Histologic Features of Syphilitic Gastritis

A Rare but Resurging Imitator of Common Diseases

Naziheh Assarzadegan, MD,[1] Jiayun M. Fang, MD,[1] Lysandra Voltaggio, MD,[2] Robert H. Riddell MD,[3] Elizabeth A. Montgomery, MD,[4] Oliver G. McDonald, MD,[4] Ryan Coates, MD,[5] Fatima Carneiro, MD,[6] Gregory Y. Lauwers, MD,[7] Michal Kamionek,[8] Laura W. Lamps, MD,[1] and Maria Westerhoff, MD[1]

From the [1]Department of Pathology, University of Michigan, Ann Arbor, MI, USA; [2]Department of Pathology, Johns Hopkins University School of Medicine, Baltimore, MD, USA; [3]Pathology and Laboratory Medicine, Mount Sinai Hospital, University of Toronto, Toronto, Canada; [4]Department of Pathology, University of Miami Miller School of Medicine, Miami, FL, USA; [5]Mountain States Pathology, Colorado Springs, CO, USA; [6]Institute of Molecular Pathology and Immunology of the University of Porto, Faculty of Medicine of the University of Porto, Centro Hospitalar Universitário São João, Porto, Portugal; [7]Department of Pathology, H. Lee Moffitt Cancer Center, Tampa, FL, USA; and [8]Atrium Health University City, Charlotte, NC, USA.

ABSTRACT

Objectives: The range of histopathologic features of gastric syphilis is not well described. Here we describe the clinicopathologic findings of eight patients with syphilitic gastritis.

Methods: A search of our Pathology Data System (2003-2022) and multiple other institutions identified eight patients with syphilitic gastritis. Clinical information, pathology reports, and available slides were reviewed.

Results: Lesions predominated in middle-aged adults (mean age, 47.2 years; range, 23-61 years) with a propensity for men (n = 7). Three patients had a documented history of human immunodeficiency virus. Clinical presentations included weight loss, abdominal pain, hematochezia, fever, dyspepsia, nausea and vomiting, hematemesis, anemia, and early satiety. Endoscopic findings included ulcerations, erosions, abnormal mucosa, and nodularity. All specimens shared an active chronic gastritis pattern with intense lymphohistiocytic infiltrates, variable plasma cells, and gland loss. Prominent lymphoid aggregates were seen in four specimens. The diagnosis was confirmed either by immunostain for *Treponema pallidum* (n = 7) or by direct immunofluorescence staining and real-time polymerase chain reaction (n = 1). All patients with available follow-up data showed resolution of symptoms after antibiotic therapy (n = 4).

Conclusions: Recognition of the histologic pattern of syphilitic gastritis facilitates timely treatment, prevents further transmission, and avoids unnecessarily aggressive treatment.

KEY POINTS

- Syphilis is a great clinical and pathologic imitator of other gastric diseases, including lymphoproliferative disorders, infiltrating carcinomas, and other infectious processes.
- The histologic features of syphilitic gastritis are those of a marked lymphohistiocytic infiltrate with prominent plasma cells, lymphoid aggregates, and only mild to moderate acute inflammation.
- Syphilitic gastritis should be considered in patients at risk for sexually transmitted diseases who have gastric ulcers and in patients in whom *Helicobacter pylori* is not detected.

KEY WORDS

Human immunodeficiency virus (HIV); Syphilis; *Treponema pallidum*; Gastritis; Lymphoma; Men who have sex with men (MSM); Gastric pathology

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Corresponding author: Naziheh Assarzadegan, MD; naziheha@umich.edu.

INTRODUCTION

The incidence of syphilis is on the rise worldwide. The introduction of penicillin and public health measures in the United States led to a decline in syphilis from the mid-1950s until the early 1980s, when syphilis resurged in association with human immunodeficiency virus (HIV). Following historically low case numbers in 2000 and 2001, the incidence of syphilis has risen annually, including a 6.8% increase from 2019 to 2020. Most cases are seen in men, especially men who have sex with men (MSM); however, the incidence of syphilis has also increased substantially in recent years among women, with a 147% increase from 2016 to 2020.[1] This suggests that the heterosexual syphilis epidemic also continues to increase rapidly.[1]

Syphilis (caused by *Treponema pallidum*) is often referred to as a "great imitator" because of its variable and subtle clinical presentations. Gastric syphilis is rare but has been well described since the 18th century.[2] Gastric involvement is reportedly observed in only 1% of patients with syphilis.[3] The endoscopic findings include erosions, ulcers, thickened gastric folds, nodularity, masses, and linitis plastica, all of which can mimic other etiologies, including other infections, carcinoma, and lymphoma. Most pathologists have only limited experience with the histologic features of syphilitic gastritis, and a high index of suspicion is necessary. To increase awareness of syphilitic gastritis, we studied the clinicopathologic features of eight affected patients diagnosed over a period of 19 years. To the best of our knowledge, this represents the largest case series of syphilitic gastritis to date.

MATERIALS AND METHODS

The study protocol was approved by the University of Michigan Institutional Review Boards. The study included eight unique cases of syphilitic gastritis identified by seven pathologists between April 2003 and April 2022. The cases consisted of collected specimens from the consultation service at the University of Michigan (n = 3); Johns Hopkins (n = 1); University of Miami (n = 1); University Hospital of Coimbra, Portugal (n = 1); and University of Toronto, Canada (n = 1). The one case from Portugal was previously published and was provided by two authors included in this study (F.C. and G.Y.L.).[4]

These cases were diagnosed as syphilitic gastritis in the absence of knowledge of laboratory findings, based on recognition of an unusual destructive gastritis pattern with an intense lymphohistiocytic infiltrate, prominent plasma cells, and lymphoid aggregates. All cases were centrally reviewed. Routine stains performed at the time of initial evaluation were examined. Pertinent clinicopathologic features, including demographic information, history of MSM, HIV infection, *Helicobacter pylori* and other infections, clinical presentation, endoscopic appearance, syphilis serology testing, involvement of other parts of the gastrointestinal tract, medication list, pathologic differential diagnoses, clinical course, treatment, and outcome, were documented.

RESULTS

Patient Characteristics and Clinical Presentations

The patients consisted of seven men and one woman between the ages of 23 and 61 years (mean age, 47.2 years). Two patients had a documented history of HIV infection. No MSM history was documented in any of the men. Presenting symptoms and laboratory data included weight loss (n = 3), abdominal pain (n = 2), fever (n = 2), hematochezia (n = 2), elevated liver transaminases (n = 2), dyspepsia (n = 2), nausea and vomiting (n = 1), diarrhea (n = 1), hematemesis (n = 1), anemia (n = 2), early satiety (n = 1), and unknown (n = 1). The demographics and clinical presentations of all eight patients are summarized in TABLE 1.

Gastric Ulcers Are the Most Common Endoscopic Finding in Syphilitic Gastritis

Endoscopic findings were available for seven of our patients. Syphilitic gastritis cases were most commonly described as having ulcerated or eroded gastric mucosa (five of seven patients with available endoscopic reports). One patient had a single large gastric ulcer in the gastric fundus with heaped-up edges and surrounding edema. Another had red, friable erosions in the gastric body. The third patient had a large gastric fundus ulcer and diffuse moderate inflammation characterized by erosions and erythema in the entire examined stomach FIGURE 1. Another patient was found to have multiple, nonhealing ulcers on two endoscopic examinations followed by diffuse gastric mucosal thickening on subsequent endoscopy. The fifth patient with available endoscopy showed gastric nodularity. The sixth patient's endoscopy demonstrated linear erosions with oozing blood and adherent clots. Our seventh patient's endoscopy was reported as abnormal antral mucosa with duodenal scarring. The initial differential diagnosis based on the endoscopic features included lymphoma (n = 4), gastric carcinoma (n = 2), and systemic disease not otherwise specified (n = 2).

Syphilitic Gastritis Has a Destructive Lymphohistiocytic Pattern of Inflammation

Seven of the collected specimens were biopsy samples while one was a resection. In addition to gastric biopsies, one of the patients had a concurrent liver biopsy, another had tandem esophageal and colonic biopsies, and three patients had colon and rectum biopsies. In the patient with gastric resection, prior biopsy specimens were not available for review. The histologic findings are summarized in TABLE 2. FIGURE 2, FIGURE 3, FIGURE 4, FIGURE 5, and FIGURE 6 illustrate the biopsy findings of five biopsy specimens. FIGURE 7 represents the findings in the resection from specimen 6. All biopsy specimens shared a destructive pattern of gastritis characterized by an intense lymphohistiocytic infiltrate, prominent plasma cells, and gland loss. A lymphoma was considered for specimens from three patients based on prominent lymphoid aggregates, and these were evaluated for a hematolymphoid malignancy. Langerhans cell histiocytosis was considered in one patient based on prominent lymphohistiocytic inflammation and focal prominence of eosinophils. Spirochetes were demonstrated by immunohistochemical stain for *T pallidum* in seven biopsy samples and by direct immunofluorescence and polymerase chain reaction

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TABLE 1 Demographic and Clinical Characteristics of Eight Patients With Syphilitic Gastritis

Case No.	Specimens	Age, y	Sex	Clinical Presentation	Endoscopy	HIV Status	MSM	Prior Syphilis Diagnosis and Serology Testing for Syphilis	Medications	Extent of GI Tract Involvement	Other Coinfections
1	Stomach and colon	45	M	Weight loss, diarrhea, hematemesis, hematochezia	Diffuse gastric ulcers	Unknown	Unknown	Unknown	Unknown	Stomach and colon	No
2	Esophagus, stomach, and colon	61	M	Unknown	Unknown	Positive	Unknown	Unknown	Unknown	Esophagus, stomach, and colon	No
3	Stomach and liver	40	M	Fever, abdominal pain, weight loss	Single gastric ulcer in the fundus with heaped edges, surrounding edema	Unknown	Unknown	Unknown	Unknown	Stomach and liver	No
4	Stomach	59	M	Early satiety, dyspepsia, weight loss	Red, friable, superficial ulceration in the gastric body, antrum spared	Unknown	Unknown	Unknown	Unknown	Stomach	No
5	Stomach	55	F	Nausea and vomiting	Nodular gastritis	Unknown	Not applicable	Unknown	Unknown	Stomach	No
6	Stomach	35	M	Dyspepsia	Multiple, nonhealing ulcers and diffuse gastric mucosal thickening	Negative Unknown at the time of diagnosis	Unknown	Unknown	Unknown	Stomach	No
7	Stomach	23	M	Abdominal pain, anemia	"Oozing" linear erosions with adherent clots	Positive	Unknown	Syphilis IgM and IgG +; RPR –	Unknown Noncomplaint with HAART	Stomach Rectum biopsy: – for *Treponema* IHC + for chlamydia and gonorrhea	Yes: *Helicobacter pylori*
8	Stomach	60	M	Anemia	Abnormal antral mucosa with duodenal scarring	Positive	Unknown	Unknown	Bictegravir for HIV	Stomach and colon	Yes: CMV gastritis

CMV, cytomegalovirus; GI, gastrointestinal; HAART, highly active antiretroviral therapy; HIV, human immunodeficiency virus; IgG, immunoglobulin G; IgM, immunoglobulin M; IHC, immunohistochemistry; MSM, men who have sex with men; RPR, rapid plasma reagin.

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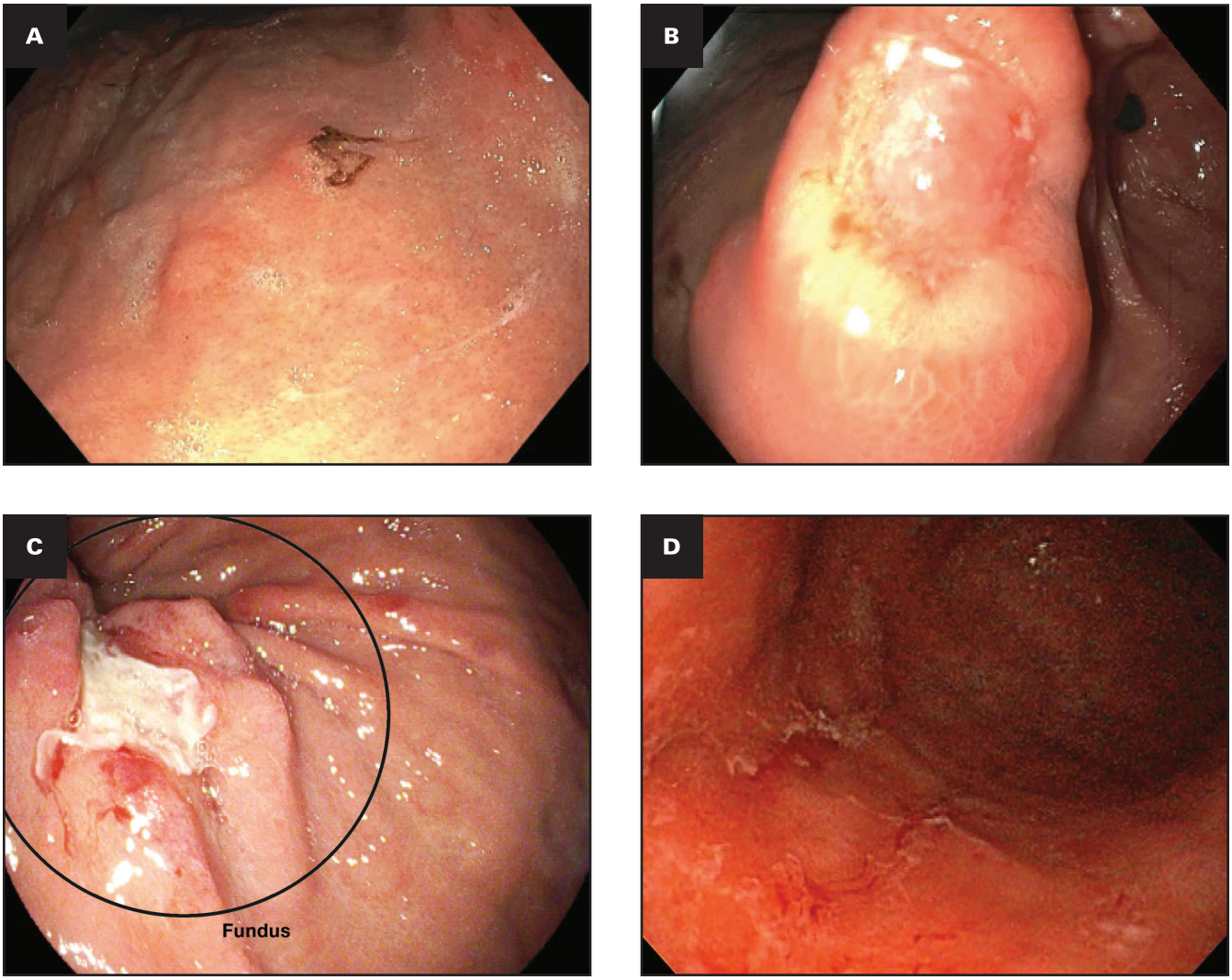

FIGURE 1 Select endoscopic images of syphilitic gastritis. **A**, **B**, Patient 1. **A**, Multiple gastric ulcers (with brown pigmentation) and diffuse erythema in the entirely examined stomach. **B**, One large ulcer with raised edges in the gastric fundus. **C**, Patient 3: single large gastric ulcer in the gastric fundus with heaped edges and surrounding edema. **D**, Patient 4: red, friable, superficial ulcerations in the gastric body. **A**, **B**, Images courtesy of Dr Michael Burkholz. **C**, Image courtesy of Dr Vivek Kumbhari.

TABLE 2 Summary of Histologic Features and Demographics

Characteristic	No.
Destructive active chronic gastritis pattern	8
Prominent plasma cells	5
Prominent lymphohistiocytic inflammation	8
Prominent lymphoid follicles	4
Atrophic mucosa with intestinal metaplasia	2
Inflammatory spillover into the superficial submucosa	8
MSM, HIV history mentioned	3
Lymphoma workup	2

HIV, human immunodeficiency virus; MSM, men who have sex with men.

in the resection sample FIGURE 7. Concurrent *H pylori* infection was documented in one of eight patients. The remaining patients had negative *H pylori* staining in six and equivocal results in one. In three patients who also had biopsies from other parts of the gastrointestinal tract, syphilis was shown to involve the esophagus in one and the colon in three. Hepatic involvement was detected in the one patient who had a concurrent liver biopsy. The rectal biopsy specimens in one patient showed acute colitis/proctitis, which was negative for syphilis by immunostain but positive for gonorrhea/chlamydia nucleic acid testing.

Initial Pathologic Impressions Suggested Other Possibilities

Similar to the initial clinical impressions, none of the initial pathologic differential diagnoses included syphilis. Initial concerns included lymphoma (n = 4), Langerhans cell histiocytosis (n = 1), autoimmune gastritis (n = 2), and refractory *H pylori* infection (n = 3), which were excluded based on negative pertinent evaluations.

Patients Improved Upon Completion of Treatment

Clinical follow-up was available for four patients, whose symptoms and endoscopic abnormalities improved upon completion of

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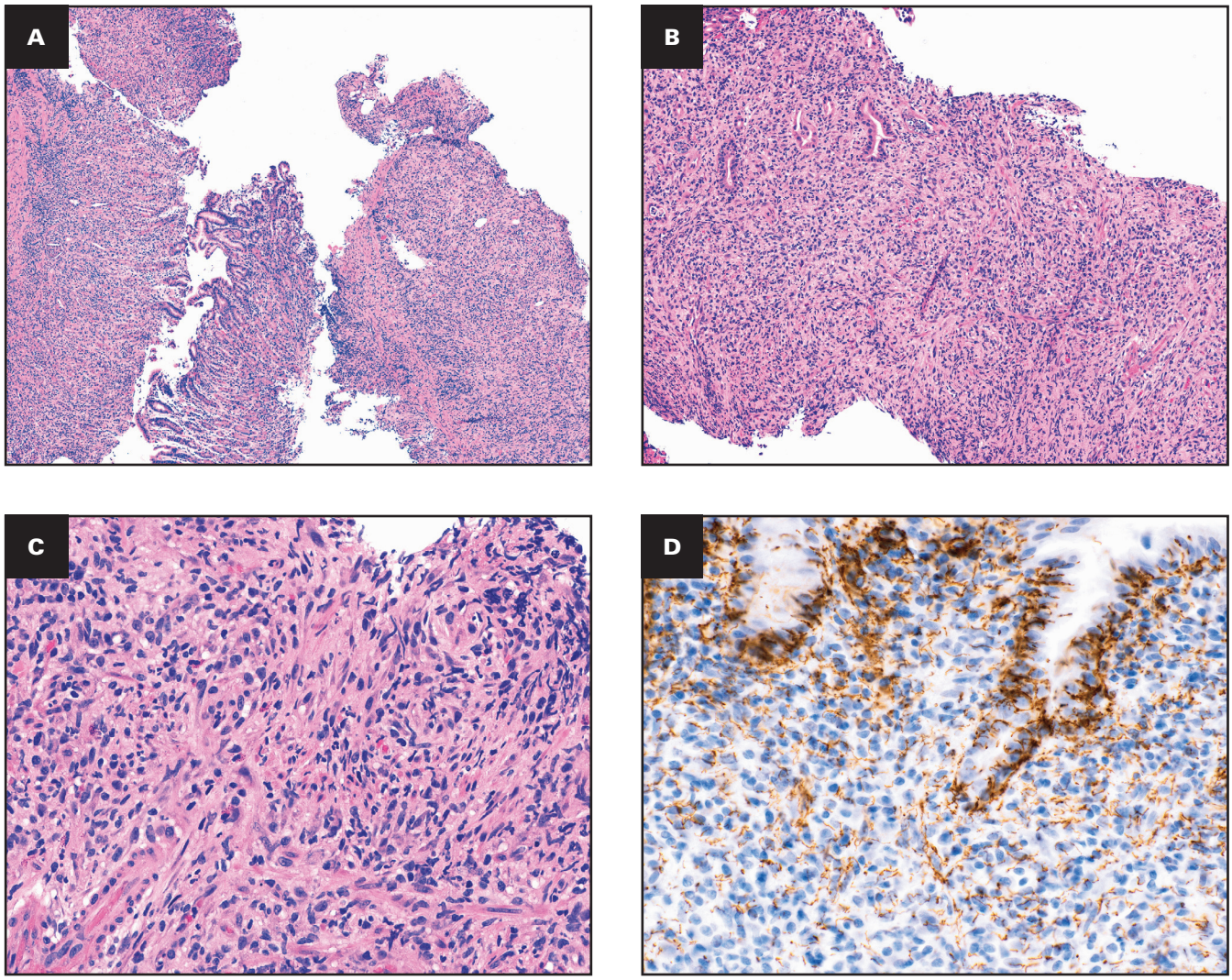

FIGURE 2 Patient 1: a 45-year-old man without a documented history of human immunodeficiency virus or having sex with men. **A**, **B**, The biopsy specimens show a destructive pattern of active chronic gastritis with expansion of the lamina propria by an intense inflammatory infiltrate (H&E; **A**, ×4; **B**, ×10). **C**, Higher magnification shows that the infiltrate is composed of lymphocytes, histiocytes, eosinophils, and plasma cells (H&E, ×40). **D**, Numerous spirochetes are demonstrated by immunohistochemical staining for *Treponema pallidum* (×40).

antibiotic therapy. Six patients had available serologic studies for syphilis, which showed positive rapid plasma reagin (RPR) titers. One patient developed a palmar rash 2 weeks following his initial presentation indicative of secondary syphilis. Another patient was diagnosed with neurosyphilis a year after the initial diagnosis of syphilitic gastritis.

In another patient, the clinician treated the marked gastritis empirically for *H pylori* despite his *Helicobacter* being eradicated successfully many years before. This second course of *H pylori* triple therapy resulted in improved endoscopy symptoms and pathology. RPR serology and immunostaining for syphilis were then ordered on the pretherapy biopsy specimens and found to be positive. The patient also developed an oral ulcer at the time of his second course of *H pylori* treatment that resolved quickly but that was not biopsied. The sixth patient in our series underwent a partial gastrectomy following suspicion for a neoplastic process, a negative *H pylori* evaluation, and gastric ulcers that failed to respond to proton pump inhibitors. After the diagnosis of syphilitic gastritis was established on the resection specimen, the patient was treated with disease-appropriate antibiotics and his symptoms improved. The eighth patient in our series received appropriate antibiotics and his antrum biopsy specimens were essentially normal 1 year after the initial diagnosis.

DISCUSSION

Syphilis, a sexually transmitted disease with a rising incidence, is caused by *T pallidum*, a bacterium that penetrates the skin through minor abrasions.[1] The bacteria spread within the body via hematogenous dissemination, with the potential to involve any organ, including the stomach.[1]

Syphilitic gastritis, also known as luetic gastritis, is rare and can occur in any stage of syphilis; however, about 50% of cases are noted in the secondary stage.[5] Generally, the clinical manifestations of

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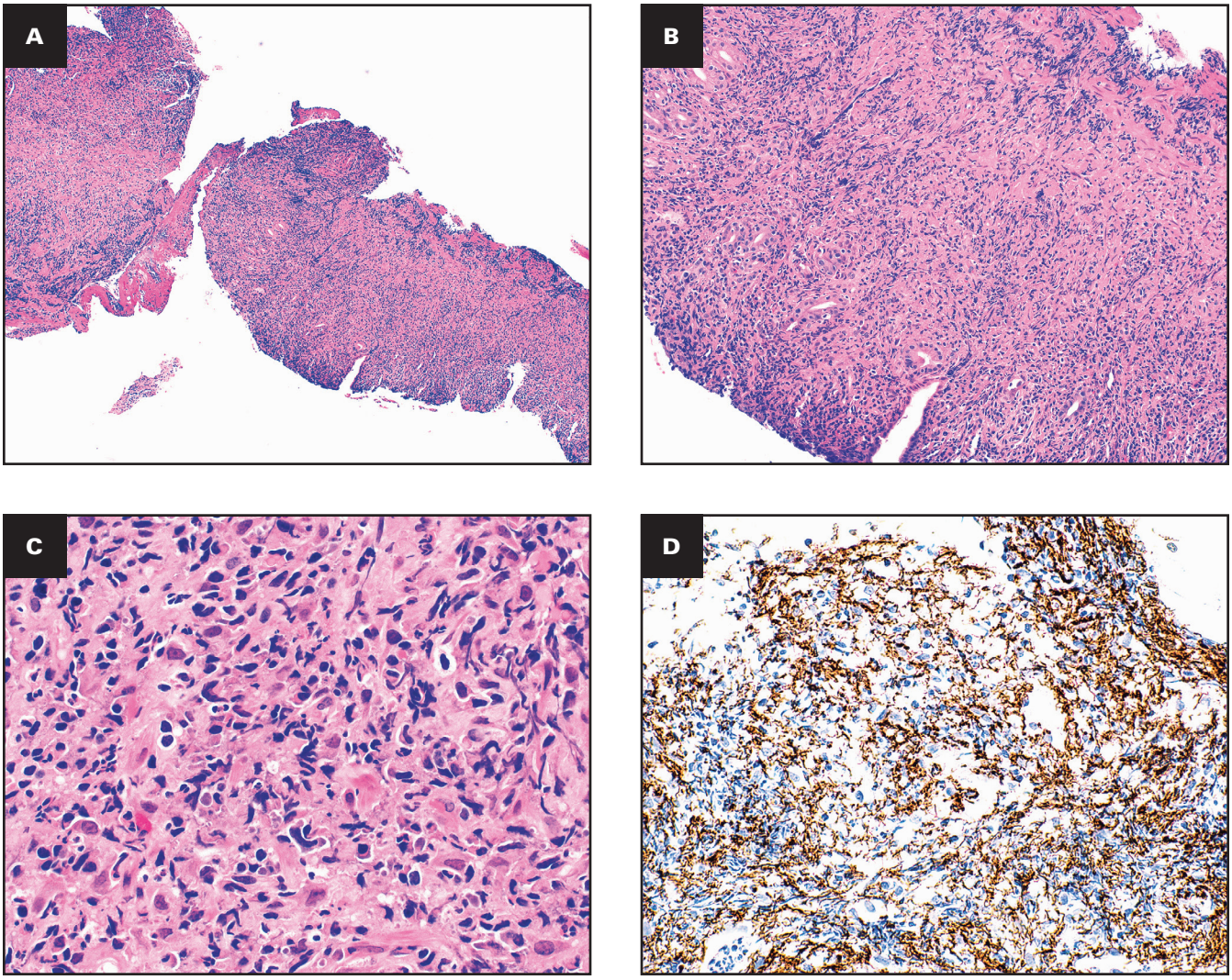

FIGURE 3 Patient 2: a 61-year-old human immunodeficiency virus–positive man without a documented history of having sex with men. **A**, **B**, The biopsy specimens show almost complete effacement of the mucosa by a marked inflammatory infiltrate identical to that seen in patient 1 (H&E; **A**, ×4; **B**, ×10). **C**, Higher magnification shows that the infiltrate is composed of lymphocytes, histiocytes, eosinophils, and plasma cells (H&E, ×40). **D**, Numerous spirochetes are demonstrated by immunohistochemical staining for *Treponema pallidum* (×40).

syphilitic gastritis are nonspecific. In addition, the clinicopathologic clues for recognizing syphilitic gastritis such as HIV infection and MSM history are not always documented or provided. We undertook this case series because recent literature has better elucidated the pathologic appearance of colorectal syphilis,[6,7] but histologic findings in syphilitic gastritis are not as well described. In this series, syphilitic gastritis was not included as the initial clinical or pathologic differential diagnosis for any of the cases; in fact, the clinical differential diagnoses included carcinoma (n = 2), systemic diseases (n = 2), malignancy (n = 1), and lymphoma (n = 3).

According to a systematic literature review covering 50 years by Mylona et al,[5] epigastric tenderness is the most common sign of syphilitic gastritis. Other clinical signs that may be found on physical examination include painless chancres, typically in the primary phase of syphilis, and diffuse adenopathy with a skin rash, seen in the secondary phase. However, in about two-thirds of patients with syphilitic gastritis, these other symptoms of syphilis are absent.[8] One of the patients in our series developed a palmar rash 2 weeks after the initial presentation, and another patient reported development of an oral ulcer a few weeks after the onset of his symptoms.

Endoscopic examination of patients with syphilitic gastritis may reveal more than one type of lesion, including large and/or multiple ulcers, erosions, nodular mucosa, thickened folds, luminal narrowing and wall rigidity, and masses.[5] A brown or purplish discoloration of ulcer edges has been reported by some observers as a characteristic finding of late stages of syphilitic gastritis. The etiology of this discoloration is unclear but has been proposed to result from fibrotic and obliterating vasculitis of the submucosa or high density of microorganisms.[5,9,10] In our series, the most common endoscopic findings were gastric ulcers (either single or multiple) with surrounding edema and inflammation (n = 4). The brown or purplish discoloration was evident in one of our patients FIGURE 1A. Gastric nodularity was described in one patient in our series. Because of the overall nonspecific clinical presentation, pathologists can play a pivotal role in patient care through awareness of the characteristic histologic findings in syphilitic

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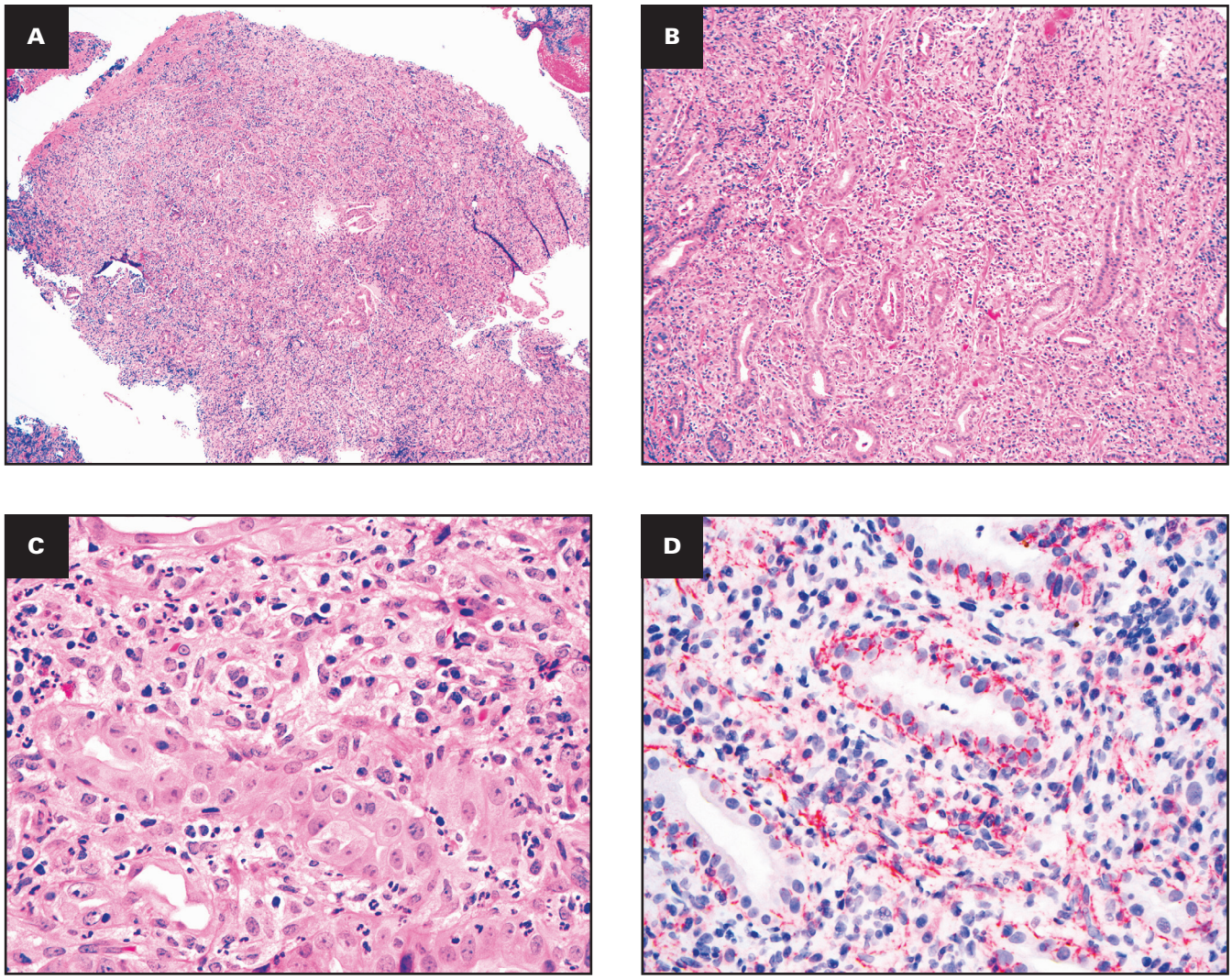

FIGURE 4 Patient 3: a 40-year-old human immunodeficiency virus–negative man without a documented history of having sex with men. **A**, **B**, The biopsy specimens show a full mucosal thickness destructive gastritis pattern (H&E; **A**, ×4; **B**, ×10). **C**, Higher magnification shows the expansion of the lamina propria by a lymphohistiocytic infiltrate with prominent plasma cells, along with mild neutrophilic inflammation of the epithelium (H&E, ×40). **D**, Numerous spirochetes are demonstrated by immunohistochemical staining for *Treponema pallidum* (×40).

gastritis. The most useful histopathologic features for the diagnosis of syphilitic gastritis include a destructive, active chronic gastritis characterized by an intense lymphohistiocytic infiltrate that can mimic a lymphoma, often with lymphoid aggregates, variable plasma cells, and gland loss. Historically, plasma cells were said to be the major inflammatory constituent in syphilis, but in our series, syphilis involving the tubular gastrointestinal tract was less plasmacytic and much more likely to be associated with an intense lymphohistiocytic infiltrate. Hence, it is important for the pathologists not to be overly reliant on a prominence of plasma cells as the diagnostic clue for syphilis. The inflammatory infiltrate often spills over into the superficial submucosa, and this can be another useful clue if the submucosa is sampled. Other histologic features that may be present include shallow erosions in the gastric mucosa; vasculitis; perivascular inflammation, known as perivascular cuffing; and atrophic gastritis.[5,8,11] Due to the intensity of inflammation and the destructive pattern, lymphoma and lymphoproliferative processes are a common consideration. Indeed, in our series, four of five patients were initially worked up for lymphoma and Langerhans cell histiocytosis. This highlights the importance of a high index of suspicion to accurately distinguish syphilitic gastritis from lymphoproliferative processes and to ensure appropriate management while avoiding overtreatment.

Confirmation of a diagnosis of syphilitic gastritis is based on the detection of *T pallidum* in biopsy specimens. However, various stains used for the diagnosis of syphilis can be difficult to interpret and may not be widely available. Moreover, the spirochetes may not be demonstrated by routine silver stains performed for *Helicobacter* detection. In a recent study of hepatic syphilis, *Treponeme* immunostain was negative in 4 of their 14 confirmed cases, indicating that a negative immunostain does not exclude the possibility of syphilis.[7] The diagnosis of syphilitic gastritis may therefore rely on laboratory tests such as RPR or more specific serologies. A better understanding of the histologic features of syphilitic gastritis

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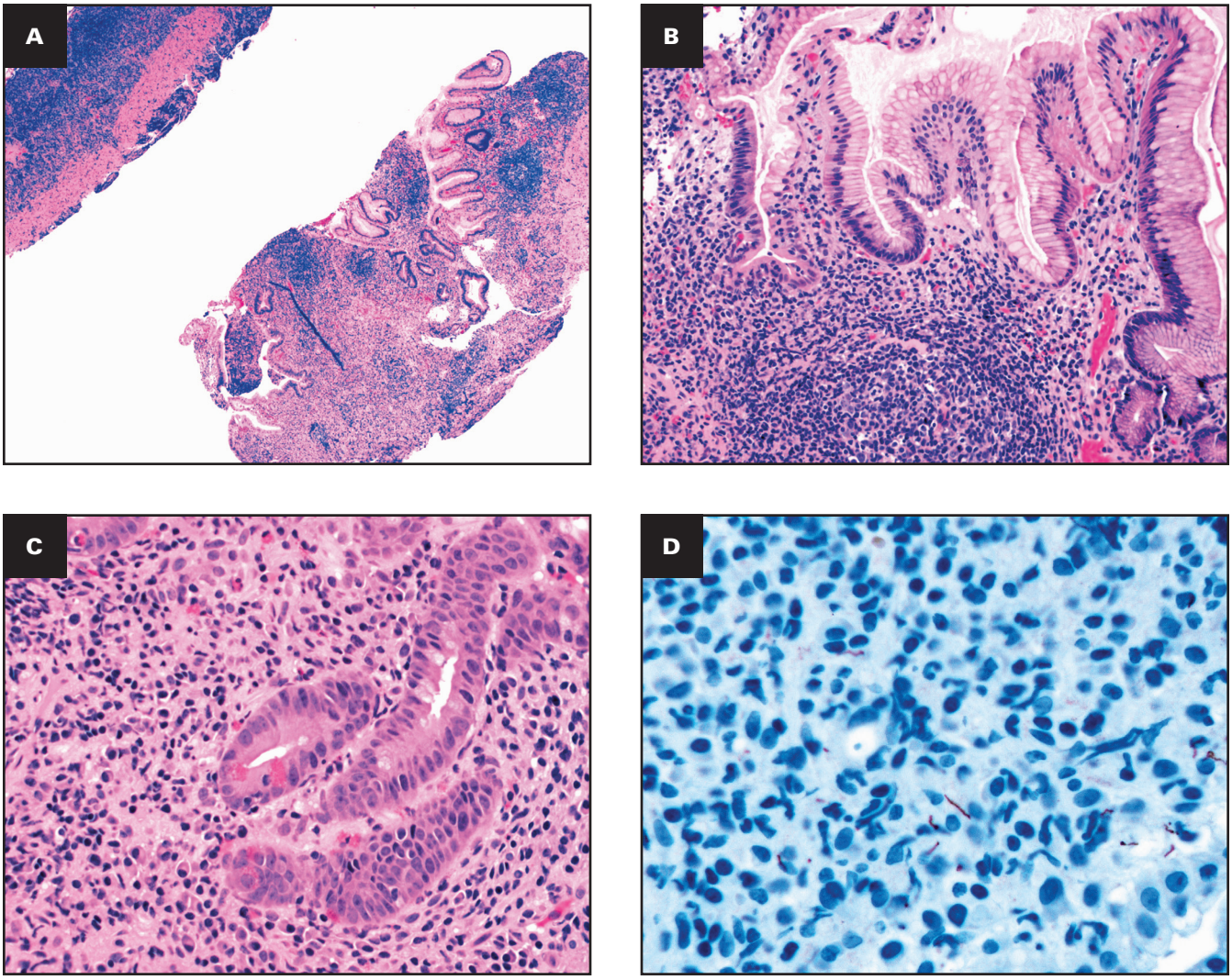

FIGURE 5 Patient 4: a 59-year-old man without a documented history of human immunodeficiency virus or having sex with men. **A**, **B**, The biopsy specimens from this patient also show a destructive chronic active gastritis pattern with prominent lymphoid follicles. No intraepithelial lymphocytes or lymphoepithelial lesions are seen (H&E; **A**, ×4; **B**, ×10). **C**, Higher magnification shows a polymorphous infiltrate composed of lymphocytes, histiocytes, eosinophils, prominent plasma cells, and a focus of intestinal metaplasia (H&E, ×40). **D**, Immunostain for *Treponema pallidum* highlights the spirochetes (×40).

aids in selecting which patients may require additional clinical testing. Although knowledge of HIV + MSM patient status is an additional helpful clue as syphilis disproportionately affects men who have sex with men, syphilitic gastritis should be considered in any case of intense active chronic gastritis with a destructive pattern regardless of sex and sexuality. This is because some patients may have unrecognized risk factors, and the true clinical spectrum of syphilitic gastritis is not well understood. This was indeed illustrated in our series. Syphilitic gastritis affected one woman, and only three patients had documented history of HIV; none of the male patients were known to be MSM.

Syphilitic gastritis can also be confused with other infectious gastritides, especially *Helicobacter* gastritis. In contrast to *Helicobacter* gastritis, which can exhibit a top-heavy lamina propria infiltrate of plasma cells with active inflammation, in the absence of gland destruction, syphilitic gastritis exhibits a destructive lymphohistiocytic infiltrate with admixed plasma cells involving the full thickness of both antral and oxyntic mucosa. Neutrophils are typically not prominent in syphilitic gastritis. Prominent lymphoid follicles have been associated with *Helicobacter* gastritis but were seen in four of our patients with syphilitic gastritis and therefore are not a reliable histologic feature to distinguish the two. Viral infections, particularly Epstein-Barr virus (EBV) gastritis, can also induce a dense and diffuse inflammatory response entering the differential diagnosis of syphilitic gastritis. However, a few subtle histologic features may provide helpful clues. For example, in EBV gastritis, the infiltrate consists of predominantly lymphocytes of variable sizes (mixed small, intermediate, and large) and a less prominent population of plasma cells and histiocytes. Intraepithelial lymphocytes and lymphoepithelial lesions, which can be seen in EBV gastritis, are not a feature of syphilitic gastritis. Similar to syphilitic gastritis, neutrophils are only focally present in EBV gastritis.[12] EBV in situ hybridization was performed in one of the patients in our series and was negative. Coinfection of multiple

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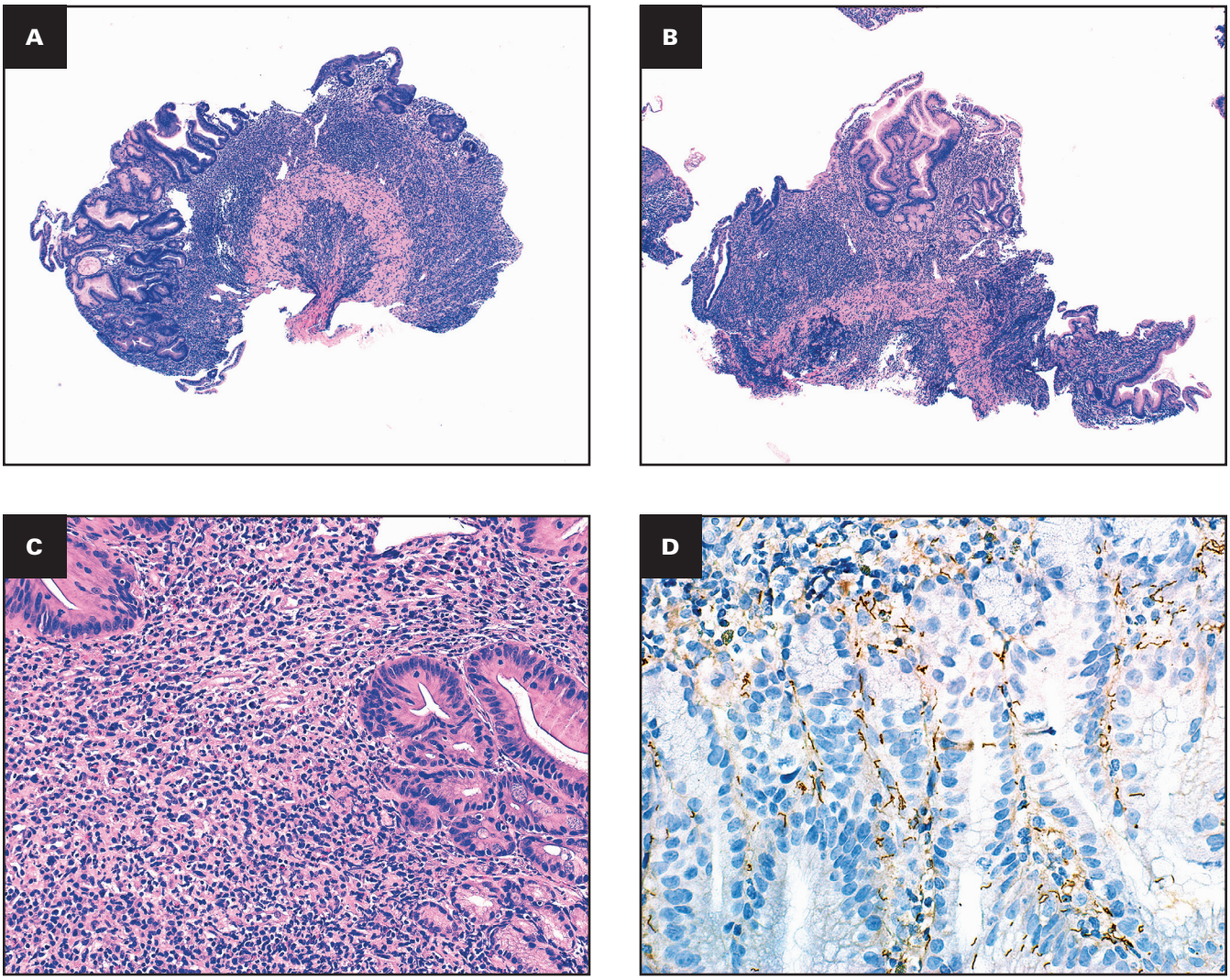

FIGURE 6 Patient 5: a 55-year-old woman without a documented history of human immunodeficiency virus. **A**, The biopsy specimens show a destructive active chronic gastritis pattern with prominent lymphoid follicles. Note the deep inflammatory involvement that includes submucosa. No intraepithelial lymphocytes or lymphoepithelial lesions are seen (H&E, ×4). **B**, **C**, Higher magnification shows a polymorphous infiltrate composed of lymphocytes, histiocytes, eosinophils, prominent plasma cells, and foci of intestinal metaplasia (H&E; **B**, ×10; **C**, ×40). **D**, Immunostain for *Treponema pallidum* highlights the spirochetes (×40).

infectious diseases is of course possible, and indeed, two of the patients in this series had concomitant *H pylori* gastritis and cytomegalovirus gastritis.

Other gastritides in the differential diagnosis include autoimmune gastritis and lymphocytic gastritis. A few subtle histologic findings may provide clues to assist in resolving this differential diagnosis. It is worth noting that syphilitic gastritis occasionally displays an atrophic gastritis-like pattern.[5] Two of our patients' biopsy specimens showed atrophic oxyntic mucosa with foci of intestinal metaplasia, raising concern for autoimmune metaplastic atrophic gastritis **FIGURES 5-6**. However, there was no enterochromaffin-like cell hyperplasia on chromogranin stain, and the antrum was involved similarly. Lymphocytic gastritis, on the other hand, is a rare pattern of chronic gastritis characterized by intraepithelial lymphocytosis (>25 intraepithelial lymphocytes per 100 epithelial cells). It is most often associated with celiac disease, medications such as nonsteroidal anti-inflammatory drugs, angiotensin receptor inhibitors (sartans), and checkpoint inhibitors and *H pylori* infection.[13] In our series and the literature, syphilitic gastritis does not typically feature isolated intraepithelial lymphocytosis.

The degree of chronic inflammation and destructive appearance in syphilitic gastritis may raise concern for a malignancy such as lymphoma, but this can be distinguished using immunohistochemistry and also flow cytometry, as well as by a lack of gene rearrangements/clonality, although there have been recent reports of the unusual ability of syphilis (cutaneous and neurosyphilis) to mimic a T-cell lymphoma with T-cell receptor rearrangements.[14,15] The stomach is the most common site for gastrointestinal lymphoma.[16] Extranodal marginal zone lymphoma (mucosa-associated lymphoid tissue [MALT]) lymphoma is the most common gastric lymphoma and is highly associated with *H pylori* infection. Biopsy specimens of MALT lymphoma show lymphoepithelial lesions and destructive infiltration by small- to medium-sized lymphocytes admixed with monocytoid cells. Plasmacytic differentiation is seen in

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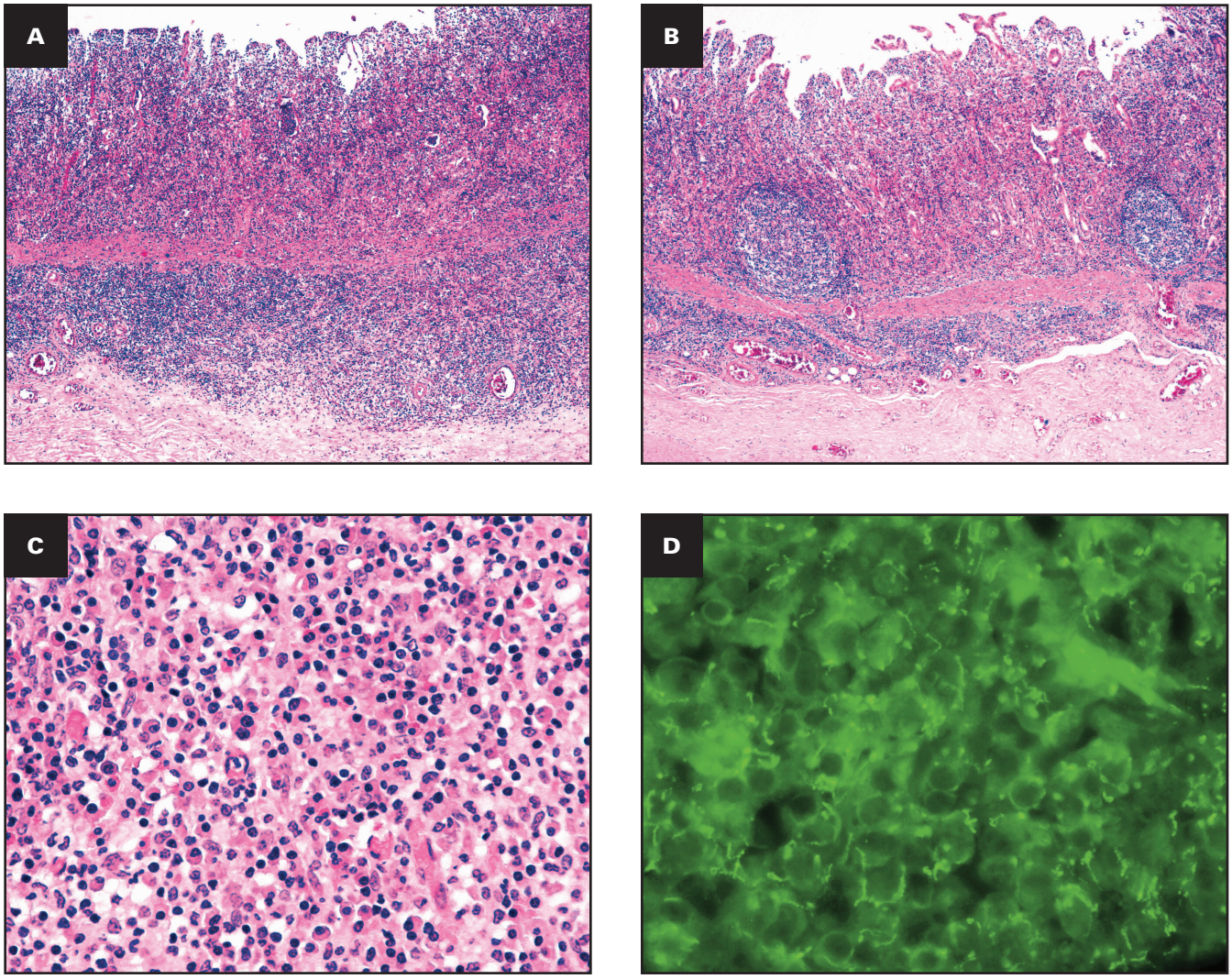

FIGURE 7 Patient 6: a 35-year-old man without a documented history of human immunodeficiency virus. **A**, **B**, Gastrectomy specimen shows a destructive active chronic gastritis with prominent lymphoid follicles and spillover into the superficial submucosa (H&E, ×10). **C**, Higher magnification shows the prominence of plasma cells (H&E, ×40). **D**, Specific immunofluorescence staining of pathogenic treponemes with monoclonal antibody. The FITC-labeled mouse antitreponemal 37-kDa monoclonal antibody stain demonstrates numerous spirochetes in thin-section specimens by the use of a ×100 oil objective and a ×10 ocular.

up to one-third of cases. Another common gastric lymphoma is diffuse large B-cell lymphoma, which is characterized by a diffuse infiltration of large cells with vesicular nuclei.[16] Immunohistochemistry to characterize the inflammatory cells is useful in distinguishing lymphoma from the mimics. In three of our patients for whom lymphoma was suspected, immunostains were performed. The inflammatory infiltrate showed a polymorphous infiltrate with a mixed population of CD20 and CD3 cells and lacked clonality by κ and λ. CD5, CD23, and BCL-2 were negative. In one patient, the diagnosis of Langerhans histiocytosis was considered based on the prominence of histiocytes and eosinophils, but the infiltrate was negative for CD1a. The histologic findings of mimickers of syphilitic gastritis are summarized in **TABLE 3**.

As our series shows, involvement of other parts of the gastrointestinal tract, such as the colon, liver, and esophagus, is common. It is worth comparing syphilitic gastritis with colorectal syphilis, which has been described in detail.[6] Sexually transmitted infectious colitis also can exhibit lymphohistiocytic inflammation with prominent lamina propria plasma cells, mild crypt architectural distortion, and incongruously less active inflammation than the chronic inflammation present. In three of our patients with colonic biopsy specimens involved by syphilis, the same destructive lymphohistiocytic process that was present in the gastric biopsy specimens involved the colon as well.

In conclusion, the histologic features of syphilitic gastritis are those of a marked lymphohistiocytic infiltrate with prominent plasma cells, lymphoid aggregates, and only mild to moderate acute inflammation. Syphilis is a great clinical and pathologic imitator of other gastric diseases, including lymphoproliferative disorders, infiltrating carcinomas, and other infectious processes; thus, recognition of this pattern is critical in making a diagnosis.

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TABLE 3 Differential Diagnosis of Syphilitic Gastritis

Mimic	Description
Helicobacter pylori infection	Active chronic gastritis, usually in the superficial aspect, can involve deeper aspect of the mucosa Typically not destructive Positive *H pylori* immunostain
Lymphoproliferative disorders and lymphoma	Can have destructive gastritis pattern Lymphoepithelial lesions are more common Immunostains are essential for distinction
Epstein-Barr virus gastritis	Chronic gastritis with prominent lymphocytes of variable sizes Less prominent population of plasma cells Essentially lack of neutrophilic activity or only focal
Autoimmune atrophic metaplastic gastritis	Predominantly chronic gastritis pattern Activity less common Predominantly involves the oxyntic mucosa and spares the antrum Enterochromaffin-like cell hyperplasia (chromogranin stain)

Many physicians may not be aware of syphilitic gastritis as an entity. As the incidence of syphilis is on the rise, awareness of the clinicopathologic features in several organ systems will help physicians achieve the correct diagnosis. Syphilitic gastritis should be considered in patients at risk for sexually transmitted diseases who have gastric ulcers and in patients with a destructive active gastritis pattern in whom *H pylori* is not detected. Treatment of syphilitic gastritis involves penicillin, with dosage depending on the clinical stage of the disease. In most cases, complete resolution of the symptoms is observed following treatment.[5] As the history of HIV and MSM is not always documented or present and syphilis can involve women as well, a high index of suspicion is required for the diagnosis. Most pathologists receive little if any clinical and endoscopic information with their biopsy specimens. Therefore, recognition of the key histologic features described in this series (intense lymphohistiocytic inflammation, plasma cells, and gland loss) are often helpful in prompting the pathologists to perform the immunostain and arrive at the correct diagnosis. Finally, recognition of syphilitic gastritis has important clinical implications as it is easily treatable, and the diagnosis can prevent further unnecessary testing and aggressive treatments, including potential gastrectomy **FIGURE 7**.

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