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Case Report

Primary Appendiceal Lymphoma Presenting as Perforated Acute Appendicitis

Acute perforated appendicitis is a very rare initial presentation of appendiceal lymphoma. A case of primary lymphoma of the appendix in a 42-year-old female is reported here. The symptom was pain in the right lower quadrant of the abdomen. Surgical intervention was performed under clinical diagnosis of acute appendicitis. Grossly, the resected appendix was gangrenous and perforated. Light microscopy revealed transmural infiltration by diffuse large B-cell lymphoma with angioinvasion and tumor necrosis, resulting in perforated acute suppurative appendicitis. To the best of our knowledge, only 4 cases of well-documented primary diffuse large B-cell lymphoma of appendix have been reported in the world literature.

Malignant lymphoma comprises 1% to 4% of the malignant neoplasms of the gastrointestinal tract,[1] but appendiceal lymphomas are exceedingly rare and often diagnosed postoperatively. The clinical findings are nonspecific, leading to a delay in diagnosis. We present a case of primary diffuse large B-cell lymphoma of the appendix with perforated acute appendicitis.

CASE REPORT

A 42-year-old female suffered from abdominal pain and fever for 2 days. There were epigastric distress, nausea and vomiting initially. The epigastric pain shifted to the right lower quadrant on the second day when she visited our emergency room. On physical examination, tenderness and rebounding pain were noted over the right lower quadrant of the abdomen. Laboratory examination revealed white cell count of 5,290/mm^3 with 84.9% neutrophils. Serum lactic dehydrogenase level was within normal limit (258 U/L). The patient then received laparoscopic appendectomy under clinical diagnosis of acute appendicitis.

Pathologic finding and follow-up study

The specimen consisted of 8 pieces of resected appendix, measuring 7 cm in length and 3.7 cm in maximal diameter after reconstruction. The wall was markedly thickened and the lumen obliterated. Gangrene with perforation near the tip was observed (Fig. 1). Histologically, normal appendiceal architecture was almost totally effaced by diffuse infiltrate of large atypical lymphocytes with irregular nuclei, prominent nucleoli and many mitotic figures. The tumor infiltrated through the muscularis propria into the subserosa. Angioinvasion by tumor cells with coagulative tumor necrosis was observed (Fig. 2). The atypical lymphocytes were immunoreactive to CD20 (B-cell marker) and negative for CD3 (T-cell marker). Other part of the appendix showed transmural polymorphonuclear leukocytes (PMN) infiltration and microabscess formation. Both tumor necrosis and polymorphonuclear (PMN) leukocytes infiltration were present

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around the perforated site. The pathologic diagnosis was primary appendiceal diffuse large B-cell lymphoma with perforated acute suppurative appendicitis.

Fig. 1. Part of appendectomy specimen showing gangrene and perforation near tip region.

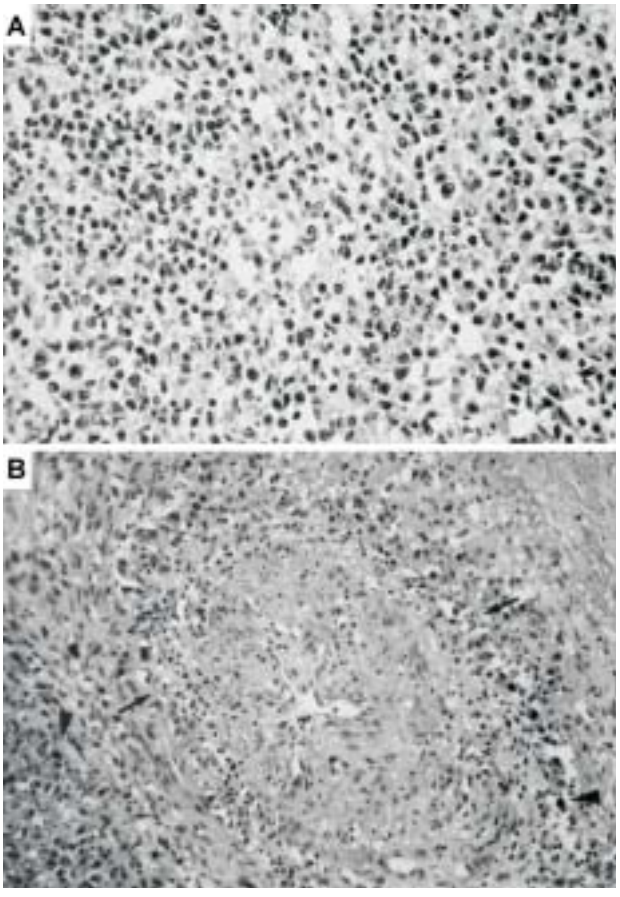

Fig. 2. Diffuse large B-cell lymphoma showing large atypical lymphocytes (**A**) with angioinvasion (**B**) (hematoxylin and eosin X400). Atypical lymphocytes (arrow head) are seen between inner elastin menbrane (arrows) and muscular layer.

After operation, a neck and thoracic computed tomography (CT) scan was performed which showed multiple but small lymph nodes of variable sizes over bilateral carotid spaces, posterior triangle of submandibular area, left axilla, retroperitoneum, and mesentery. The image impression was in favor of reactive lymphadenopathy.

DISCUSSION

The incidence of primary appendiceal lymphoma has been estimated at 0.015% of all appendiceal specimens (11/71,000).[2] In our hospital, of 4458 appendectomy specimens (13 years, 1990 to 2003), only this 1 was of primary appendiceal lymphoma. The incidence is 0.022%. In literature review of 68 reported cases, there were 37 males, 25 females and 6 cases of unknown gender. Forty-seven reported cases used old nomenclature, such as lymphosarcoma or lymphoblastic sarcoma. Another 29 cases reported in the recent 3 decades have been 9 cases of Burkitt's lymphoma, which is the majority, 2 cases of mantle cell lymphoma, 1 case of marginal zone B-cell lymphoma, 3 cases of T-cell lymphoma, and 4 cases of diffuse large B-cell lymphoma. However, since cases of lymphoblastic sarcoma and diffuse large cell lymphoma in the old literature were not further classified, the case number of diffuse large B-cell lymphoma may be underestimated. Clinicopathological features of these cases and our case are summarized in Table 1.

Primary appendiceal lymphoma may present clinically as acute appendicitis. In a review of 68 patients with appendiceal lymphoma, 43 presented with acute or subacute right lower quadrant pain. Others were either incidentally found or presented with nonspecific symptoms, such as abdominal pain, anorexia, nausea, vomiting, fever, weight loss, and right lower quadrant mass.[1] Acute appendicitis and angioinvasion with tumor necrosis were not described in the previous case reports. Therefore, it is not known whether, in addition to obstruction, acute appendicitis and angioinvasion play a role in the symptoms and signs of the primary appendiceal lymphoma. In our patient, both obstruction and angioinvasioin with tumor necrosis could play a role in the pathogenesis of the perforated acute appendicitis.

Table 1. Literature review of 68 cases of primary malignant lymphoma of the appendix

Number of cases	Type	Age (yr)/Sex	Diameter (cm)	Authors	Year
1	Burkitt's	Young/	-	Nanji *et al*.	1983
1	Burkitt's	Young/	-	Ghani *et al*.	1984
1	Burkitt's	3/F	-	Caine *et al*.	1990
1	Diffuse large B-cell	48/F	-	Shimada *et al*.	1990
1	Small cell, cleaved	65/M	-	Carpenter *et al*.	1991
1	Lymphoblastic	75/M	3.5	Rao *et al*.	1991
1	Burkitt's	17/M	-	Carstensen *et al*.	1993
25	Lymphoblastic sarcoma				
9	Giant follicular lymphoblastoma				
3	Lymphosarcoma, unclassified		-		
3	Well-differentiated lymphocytic				
3	Diffuse large cell				
3	Burkitt's				
1	Unknown	25.7 (mean)/ 19 F, 24 M 4 unknowns	-	Pasquale *et al*. *	1994
1	Burkitt's	25/M	2.2	Krepel *et al*.	1996
1	Anaplastic large T-cell	24/F			
1	Diffuse large B-cell	69/M	-	Muller *et al*.	1997
1	Marginal zone B-cell	74/M			
1	Primary nasal NK/T-cell	20/ M	-	Tsujimura *et al*.	2000
1	Diffuse large B-cell	66/M	3	Katz *et al*.	2002
2	Mantle cell				
1	Diffuse large B-cell				
1	Non-Hogkin's lymphoma				
1	Large cell undifferentiated	54 (mean)/ 4 M, 1 F	3.8 (mean)	Pickhardt *et al*.	2002
1	Primary T-cell	84/F	-	Kitamura *et al*.	2002
1	Burkitt's	12/M	-	Bissen *et al*.	2002
1	Diffuse large B-cell	42/F	3.7	Present case	2004

* In the 68 cases reviewed, 47 cases were reported before 1968, when the old nomenclature, lymphosarcoma, was used. The mean age of the 47 cases was 25.7 years old, including 19 females, 24 males and 4 unknowns.

According to the previous reported cases[8,10,13,14] and the present case, the average appendiceal diameter at pathologic examination is approximately 3.5 cm. The Armed Forces Institute of Pathology reported 5 cases of non-Hodgkin's lymphoma of the appendix discovered retrospectively on CT scan where the maximal appendiceal diameter ranged from 2.5 to 4.0 cm as demonstrated by CT scan.[14] Therefore, it is suggested that appendiceal neoplasm should be considered when the diameter reaches 3 cm.

Guidelines for therapy of primary appendiceal lymphoma are unclear because of its rarity. In this patient, since the disease had extended beyond the appendix (T3N2M0), further adjuvant chemotherapy with CHOP (cyclophosphamide, hydroxydoxorubicin, vincristine, prednisolone) was performed. There was no evidence of recurrence 6 months after operation. However, close follow-up is certainly recommended.

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