**73**:378–383.

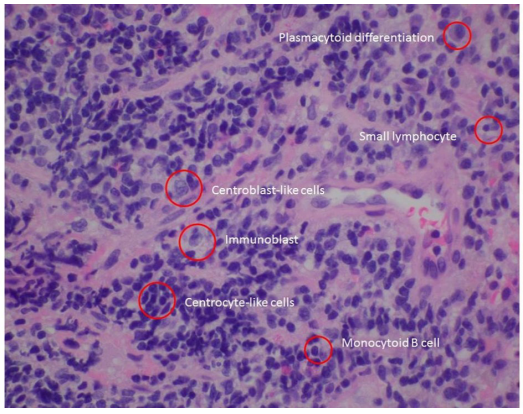

Figure 1 MALT lymphoma has a polymorphous lymphoid infiltrate that can include small lymphocytes, monocytoid B cells, centrocyte-like cells and cells with plasmacytoid differentiation. Scattered immunoblasts and centroblast-like cells may also be seen. MALT, mucosa-associated lymphoid tissue.

HISTOLOGY AND ANCILLARY STUDIES

The revised 2016 WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues describes MALT lymphoma as comprised primarily of monocytoid B cells, centrocyte-like cells and small lymphocytes. However, plasmacytoid differentiation, scattered immunoblasts and transformed centroblast-like cells may also be seen (figure 1). In many cases, a lymphoepithelial lesion of >3 monocytoid lymphocytes in the epithelium with distortion or destruction of glands is also seen.[2 6] Tumour cells may invade nearby reactive germinal centres.[2 6] Though WHO does not directly address histological findings specific to the colon, others have described that this atypical cell population may form diffuse sheets within the colonic mucosa or submucosa, or even extend to the muscularis propria[6 16] (figure 2).

One should be careful avoid mistaking scattered, larger, transformed cells for tingible-body macrophages within nearby germinal centres. The MALT lymphoma primarily consists of small to medium cells, and sheets of large cells should be absent. If sheeting is present, a diffuse large cell lymphoma should be considered.[2] Additional morphological mimics are discussed in the Differential diagnosis section.

Immunophenotypically, MALT lymphoma, including those in the colon, coexpress the B cell markers CD19, CD20 and

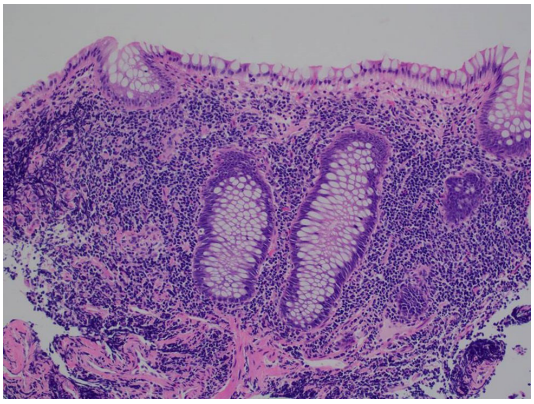

Figure 2 MALT lymphoma. A prominent lymphoid infiltrate is seen that distorts the crypts, and can involve the mucosa and/or submucosa. Lymphoepithelial lesions are a nonspecific, but frequent finding. MALT, mucosa-associated lymphoid tissue.

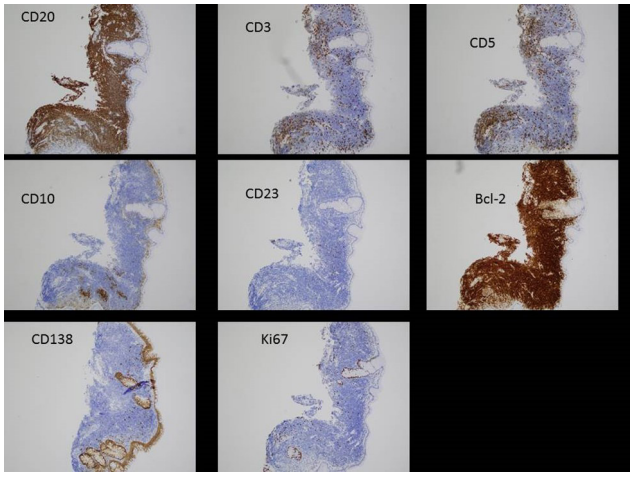

Figure 3 Immunohistochemical profile of typical MALT lymphoma. MALT lymphoma is positive for CD20, but negative for CD5 and CD10. CD3 is negative in addition. CD23 staining demonstrates a lack of follicular architecture. Bcl-2 is usually positive, and CD138 is mostly negative. The Ki-67 proliferation index is typically low. MALT, mucosa-associated lymphoid tissue.

CD79a, but are typically negative for CD5 and CD10, though rare cases may show CD5 reactivity.[7 16 18] CD43 may aid in diagnosis when it is positive, but is variable. Bcl-2 and Bcl-6 expression can be variable, but Bcl-1 is negative. MALT lymphomas are negative for the T cell markers CD3 and CD23.[16 18] The Ki-67 proliferation rate may vary, but can be low[7 18] (figure 3).

A small number of studies have described Bcl-10 expression in MALT lymphomas, with moderate to strong nuclear staining seen in lesions with t(11;18) and t(1;14) rearrangements, which occur more frequently in GI lesions than non-GI lesions. These GI MALT lymphomas are also associated with weak to negative MALT1 expression.[19 20] These immunohistochemical profiles are in contrast to t(14;18) MALT lymphomas, which are not frequent within the GI tract, but have strong cytoplasmic expression for both Bcl-10 and MALT1.[19] Bcl-10 reactivity in colon MALT lymphomas specifically are less studied in the English literature (article in Chinese).[21] MALT lymphomas that lack translocations show moderate and weak cytoplasmic expression of Bcl-10 and MALT1, respectively (table 1).[19]

PATHOGENESIS AND MOLECULAR GENETIC FEATURES

MALT lymphomas can display recurrent cytogenetic abnormalities. These include t(1;14)(p22;q32), t(11;18)(q21;q21) and t(14;18)(q32;q21) translocations that affect the nuclear factor kappa-light-chain-enhancer of activated B-cells (NF-kB)pathway and trisomies of chromosomes 3 and 18.[2 22] Within the intestine, however, the most common findings are +3 (75%), t(11;18)

Table 1 Bcl10 and MALT1 immunoreactivity in MALT Lymphoma*

Case	Bcl-10	MALT1
Reactive tonsil follicle	Cytoplasmic (high/mod)	Cytoplasmic (high/mod)
t(1;14) MALT lymphoma	Nuclear (strong)	Cytoplasmic (weak)
t(11;18) MALT lymphoma	Nuclear (mod)	Negative
t(14;18) MALT lymphoma	Cytoplasmic (strong)	Cytoplasmic (strong)
No translocation MALT lymphoma	Cytoplasmic (mod)	Cytoplasmic (weak)

*Adapted from Ye *et al*.[19]
MALT, mucosa-associated lymphoid tissue.

(12%–56%), +18 (25%), and t(1;14) (0%–13%); moreover, cytogenetically normal cases are also frequently seen.[2 19 23] The t(11;18) translocation is not region-specific and can be seen in samples from patients in North America, Europe and Asia.[24] Cases of gastric MALT lymphoma with t(11;18) and t(1;14) are enriched in cases that did not respond to *H. pylori* eradication[20 25]; however, it is unclear whether the same effect is seen in colon-based lesions.[26]

The t(11;18)(q21;q21) translocation creates a fusion gene of apoptosis inhibitor 2 (also named BIRC2) on chromosome 11 and MALT lymphoma-associated translocation 1 (MALT1) on chromosome 18. The BIR domain of the fusion protein mediates self-oligomerisation.[22] The t(1;14)(p22;q32) translocation moves the BCL10 gene on chromosome 1 behind the immunoglobulin heavy chain (IGH) enhancer on chromosome 14. Increased BCL10 is then thought to form oligomers via its CARD domain and trigger MALT1 oligomerisation.[22] The downstream effect of both translocations is oligomerised MALT1, which promotes the degradation of IkB leading to release of NF-kB. Free NF-kB then goes to the nucleus and promotes proliferation and survival.[22] A study in isolated human colonic epithelial cells suggests that NF-kB can additionally in turn increase expression of BCL10 leading to NF-kB-BCL10 transcriptional loop.[27] However, a pathogenic summary of MALT lymphomas that lack translocations and contain only trisomies or normal karyotype has not been fully detailed.

Testing colonic MALT lymphomas for clonality via Immunoglobulin heavy chain gene (IGH)rearrangement is, somewhat counterintuitively, not a very sensitive diagnostic approach. One study, using fluorescent in situ hybridisation (FISH), was able to identify IGH rearrangement in only 50% intestinal MALT lymphoma (n=14) cases.[4] Another investigation using PCR could identify clones in only approximately 70% of cases using combined IGH,Immunoglobulin light chain kappa (IGK) and Immunoglobulin light chain Lambda (IGL)primers.[28] An additional study was able to increase the sensitivity by using primer sets for partially rearranged IGH along with IGK and IGL, however, the expanded primer sets were considered too expansive for clinical utility.[29] Furthermore, caution should be taken in using PCR because false positive results may be seen in reactive hyperplasia to infectious agents such as *H. pylori* in chronic active gastritis.[6]

More expansive molecular genetic testing, such as next generation sequencing, is not necessary for the diagnosis of colonic MALT lymphoma, as the results are not specific. Allowing for this limitation, however, mutations can be found in colon MALT lymphoma. P53 and Ataxia Telangiecstasia mutated gene (ATM) deletions were identified by FISH in 28% and 14% of intestinal MALT lymphoma in a small series (n=14).[4] Other infrequent findings seen with next-generation sequencing include mutations in TNFAIP3 and MYD88 L265P, which can also be seen in other B cell neoplasms.[2]

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of expanded lymphocyte populations in the colon can be challenging. Morphologically, a variety of other lesions are composed of small lymphocytes that may invade the epithelium or expand the lamina propria. A number of these also share the CD5 and CD10 negative expression profile of MALT lymphoma. Most, however, may be distinguished based on careful histological examination, further immunophenotype, and with limited additional cytogenetic findings. The differential includes follicular lymphoma, lymphoplasmacytic lymphoma (LPL), mantle cell lymphoma, large cell lymphomas, intestinal T cell lymphomas, inflammatory lesions including syphilitic colitis and benign reactive hypertrophy.

Follicular lymphomas within the GI tract canonically occur in the small intestine either primarily or secondarily after systemic disease.[5 30] Primary duodenal-type follicular lymphoma, like MALT lymphoma, is often found incidentally and without significant systemic symptoms. However, it presents as multiple small polyps, polypoid lesions or white spots on endoscopy, and is typically located in the duodenum. Only rare (about 20) cases of follicular lymphoma of the colon are described.[30 31] At least seven of these cases were examples of secondary involvement after systemic or duodenal disease. Two cases were also initially called MALT lymphoma on initial biopsy, but reclassified after resection and further immunohistochemical studies. Follicular lymphomas are differentiated from MALT lymphoma by coexpression of CD10 and Bcl2, lack of CD43 and the presence of a t(14;18)(q32;q21)(IGH/BCL2) translocation.[30] Though a t(14;18)(q32;q21)(IGH/MALT1) translocation can be seen in some MALT lymphomas, they are found in non-gastric sites.[19]

LPL is a morphological and immunohistochemical pitfall. Like MALT lymphoma, a polymorphous infiltrate of small lymphocytes, including some with plasma cell differentiation, is seen. LPL is also negative for CD5 and CD10. LPL plasma cells often express CD19. Molecular testing for mutations in MYD88 L265P can be helpful, and is a characteristic finding in LPL. However, a small percentage (~6%–9%) of MALT lymphomas also harbours this mutation.[2] Other mutations common to LPL are in CXCR4, CD79B and ARID1A.[2] Location is a key dividing characteristic with MALT lymphoma, as LPL typically is located in bone marrow and lymph nodes, with only very rare occurrence in the GI tract.[21] Further complicating matters, both lymphomas may also present with IgM paraproteins.[32] In a series of 44 Waldenstrom's macroglobulinaemia involving extramedullary sites, the colon was involved in one case, while four cases were called MALT lymphoma, showing how distinction may not always be possible.[32]

Mantle cell lymphoma, may arise in the colon, but frequently has multiple lesions, instead of a single lesion. These also typically express CD5 and Bcl1, and have characteristic t(11;14)(q13;q32) CCD1/IGH rearrangement on cytogenetic investigation.[2]

Large B cell lymphomas such as diffuse large B cell lymphoma (DLBCL), when extranodal, frequently occur in the GI tract, and DLBCL is the most common type of colorectal lymphoma.[5 6] Clinical B symptoms and laboratory findings such as increased LDH are more characteristic. Histologically, the cells are large and form sheets and are thus easily distinguished on morphology. By immunophenotype, however, non-GC type DLBCLs will be negative for CD10, and many cases will be negative for CD5. Thus, morphology would guide the diagnosis and workup in these and other medium to large cell (eg, 'double hit lymphoma') lesions. Large cell lymphoma may arise in association with MALT lymphoma, however, and should be excluded during histological examination.[33]

Enteropathy-associated T-cell lymphoma (EATL) canonically occurs in the small intestine (>90%), but may be multifocal and may be seen in the colon. This lesion is associated with celiac disease and refractory celiac disease, and thus, unlike MALT lymphoma, clinical symptoms are often present. Laboratory investigation may also show elevated LDH. The infiltrate in EATL is polymorphous, similar to MALT lymphoma, and include pleomorphic medium to large cells with clear to eosinophilic cytoplasm, with some intraepithelial spread. However, unlike MALT lymphoma, frequent histiocytes and eosinophils may

be seen. The neoplastic cells are negative for CD5 and CD10; however, they are T-cells that express CD3, CD103, cytotoxic cytoplasmic markers, and CD30, but are negative for CD56.[2]

Monomorphic epitheliotropic intestinal T-cell lymphoma typically occurs in the small intestine, but may be seen in the colon (16%), and is composed of medium cells with moderate clear cytoplasm that may morphologically resemble marginal zone cells, and have a prominent intraepithelial component. Though the neoplastic cells are negative for CD5 and CD10, this lesion is composed of CD3-expressing T-cells rather than the B-cells that make up MALT lymphomas. The T-cells also express CD8 and CD56 and have aberrant loss of CD5 expression. Some cases may also aberrantly express CD20.[2]

Inflammatory bowel diseases (IBDs) may also display ulceration or polypoid lesions endoscopically and microscopic lymphoid infiltrates with disrupted architectural features. However, IBD should have additional distinguishing features besides gland destruction or distortion.[34] Ulcerative colitis will likely have active inflammation (crypt abscesses, etc) and epithelial changes of chronic inflammation. Crohn disease may have similar findings, or include granulomas, serositis, as well as fistulas and sinus tracts in a non-continuous fashion.[34] Furthermore, gross evidence of circular bowel wall thickening, irregular ulceration and longitudinal ulceration are additional features that favour an IBD diagnosis over a lymphoid malignancy.[35] Lymphocytic colitis is composed of increased intraepithelial T lymphocytes with reactive changes, may have basement membrane thickening, and can have some lamina propria expansion, but without gland destruction.[34] T-lymphocytes in colitis would also have retention of normal markers CD3 and CD5.

Additionally, syphilitic colitis/proctitis is another reactive condition that morphologically and endoscopically may resemble MALT lymphoma. It can manifest endoscopically as mucosal nodularity with or without ulceration and erosion and histologically show extensive and deep lymphocytic infiltrate with plasma cell differentiation, features that are frequently encountered in MALT lymphoma. These and additional features such as perivascular plasma cells, endothelial swelling, are more specifically found in the submucosa rather than just in the mucosa. When present in the mucosa, the differential also includes IBD. Mucosal active chronic crypt-centric damage and mucosal eosinophils are more limited in syphilitic colitis.[36] Treponema immunostains, as well as clinical history of HIV infection and anal pain, can be very helpful in distinguishing between MALT lymphoma and syphilitic colitis.[36]

Benign reactive lymphoid hyperplasia, such as what can be seen in the rectal 'tonsil' or enlarged ileal Peyer's patch, is composed of lymphoid follicles that may be enlarged, but have retained architecture and well-formed germinal centres. The presence of tingible body macrophages can be helpful in diagnosis.[34] The lymphoid component may be polymorphous, with plasma cells, immunoblasts and/or small lymphocytes, similar to neoplastic lesions.[6] Molecular (PCR or sequencing) tests can be falsely positive in infectious etiologies or falsely negative if the specimen is scant.[4 28] Though, MALT lymphomas may have small clonal lymphocytes that are difficult to distinguish on high power histology, overall architectural features, abnormal immunophenotype and cytogenetic analysis should clench the diagnosis.[6]

MANAGEMENT AND PROGNOSIS

Several case reports, but very few case series have described MALT lymphoma within the colon recently (table 2). Most cases are low stage when discovered.[9 30] A variety of management approaches have been described, from watchful waiting

Table 2 Recent (within 10 years) case series/reviews on colonic malt lymphoma

Study	# patients	Endoscopy	Morphology	Immunophenotype	Staging	Management	Other
Akasaka *et al*[10]	4 (median 57, range 50–64, 4F) Sx: Bleeding per rectum; faecal occult blood, constipation; abdominal pain	>3 cm elevated lesion rectum; polyp (hypoechoic) cecum; 1.8 cm sessile elevated lesion with angiectasia sigmoid; smooth elevated lesion with irregular vascular pattern rectum; Rectum (2), cecum (1), sigmoid (1)	Centrocyte-like cells in mucosa and submucosa (2), mucosa only (2)	Pos: L26 (CD20), CD79a, Bcl-2 Neg:CD5, CD10, Cyclin D1	No LAD on CT (three tested)	Rad;endoscopic resection (2); sigmoid colectomy	No recurrence at 9 mo and 6 years (only f/u for 2)
Kim *et al*[7]	8 (median 60, range 17–72; 6M, 2F) Sx: Palpable mass(1), haematochezia (3), wt loss (2), mucoid stool (1), abd pain (4, for >1.2 cm size), ASx (1)	Polypoid (5), mucosal/submucosal thickening (3), ulcerated (2). 1.2–3 cm. Location: ASCO (2), rectum (4), cecum (1), appy orifice (1), SIGCO (1), ICV (3), TRANSCO (1), multiple (4)	N/A	N/A	IE (4), IIE (1), NA (3)	Surg (2), Chemo (2), Rit (1), ChemoRad (1), SurgChemo (1), endoscopic polypectomy (1), RadHPE (1)	Helicobacter pylori neg (3), NA (5)
Jeon *et al*[9]	51 (21M/30F, median 60, IQR 55–71), Sx: ASx (26), Abd pain (10), stool blood (9), constip/diarr/tenesmus (5), obstruction (1), B Sx (1), elevated LDH (4)	Appearance: subepithelial tumour (26), polyposis (10), epithelial mass (7), ileitis (8); Lesions:single (27), multiple (16);Location: TI (8), CEC (7), ASCO (3), TRANSCO (2), DESCO (2), SIGCO (5), REC (20), mult (4)	N/A	Selected as: Pos: CD19, CD20, CD79a, Bcl-2 Neg: CD3, CD5, CD10, cyclin D1, Bcl-6 Low Ki-67 index	I (37), II (5), IIE (2), IV (7)	EMR (17), Surg (8), Rad (12), Chemo (4), EMR +Rad (4), Surg +Rad (1), Obs (5)	8 EMR cases had positive margins
Fischbach (German, abstract in English)[14]	7 (5M/2F, range 47–75), Sx: ASx (4), fatigue (2), change in bowel habits (2), obstipation (2)	Single (6); Obstructive tumours (2), polyps (3), flat (1), vascular angiectasia (1)	N/A	N/A	N/A	Polypectomy, surg resection, H.pylori eradication Rx, systemic immune chemo	F/u 0–57 months: complete remission (5), unknown (2)

ASCO, ascending colon; ASx, asymptomatic; CEC, cecum; chemo, chemotherapy; DESCO, descending colon; EMR, endomucosal resection; HPE, *H. pylori* eradication; ICV, ileocecal value; LAD, lymphadenopathy; LDH, lactate dehydrogenase; N/A, not available; Neg, negative; Obs, observation; Pos, positive; Rad, radiation; REC, rectum; Rit, rituximab; SIGCO, sigmoid colon; surg, surgery; Sx, symptoms; TRANSCO, transverse colon.

to tactics including local excision via endomucosal resection, surgical resection (partial colectomy), radiotherapy, chemotherapy, immune therapy (rituximab) and antibiotics in varying combinations.[7 10 11 15]

French and American groups have recently addressed management approaches for colorectal non-Hodgkin lymphomas and give some specific attention to MALT lymphoma.[37 38] The French intergroup concluded that there is no consensus, but excision, rituximab, alkylating agent are used, and watchful waiting can be justified. They disparage radiotherapy due to mobility of the gut and associated risk of toxicity.[37] The American study gives no specific recommendations, noting a paucity of data.[38] However, it notes that higher stage lesions can be treated with systemic therapy.[38] Some groups suggested treatment algorithms for colorectal non-Hodgkin lymphomas based on the stage (Paris staging system) and the histological type of the lymphoma.[38]

MALT lymphoma of the colon is a low-grade B-cell neoplasm, and has an excellent prognosis, which probably contributes to a paucity of studies and lack of management consensus. Despite varying management approaches, most studies show patients alive at the end of follow-up periods ranging from 9 months to 6 years.[7 10 11] Recurrence is very rarely described. The most expansive study aimed at colorectal MALT lymphoma, a recent study with 51 cases of colorectal (rectum 39% of cases), described 5-year progression-free survival at 92% and overall survival at 94%.[9] In this series, only one patient died from colorectal MALT lymphoma (peritonitis secondary to perforation during chemotherapy for relapsed MALT lymphoma), resulting in a disease-specific survival of 98% at 5 years.[9] Interestingly, five patients were observed without treatment and the disease did not progress.[9]

CONCLUSIONS

Extranodal marginal zone lymphoma of MALT lymphoma occurs very rarely within the colon. Similar to MALT lymphoma in other locations, the clinical presentation is mild and can often be asymptomatic and discovered incidentally. Though the morphological and immunophenotypic features are similar to MALT lymphoma at other sites, the cytogenetic profile within the colon is somewhat more distinct. Molecular testing on small colonic biopsy samples should be done with caution due to lack of sensitivity and specificity. Treatment approaches are diverse, likely due to the paucity of progression almost regardless of treatment plan. The less common high stage cases may be treated systemically. The overall prognosis for MALT lymphoma of the colon is excellent.

Take home messages

- Extra-nodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) occurs very rarely within the colon.
- Clinical presentation is mild and can often be asymptomatic and discovered incidentally.
- Though the morphological and immunophenotypic features are similar to MALT lymphoma at other sites, the cytogenetic profile within the colon is somewhat more distinct.
- Molecular testing on small colonic biopsy samples should be done with caution.
- Treatment approaches are diverse.
- The less common high stage cases may be treated systemically and the overall prognosis for MALT lymphoma of the colon is excellent.

Handling editor Runjan Chetty.

Contributors SA (primary haematopathologist): evaluated the histopathology of the selected imaged cases, conducted immunophenotypic workup, and helped in supervising, writing and editing the review. NH (pathologist): gathered all the clinicopathologic information and took photomicrographs. He wrote the primary draft of the manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; internally peer reviewed.

ORCID iD

Saja Asakrah http://orcid.org/0000-0002-0037-2707

REFERENCES

1 Isaacson PG. Gastrointestinal lymphomas of T- and B-cell types. *Mod Pathol* 1999;12:151–8.
2 Swerdlow SH, Campo E, Harris NL. *WHO classification of tumours of haematopoietic and lymphoid tissues*. 2. WHO Press, 2017.
3 Zucca E, Conconi A, Pedrinis E, *et al*. Nongastric marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue. *Blood* 2003;101:2489–95.
4 Zhang G-P, Cao P-F, Feng L-J. Detection and clinical significance of genes in primary gastrointestinal malt lymphoma. *Tumour Biol* 2014;35:3223–8.
5 Howell JM, Auer-Grzesiak I, Zhang J, *et al*. Increasing incidence rates, distribution and histological characteristics of primary gastrointestinal non-Hodgkin lymphoma in a North American population. *Can J Gastroenterol* 2012;26:452–6.
6 Burke JS. Lymphoproliferative disorders of the gastrointestinal tract: a review and pragmatic guide to diagnosis. *Arch Pathol Lab Med* 2011;135:1283–97.
7 Kim MH, Jung JT, Kim EJ, *et al*. A case of mucosa-associated lymphoid tissue lymphoma of the sigmoid colon presenting as a semipedunculated polyp. *Clin Endosc* 2014;47:192–6.
8 Abbas H, Niazi M, Makker J. Mucosa-associated lymphoid tissue (MALT) lymphoma of the colon: a case report and a literature review. *Am J Case Rep* 2017;18:491–7.
9 Jeon MK, So H, Huh J, *et al*. Endoscopic features and clinical outcomes of colorectal mucosa-associated lymphoid tissue lymphoma. *Gastrointest Endosc* 2018;87:529–39.
10 Akasaka R, Chiba T, Dutta AK, *et al*. Colonic mucosa-associated lymphoid tissue lymphoma. *Case Rep Gastroenterol* 2012;6:569–75.
11 Seo S-W, Lee S-H, Lee D-J, *et al*. Colonic mucosa-associated lymphoid tissue lymphoma identified by chromoendoscopy. *World J Gastroenterol* 2014;20:18487–94.
12 Martín Domínguez V, Mendoza J, Díaz Menéndez A, *et al*. Colon lymphomas: an analysis of our experience over the last 23 years. *Rev Esp Enferm Dig* 2018;110:762–7.
13 Doolabh N, Anthony T, Simmang C, *et al*. Primary colonic lymphoma. *J Surg Oncol* 2000;74:257–62.
14 Fischbach W. Colorectal MALT lymphoma: a rare clinical entity. *Z Gastroenterol* 2018;56:905–11.
15 Ghimire P, Wu G-Y, Zhu L. Primary gastrointestinal lymphoma. *World J Gastroenterol* 2011;17:697–707.
16 Hasegawa N, Kato K, Yamada K, *et al*. Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT) of the sigmoid colon. *Gastrointest Endosc* 2000;52:802–4.
17 Esteban JM, Gutiérrez del Olmo A, Baki W, *et al*. Colonic mucosa-associated lymphoid tissue lymphoma presenting as multiple polyposis. *Gastrointest Endosc* 2005;61:928–30.
18 Chen P-H, Lin Y-M, Yen H-H, Lin Y–M, Yen H–H. Primary mucosa-associated lymphoid tissue lymphoma of the colon. *Clin Gastroenterol Hepatol* 2011;9:e74–5.
19 Ye H, Gong L, Liu H, *et al*. MALT lymphoma with t(14;18)(q32;q21)/IGH-MALT1 is characterized by strong cytoplasmic MALT1 and BCL10 expression. *J Pathol* 2005;205:293–301.
20 Ye H, Gong L, Liu H, *et al*. Strong BCL10 nuclear expression identifies gastric MALT lymphomas that do not respond to H pylori eradication. *Gut* 2006;55:137–8.
21 He S, Guo Y, Bei C-F, *et al*. [Gastrointestinal B-cell lymphoma: a morphologic and immunohistochemical study of 194 cases]. *Zhonghua Bing Li Xue Za Zhi* 2010;39:814–8.
22 Troppan K, Wenzl K, Neumeister P, *et al*. Molecular pathogenesis of MALT lymphoma. *Gastroenterol Res Pract* 2015;2015:1–10.
23 Streubel B, Simonitsch-Klupp I, Müllauer L, *et al*. Variable frequencies of MALT lymphoma-associated genetic aberrations in malt lymphomas of different sites. *Leukemia* 2004;18:1722–6.
24 Remstein ED, Dogan A, Einerson RR, *et al*. The incidence and anatomic site specificity of chromosomal translocations in primary extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) in North America. *Am J Surg Pathol* 2006;30:1546–53.

25 Liu H, Ruskon-Fourmestraux A, Lavergne-Slove A, *et al*. Resistance of t(11;18) positive gastric mucosa-associated lymphoid tissue lymphoma to Helicobacter pylori eradication therapy. *Lancet* 2001;357:39–40.
26 Grünberger B, Wöhrer S, Streubel B, *et al*. Antibiotic treatment is not effective in patients infected with *Helicobacter pylori* suffering from extragastric malt lymphoma. *J Clin Oncol* 2006;24:1370–5.
27 Borthakur A, Bhattacharyya S, Anbazhagan AN, *et al*. Prolongation of carrageenan-induced inflammation in human colonic epithelial cells by activation of an NFκB-BCL10 loop. *Biochim Biophys Acta* 2012;1822:1300–7.
28 Zhang J-F, Zhang S-X, Li J. [Molecular Pathological Diagnosis of Mucosa-associated Lymphoid Tissue Lymphoma]. *Zhongguo Shi Yan Xue Ye Xue Za Zhi* 2015;23:689–92.
29 Lu C, He Q, Zhu W, *et al*. The value of detecting immunoglobulin gene rearrangements in the diagnosis of B-cell lymphoma. *Oncotarget* 2017;8:77009–19.
30 Iwamuro M, Kondo E, Takata K, *et al*. Diagnosis of follicular lymphoma of the gastrointestinal tract: a better initial diagnostic workup. *World J Gastroenterol* 2016;22:1674–83.
31 Iwamuro M, Okada H, Takata K, *et al*. Colorectal manifestation of follicular lymphoma. *Intern Med* 2016;55:1–8.
32 Lin P, Bueso-Ramos C, Wilson CS, *et al*. Waldenstrom macroglobulinemia involving extramedullary sites: morphologic and immunophenotypic findings in 44 patients. *Am J Surg Pathol* 2003;27:1104–13.
33 Katsumata R, Matsumoto H, Motoyasu O, *et al*. Primary colorectal lymphoma comprising both components of diffuse large B-cell lymphoma and mucosa-associated lymphoid tissue lymphoma combined with cytomegalovirus colitis. *Clin J Gastroenterol* 2016;9:59–62.
34 Cardona DM, Layne A, Lagoo AS. Lymphomas of the gastro-intestinal tract - pathophysiology, pathology, and differential diagnosis. *Indian J Pathol Microbiol* 2012;55:1–16.
35 Zhang T-Y, Lin Y, Fan R, *et al*. Potential model for differential diagnosis between Crohn's disease and primary intestinal lymphoma. *World J Gastroenterol* 2016;22:9411–8.
36 Arnold CA, Roth R, Arsenescu R, *et al*. Sexually transmitted infectious colitis vs inflammatory bowel disease: distinguishing features from a case-controlled study. *Am J Clin Pathol* 2015;144:771–81.
37 Matysiak-Budnik T, Fabiani B, Hennequin C, *et al*. Gastrointestinal lymphomas: French intergroup clinical practice recommendations for diagnosis, treatment and follow-up (SNFGE, FFCD, GERCOR, UNICANCER, SFCD, SFED, SFRO, SFH). *Dig Liver Dis* 2018;50:124–31.
38 Gay ND, Chen A, Okada CY. Colorectal lymphoma: a review. *Clin Colon Rectal Surg* 2018;31:309–16.