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OBSERVATION

Mesenteric lymph node cavitation syndrome

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Abstract

The mesenteric lymph node cavitation syndrome consists of central necrosis of mesenteric lymph nodes and may occur with either celiac disease or a sprue-like intestinal disease that fails to respond to a gluten-free diet. Splenic hypofunction may also be present. The cause is not known but its development during the clinical course of celiac disease is usually indicative of a poor prognosis for the intestinal disorder, a potential for significant complications including sepsis and malignancy, particularly T-cell lymphoma, and significant mortality. Modern abdominal imaging modalities may permit earlier detection in celiac disease so that earlier diagnosis and improved understanding of its pathogenesis may result.

Key words: Mesenteric lymph node; Celiac disease; Yersinia infection; Tuberculosis; Kikuchi disease; Hyposplenism; Lymphoma

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INTRODUCTION

Over 50 years ago, mesenteric lymph node changes were described in celiac disease[1-3]. At that time, definition of most changes in abdominal lymphoreticular structures relied largely on surgical observation or postmortem evaluation. In addition, altered abdominal lymphoreticular function was also evident, reflected in reduced splenic function[4-6]. In recent years, refinements in abdominal imaging, i.e. ultrasound, computed tomography (CT), magnetic resonance imaging (MRI) and positron emission tomography, have led to improved and earlier documentation of lymphoreticular changes in celiac disease. Neoplastic (i.e. lymphoma) and non-neoplastic changes, including mesenteric lymph node cavitation, have been recorded.

MESENTERIC LYMPH NODE CAVITATION SYNDROME

Detailed descriptions of this entity appeared largely in the French literature[7-9]. These reports described an unusual syndrome that seemed to complicate the clinical course of adult celiac disease. While typical small intestinal mucosal biopsy changes of celiac disease were present, the most intriguing observation was the definition of cavitated mesenteric lymph nodes. In addition, splenic atrophy or splenic hypofunction appeared to be present, raising the spectra of impaired immune function and a specific infectious cause.

Matuchansky and collegues[10], in a seminal report, noted details of 6 cases that included 4 females and 2 males. Within the jejunoileal mesenteric nodes, pseudocystic lesions were detected that consisted histologically of a large central cavity occupied by hyaline-type material surrounded by fibrous tissue and lymph node remnants. Evidence of mesenteric panniculitis or malignant lymphoma was not detected. Persistent diarrhea or childhood diarrhea along with malabsorption accompanied the small intestinal changes. An unequivocal mucosal response to a gluten-free diet was shown in some cases confirming that celiac disease was present. In others, a definitive response to a gluten-free diet could not be documented suggesting

that either a resistant form of celiac disease or sprue-like intestinal disease was present. Similar features have been noted with other complicating disorders (e.g. lymphoma) in both adult celiac disease or sprue-like intestinal disease[11]. Microscopic examination of the lymph nodes in these cases usually shows some common features. Atrophic cavitated lymph nodes are usually present without evidence of infection or malignancy in the lymph nodes. Central acidophilic lipid-containing fluid is usually present surrounded by a rim of residual lymph node tissue that includes follicles, sinus and capsular components. The changes historically have appeared to be confined to the mesenteric lymph node chain.

HYPOSPLENISM

Another important, although not essential[4-6], component of this clinical syndrome appears to be splenic atrophy or splenic hypofunction. While splenic changes have been previously noted in other intestinal disorders (e.g. inflammatory bowel disease)[12], mesenteric lymph node cavitation was seen only in those with pathological changes of celiac disease or sprue-like small intestinal disease, and not with inflammatory bowel disease[10]. In early studies, splenic atrophy was often defined structurally during postmortem evaluation or abdominal surgery. More recently, these changes tended to be defined with modern imaging methods. Hyposplenism, indicative of reduced splenic function, appeared to reflect this structural change in the spleen, and depending on its mode of measurement, seemed to be quite common in celiac disease[6]. The latter disorder may be suspected from a peripheral blood smear with Howell-Jolly bodies, monocytosis, lymphocytosis and increased platelet counts, and confirmed with pitted red blood cells counts or radiolabeled colloid scanning of the spleen[13-15]. In celiac disease, for example, 76.2% of patients were found to have pitted red blood cells[6]. These may also occur during the clinical course of many other disorders, apart from celiac disease or sprue-like intestinal disease[13-15]. These disorders include dermatitis herpiformis[16], collagenous sprue[17], collagenous colitis[18] and abdominal lymphoma[14,19], all disorders intimately linked to celiac disease[19-21]. Hyposplenic patients have been reported to be at increased risk for bacterial sepsis, especially with encapsulated organisms such as pneumococcus, sometimes with a fatal outcome[22], so vaccination using the pneumococcal conjugate has been recommended[14]. The risk of sepsis appears to be more significant if a diagnosis of celiac disease is established during adult years rather than in childhood[23]. There may also be a higher risk for vascular, autoimmune and thrombotic disorders along with solid tumors[14]. In celiac disease with associated autoimmune or malignant complications, IgM memory B-cells were reduced suggesting a possible mechanism leading to infections by encapsulated bacteria[14]. Resolution of reduced splenic function appears to be possible, but only after improvement of small intestinal mucosal changes has occurred[6].

LONG-TERM NATURAL HISTORY AND COMPLICATIONS

Most early reports indicated that cavitation of mesenteric lymph nodes was associated with a very poor prognosis with a mortality of about 50%[24]. Nevertheless, dramatic improvement has also been recorded with complete normalization of the mesenteric lymph nodes[25,26].

In celiac disease with associated dermatitis herpetiformis, recurrent diarrhea, steatorrhea and protein-losing enteropathy were defined followed later by hyposplenism, mesenteric lymph node cavitation and malignant lymphoma of the small intestine[27]. In another case of mesenteric lymph node cavitation, lymphoma also developed with a sprue-like intestinal lesion that did not respond to a gluten-free diet[28]. Cavitation of mesenteric lymph nodes may also occur without celiac or other small bowel disease[29]. Bacterial infections may be associated with necrosis of lymph nodes (e.g. mycobacteria, *Yersinia*) and lymph node cavitation has been reported with Whipple's disease[30]. Necrotizing lymphadenitis may also occur with systemic lupus erythematosus[31], and this appears to be pathologically similar to Kikuchi-Fujimoto disease, a self-limited form reported in young Asian adults[32]. In celiac disease, however, malignant lymphoma may also be the cause of necrotic mesenteric lymph node changes[33]. In one report, these necrotic lesions were seen in the liver and spleen due to hepatosplenic type lymphoma, a rare type of peripheral T-cell lymphoma with T-cell receptor rearrangement[33]. In a more recent case report, progressive encephalopathy and focal lesions of the cerebellum and brainstem were associated with abnormal T-cell clones in a sprue-like disorder with mesenteric and mediastinal lymph node cavitation[34]. Finally, a case of necrotizing hepatitis with celiac disease and mesenteric lymph node cavitation was recently described, but lymphoma was not detected[35].

CONCLUSION

This syndrome is an intriguing entity or group of entities frequently associated with celiac disease or sprue-like intestinal disease consisting of cavitated mesenteric lymph nodes and, often, splenic hypofunction. Cavitated mesenteric nodes should be differentiated from other causes of mesenteric cystic lesions, including lymphatic cysts or cystic lymphangioma. These have also been recorded with celiac disease and hyposplenism[36]. Although diagnosis is usually confirmed by pathological evaluation of mesenteric lymph nodes, imaging studies may be very helpful. Ultrasound may show anechoic cysts up to 8 cm in size. CT may reveal low attenuation (fluid or fat) lymphadenopathy suggesting celiac disease, Whipple's disease, infections such as tuberculosis, lymphoma or necrotic metastases, including germ cell tumors[37]. Occasionally, fluid-fat levels are appreciated in the lymph node, reported only in celiac disease[37]. MRI may be useful as the fluid and fat layer may be appreciated in T2- and T1-weighted axial images, even if fluid-fat levels are not seen on CT[38]. In some cases, image-guided fine-needle aspiration of the

cyst may be performed[38]. The cause of cavitation syndrome is usually not defined. The mesenteric lymph node cavitation changes have been hypothesized to represent excess antigen exposure via damaged small bowel mucosa causing lymphoid cell depletion in the lymph nodes and spleen. Alternatively, changes may reflect necrosis in the mesenteric nodes triggered by localized immune-mediated complement activation and intravascular coagulation[38]. Specific infections and malignant lymphoma may complicate its natural history and clinical course and contribute to its poor prognosis.

REFERENCES

1 **Paulley JW**. Observation on the aetiology of idiopathic steatorrhoea; jejunal and lymph-node biopsies. *Br Med J* 1954; **2**: 1318-1321
2 **Faber M**, Meulengracht E, Vimtrup B. A rapidly progressing sprue-like syndrome with hitherto undescribed pathological changes. *Acta Med Scand Suppl* 1952; **266**: 381-392
3 **Gallus P**, Dustin P Jr. [Anatomoclinical study of a case of idiopathic sprue. Significance of intestinal and mesenteric lymph node lesions.] *Acta Gastroenterol Belg* 1960; **23**: 170-187
4 **Marsh GW**, Stewart JS. Splenic function in adult coeliac disease. *Br J Haematol* 1970; **19**: 445-457
5 **Ferguson A**, Hutton MM, Maxwell JD, Murray D. Adult coeliac disease in hyposplenic patients. *Lancet* 1970; **1**: 163-164
6 **O'Grady JG**, Stevens FM, Harding B, O'Gorman TA, McNicholl B, McCarthy CF. Hyposplenism and gluten-sensitive enteropathy. Natural history, incidence, and relationship to diet and small bowel morphology. *Gastroenterology* 1984; **87**: 1326-1331
7 **Colin R**, Hemet J, Geffroy Y. [Primary villous atrophy. Mesenteric lymph node cavitation. Splenic atrophy. Apropos of a case] *Arch Fr Mal App Dig* 1972; **61**: 451-462
8 **Marche C**, Bocquet L, Mignon M, Preel JL. [Malabsorption syndrome with mesenteric lymph node cavitation and splenic atrophy. Apropos of a new anatomo-clinical case] *Sem Hop* 1974; **50**: 879-886
9 **Hoang C**, Galian A, Maitre F, Degois T, Celerier M, Modigliani R. [Total villous atrophy, mesenteric lymph-node cavitation, splenic atrophy. An unusual form of celiac disease in adults, apropos of a new case] *Ann Pathol* 1983; **3**: 251-256
10 **Matuchansky C**, Colin R, Hemet J, Touchard G, Babin P, Eugene C, Bergue A, Zeitoun P, Barboteau MA. Cavitation of mesenteric lymph nodes, splenic atrophy, and a flat small intestinal mucosa. Report of six cases. *Gastroenterology* 1984; **87**: 606-614
11 **Freeman HJ**. Free perforation due to intestinal lymphoma in biopsy-defined or suspected celiac disease. *J Clin Gastroenterol* 2003; **37**: 299-302
12 **Palmer KR**, Sherriff SB, Holdsworth CD, Ryan FP. Further experience of hyposplenism in inflammatory bowel disease. *Q J Med* 1981; **50**: 463-471
13 **Di Sabatino A**, Rosado MM, Cazzola P, Riboni R, Biagi F, Carsetti R, Corazza GR. Splenic hypofunction and the spectrum of autoimmune and malignant complications in celiac disease. *Clin Gastroenterol Hepatol* 2006; **4**: 179-186
14 **William BM**, Corazza GR. Hyposplenism: a comprehensive review. Part I: basic concepts and causes. *Hematology* 2007; **12**: 1-13
15 **William BM**, Thawani N, Sae-Tia S, Corazza GR. Hyposplenism: a comprehensive review. Part II: clinical manifestations, diagnosis, and management. *Hematology* 2007; **12**: 89-98
16 **Corazza GR**, Bullen AW, Hall R, Robinson PJ, Losowsky MS. Simple method of assessing splenic function in coeliac disease. *Clin Sci* (Lond) 1981; **60**: 109-113
17 **Freeman HJ**. Hyposplenism, antiendomysial antibodies and lymphocytic colitis in collagenous sprue. *Can J Gastroenterol* 1999; **13**: 347-350
18 **Freeman HJ**. Functional asplenia and microscopic (collagenous) colitis. *Can J Gastroenterol* 1996; **10**: 443-446
19 **Freeman HJ**, Weinstein WM, Shnitka TK, Piercey JR, Wensel RH. Primary abdominal lymphoma. Presenting manifestation of celiac sprue or complicating dermatitis herpetiformis. *Am J Med* 1977; **63**: 585-594
20 **Weinstein WM**, Saunders DR, Tytgat GN, Rubin CE. Collagenous sprue--an unrecognized type of malabsorption. *N Engl J Med* 1970; **283**: 1297-1301
21 **Freeman HJ**. Collagenous colitis as the presenting feature of biopsy-defined celiac disease. *J Clin Gastroenterol* 2004; **38**: 664-668
22 **O'Donoghue DJ**. Fatal pneumococcal septicaemia in coeliac disease. *Postgrad Med J* 1986; **62**: 229-230
23 **Ludvigsson JF**, Olén O, Bell M, Ekbom A, Montgomery SM. Coeliac disease and risk of sepsis. *Gut* 2008; **57**: 1074-1080
24 **Howat AJ**, McPhie JL, Smith DA, Aqel NM, Taylor AK, Cairns SA, Thomas WE, Underwood JC. Cavitation of mesenteric lymph nodes: a rare complication of coeliac disease, associated with a poor outcome. *Histopathology* 1995; **27**: 349-354
25 **Arotçarena R**, Hammel P, Terris B, Guth A, Bernades P, Ruszniewski P. [Regression of mesenteric lymph node cavitation syndrome complicating celiac disease after a gluten free diet] *Gastroenterol Clin Biol* 2000; **24**: 579-581
26 **Bardella MT**, Trovato C, Quatrini M, Conte D. Mesenteric lymph node cavitation: a rare hallmark of celiac disease. *Scand J Gastroenterol* 1999; **34**: 1257-1259
27 **Freeman HJ**, Chiu BK. Small bowel malignant lymphoma complicating celiac sprue and the mesenteric lymph node cavitation syndrome. *Gastroenterology* 1986; **90**: 2008-2012
28 **Bulger K**, Griffin M, O'Brien M, Crowe J. Lymphoma in the mesenteric lymph node cavitation syndrome. *Gastroenterology* 1988; **94**: 553
29 **Tellisi N**, Al-Omishy H. Cavitation of mesenteric lymph nodes without celiac disease. *Saudi Med J* 2004; **25**: 1277
30 **de Wazières B**, Fest T, Litzler JF, Simon G, Rohmer P, Dupond JL. [Mesenteric lymph node cavitations in Whipple's disease. Apropos of a case] *J Radiol* 1993; **74**: 661-663
31 **Eisner MD**, Amory J, Mullaney B, Tierney L Jr, Browner WS. Necrotizing lymphadenitis associated with systemic lupus erythematosus. *Semin Arthritis Rheum* 1996; **26**: 477-482
32 **Hutchinson CB**, Wang E. Kikuchi-Fujimoto disease. *Arch Pathol Lab Med* 2010; **134**: 289-293
33 **Freeman HJ**. Fulminant liver failure with necrotizing foci in the liver, spleen and lymph nodes in celiac disease due to malignant lymphoma. *Can J Gastroenterol* 1996; **10**: 225-229
34 **Keller CE**, Gamboa ET, Hays AP, Karlitz J, Lowe G, Green PH, Bhagat G. Fatal CNS vasculopathy in a patient with refractory celiac disease and lymph node cavitation. *Virchows Arch* 2006; **448**: 209-213
35 **Cornelis T**, Hiele M, Vermeire S, Libbrecht L, Verslype C. A unique combination of celiac disease, mesenteric lymph node cavitation, splenic atrophy and necrotizing hepatitis. *Acta Gastroenterol Belg* 2008; **71**: 267-270
36 **Miele L**, Pierconti F, Forgione A, Vero V, Cammarota G, Molinari F, Masselli G, Capristo E, Martini M, Larocca LM, Civello IM, Gasbarrini G, Grieco A. Cystic lymphangioma of the mesentery and hyposplenism in celiac disease. *Eur J Gastroenterol Hepatol* 2007; **19**: 1026-1030
37 **Reddy D**, Salomon C, Demos TC, Cosar E. Mesenteric lymph node cavitation in celiac disease. *AJR Am J Roentgenol* 2002; **178**: 247
38 **Huppert BJ**, Farrell MA, Kawashima A, Murray JA. Diagnosis of cavitating mesenteric lymph node syndrome in celiac disease using MRI. *AJR Am J Roentgenol* 2004; **183**: 1375-1377

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