Coeliac Disease Complicating to B Cell Lymphoma and Enterocolic Fistula

Wajeeha Khalid[1], Jamaluddin[2]

Abstract

We describe the case of 66 year old male, known case of COPD and type II diabetes mellitus, with a diagnosis of coeliac disease confirmed by the elevated titers of antigliadin and antiendomysium IgG antibodies together with partial villous atrophy in jejunal histology, complicating to diffuse large B cell lymphoma presented as enterocolic fistula. Laparotomy was performed which included gastrojejunostomy to bypass the fistula, ileo-ileal anastomosis to prevent obstruction, and end-transverse colostomy. Histology was taken from fistulous tract following laparotomy suspected high-grade non-Hodgkin's lymphoma. Further supplementary reports showed immunoperoxidase studies that the tumor cells are strongly positive for LCA and negative for CD30 and S100. These findings are suggestive of high grade non Hodgkins lymphoma which is confirmed by immunohistochemistry results. The biopsy showed high proliferation and soft tissue infiltration by diffuse large B-cell lymphoma which shows extensive apoptosis secondary to a complication of coeliac disease presenting as enterocoloc fistula.

Keywords: Celiac disease, lymphoma, B-Cell,fistula.
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Introduction

Coeliac disease is stated as the inflammatory condition characterized by villous atrophy leading to steatorrhea, weight loss or other signs of nutrient or vitamin deficiency[1]. Enterocolic fistula is an abnormal connection between colon and small intestine. Inflammatory bowel diseases are known to cause enterocolic fistulas but primary lymphomas involving gastrointestinal tract accounts for only 1% - 4%[2]. Enterocolic fistula formation by primary lymphoma, which is even and an unusual presentation, accounts for approximately 9% in colon as well as in small intestine[3].

[1-2] Department of Surgery, Abbasi Shaheed Hospital and Karachi Medical and Dental College

Correspondence: Wajeeha Khalid
Department of Surgery, Abbasi Shaheed Hospital and Karachi Medical and Dental College
Email: wajeeha786@gmail.com
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The following case describes a 66-year-old male, a known case of COPD and type II diabetes, with a diagnosis of coeliac disease. This was confirmed by the elevated titres of antigliadin and antiendomysium IgG antibodies, together with partial villous atrophy in jejunal histology, complicating to diffuse large B cell lymphoma presented as enterocolic fistula, which is rarely seen, and often difficult to manage. This is because of speedy detoriation of patient, limited literature availability and reported cases.

Case Report

A 66-year-old employed coal miner presented to outpatient department of Abbasi Shaheed hospital in medicine department, with the history of smoking 40-50 pack per year, progressive shortness of breath with exertion and 3 to 4 episode of productive cough for three days, especially at night. He

got admitted on 30/4/17, was a known case of chronic obstructive pulmonary disease (COPD) and type II diabetes mellitus, on combivent inhaler, metformin, and ramipril.

Upon general examination, he looked ill and lethargic. Respiratory examination showed bilateral chest wheezes and reduced air entry were revealed with 90% oxygen saturation accompanied by hyper inflated lungs on chest x-ray (Fig.1), tachypnea (90bpm), hypertension (153/80mmHg), hyponatremia (108mmol/L), and increased urine osmolality. Computed tomography of chest and bronchoscopy was done which showed no significant findings except computed tomography pulmonary angiography showed right segmental pulmonary effusion with resolution of small bilateral effusions and several pleural nodules along with mediastinal lymphadenopathy, the largest lymph node measuring 15.9mm. Patient was recommended to repeat CT chest and bronchoscopy and to remain under follow up.

CT chest and bronchoscopy were repeated and showed persistent hilar lymphadenopathy along with 1.4cm anterior mediastinal lymph node and squamous metaplasia with no malignant cells in bronchial washings respectively, with persistent hyponatremia. Full body PET/CT scan was recommended and it showed low grade Fludeoxyglucose (18F) (FDG) uptake in mediastinal lymph nodes and pleural nodules but high grade FDG uptake in abnormal loop of proximal jejunum, indicating any jejunal abnormality (Fig 2). Patient was recommended biopsy of right posterior pleural nodule to rule out any neoplastic changes but he declined

For further workup gastroenterologist were called andenteroscopy was planned which revealed partial villous atrophy on jejunal biopsy with markedly increased intra mucosal CD8 T-lymphocytes.Serologic profile showed anti-tissue transglutaminase (tTG) antibody positive, and antiendomyseal antibody positive. These findings confirmed coeliac disease. Colonoscopy was also performed to exclude any right sided pathology of bowel along with flexible sigmoidoscopy and both were normal. Hyponatremia in the patient persisted (Na=119mmol/L). Patient was asked to commence gluten free diet and to remain under follow-up.

Patient was advised follow-ups but he did not follow with appointments. Approximately after 3 months patient came to out-patient department presenting with diarrhoea for which he described 3 to 4 daily episodes of large-volume non-bloody stool with occasional nocturnal episodes. He also had complains of weight loss (10kg), severe generalized on and off abdominal pain, fever, and drenching night sweats for which he was admitted in emergency and colonoscopy was reorganized as inpatient to find out the cause of unexplained diarrhoea and weight loss in spite of having gluten free diet. Colonoscopy showed poor bowel preparation and the scope entered in small bowel soon after distal sigmoid colon. This suspected enterocolic fistula which was confirmed by the presence of small bowel mucosa on biopsy of the specimen taken from fistula. CT abdomen was done which also confirmed fistulous tract between sigmoid colon and small bowel with nodular thickening of bowel wall (Fig 3). Whole bowel was also visualized after giving gastrograffin enema, which showed no evidence of abdominal perforations or masses that might cause intestinal obstruction. Palliative laparotomy was performed which included gastrojejunostomy to bypass the fistula, ileo-ileal anastomosis to prevent obstruction, and end-transverse colostomy. Histology following laparotomy suspected high grade non-Hodgkin's lymphoma. After histopathology, oncology opinion was planned buteventually patient expired on the same day.

Supplementary reports, the next day after the death of the patient, showed immuno peroxidase studies that the tumour cells are strongly positive for LCA (leucocyte common antigen)and negative for CD30 and S100. They showed very weak non-specific staining for AE1/AE3(pancytokeratins). These findings are suggestive of high grade non-Hodgkins lymphoma which is confirmed by immunohistochemistry results showing the tumour to have p53 deregulated CD20+ CD79+ bcl6+ CD23- MUM-1- FOX-P1- CD10- Mib-1 70% CD19+/- bcl-2- CD5.

The biopsy showed high proliferation and soft tissue infiltration by diffuse large B-cell lymphoma, which shows extensive apoptosis secondary to a complication of coeliac disease presenting as enterocoloc fistula which led to the death of the patient.

Discussion

Primary intestinal tumour leading to fistula formation occurs very rarely and involving colon is even rarer. Most common complication of coeliac disease is malnutrition, bone loss, lactose intolerance, irritability, dental defects, and lymphoma and bowel cancer, if left untreated. However, primary lymphoma of intestine caused by coeliac disease progressing to enterocolic fistula formation is unlikely the complication, when its treated[1,2]. We describe the case of 66 year old male with a diagnosis of coeliac disease confirmed by the elevated titres of antigliadin and antiendomysium IgG antibodies together with partial villous atrophy in jejunal histology, complicating to diffuse large B cell lymphoma presented as enterocolic fistula. Coeliac disease is associated with the risk of lymphoma, as a complication but most common type of lymphoma associated with celiac disease complication is diffused large B cell lymphoma, the commonest type of non-Hodgkin's lymphoma[2-4]. Most common extranodal site involved by lymphoma is gastrointestinal tract accounting for 5%-20% of all cases, although lymphoma can arise from any region of the gastrointestinal tract, the most commonly involved sites in term of its occurrence are the stomach (75%) followed by small intestine (20-30%), and colorectal sites (6%-12%) usually secondary to widespread disease[2,5]. However primary lymphoma causing enterocolic fistula was unique to this case and rarely cited in the literature, hence it was an unusual presentation[6].

Symptoms of diarrhoea with persistent hyponatremia and weight loss in this patient can be explained due to enterocolic fistula causing short bowel syndrome leading to malabsorption, causing weight loss, and decrease bile salt reabsorption, which could lead to steatorrhea. Bile acids itself

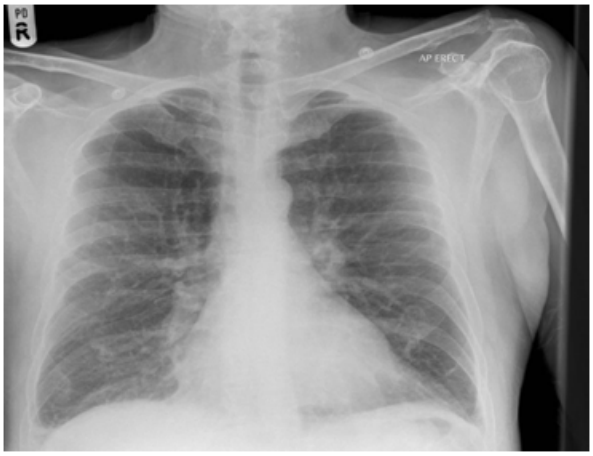

Fig 1. X-Ray chest P/ P/A view

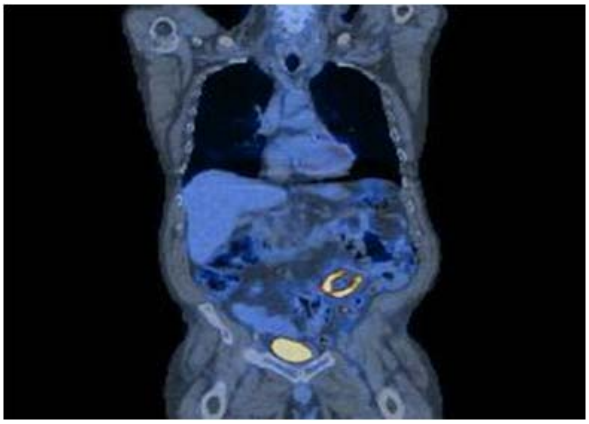

Fig 2. PET Scan; uptake in abnormal loop of proximal jejunum, indicating any jejunal abnormality

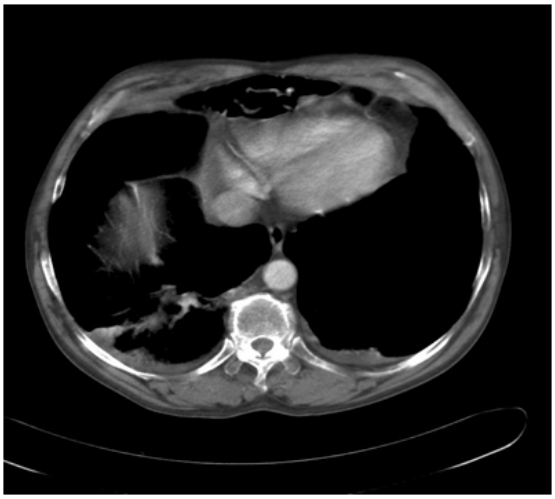

Fig 3. CT abdomen confirming fistulous tract.

cause the secretion in colon causing diarrhoea. Increased fluid load in the sigmoid colon also cannot be reabsorbed easily causing colonic fluid overload. Both of these mechanisms could lead to malabsorption of fat and fat soluble vitamins resulting weight loss. Diarrhoea could also be due to colonization of the small bowel by colonic bacteria, resulting in small bowel bacterial overgrowth. Nutritional replenishment and electrolyte balance play a central role in the management, demonstrating that the patient receiving optimal nutritional support (3000 calories per day) had mortality rate of 12%, with earlier healing of fistulas, as compared to 55% mortality among patient receiving sub optimal nutritional regimen[7]. Finally, the diagnosis of lymphoma in this case explains the patient's B symptoms (B symptoms include unexplained weight loss, fevers, and drenching night sweats). Usually enterocolic fistulas are caused by Crohn's disease but can also be seen due to prior surgery, diverticulitis, pancreatitis, foreign bodies or certain malignancies. Fistula formation can lead to debilitating complications, causing nutritional depletion and electrolyte imbalance to sepsis and even mortality. In the above mention case due to limited literature availability it is difficult to determine the fact that whether selective surgical procedure improves the prognosis or not[5,8].

Treatments modalities include localize segmental resection of the lymphoma involved intestine and its adjacent mesentery and resection of small tumours. If the small intestine is diffusely affected by lymphoma, chemotherapy plus surgery have excellent prognosis[9]. Chemotherapy after localize resection alone still remains controversial. The clinical course and the treatment of enterocolic fistula vary and depend upon aetiology and complexity. Treatment of associated infections and abscesses with antibiotics, and possibly drainage should be considered. In the above mentioned case R-CHOP chemotherapy can be considered as it has proven to improve the prognosis and shows the closing to fistula and limiting the malignancy in the patient where surgical intervention remains controversial[10].

Fistula formation is a chronic process and in its early stages, it is only confined to submucosa, which makes its early diagnosis difficult. Along with the progression of lymphoma, the fistula extents gradually to serosa and invades adjacent intestinal walls forming adhesion or fistula. Most common presenting complains of such patients are abdominal pain, diarrhoea, and weight loss which can resemble other gastrointestinal disease. However, confirmatory diagnosis still remains questionable because likewise in above case CT scan as well detected the fistula in late stages of malignancy.

Treatment options still remains unclear which is attributed to the chronicity, site, and aetiology of fistula. For definitive diagnosis, surgical laparotomy should be considered.

Conclusion

Not many evidences and explanation have been cited of entercolic fistula due to lymphoma. This is likely due to infrequent pattern of disease and less reported cases like the one mentioned above. Generally, intestinal lymphoma are presented as bowel obstruction and enterocolic fistulas are most commonly associated with Crohn's disease. In the above case, progression of lymphoma was secondary to coeliac disease with the rare presentation of enterocolic fistula. More studies of enterocolic fistula formation in this context are required in order to hypothesize the reasoning of this rare presentation.

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ANSWER OF PICTURE QUIZ

Dermatofibroma.