A rare case report of large B cell lymphoma in adult presentation as intussusception

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Abstract

Adult intussusception represents 5% of all intussusceptions. Primary gastro-intestinal lymphoma comprises 1%-4% of all gastro-intestinal malignancies 90% of them are B-cell non-Hodgkin's lymphoma (NHL). Most common NHL is diffuse large B-cell lymphoma accounts for 30-40%. Most common lymphoma causing intussusception is diffuse large B-cell lymphoma (DLBCL). We herein report a rare case of ileo-colic intussusception due to DLBCL in a 50-years-old male. Computed tomography showed ileo-colic intussusception with possibility of neoplastic etiology as a lead point. Hemicolectomy with ileo-colic anastomosis was done laparoscopically with post-operative chemotherapy. Subsequently, whole body positron emission tomography-computed tomography verified complete resolution of the malignancy. This study aims to present a rare case of ileo-colic intussusception due to non-Hodgkin's B-cell lymphoma in a patient with unusual clinical course and highlight the importance of not only the timely surgical intervention but also the significance of strict adherence to follow up and chemotherapy will completely eradicate the malignancy.

Introduction

Intussusception is described as invagination of the proximal intestinal segment (intussusceptum) within the lumen of the distal intestinal segment (intussuscipiens). Although, intussusception is common in children, it represents 5% of all intussusception and 1% to 5% of all intestinal obstruction in adults.[1] The pathogenesis is believed to be secondary to an imbalance in the longitudinal forces along the intestinal wall which can be caused by either a mass acting as a leading point or by a disorganized pattern of peristalsis (*e.g.*, an ileus in the post-operative period).[2] Unlike pediatric population, an evident etiology is established in 70-90% of cases in adults and nearly 40% of them are caused by neoplasms. Most of the lead points in small intestine are benign neoplasms, and malignancy contributes only 30%.[3] Primary gastro-intestinal lymphoma accounts for 1%-4% of all gastro-intestinal malignancies. Most frequent primary sites are stomach (50%-60%) followed by small intestine (20-30%).[4] About 90% of primary gastro-intestinal lymphoma are B-cell non-Hodgkin's lymphoma, followed by T-cell non-Hodgkin's lymphoma and Hodgkin's lymphoma. Most common part of small intestine affected by lymphoma is ileum followed by jejunum and duodenum.[5] Here we present a rare case of diffuse large B-cell non-Hodgkin's lymphoma causing intussusception.

Case Report

A 50-years-old male, resident of Hingoli district, referred to the out-patient department of our institution with two months history of chronic abdominal pain and he had also suffered from intermittent constipation and lack of appetite.

He was managed conservatively at the previous clinic for the obstructive symptoms. Pain was localized to right-lower quadrant, colicky in nature. His medical history was unremarkable. On clinical examination, abdomen was soft and non-tender. Digital rectal examination revealed presence of soft stools.

Laboratory tests of blood were within normal limits. Abdominal radiograph (Figure 1) revealed 2-3 atypical air fluid levels without obvious bowel dilatation. Contrast enhanced computed tomography (Figure 2) done at previous clinic revealed ileo-colic intussusception involving up to mid transverse colon with homogenous soft tissue density lesion in the mid-transverse colon - possibility of neoplastic etiology as lead point of intussusception, suggested histopathological correlation, multiple enlarged enhancing right paracolic nodes, terminal and distal ileal loops proximal to intussusception showing mild dilatation suggestive of bowel obstruction.

Both ileum and transverse colon were resected 5 cm from the intussusception laparoscopically using endo-stapler. The resected ends were brought together by using stapler and side to side anastomosis was done, the enterotomy site was closed with PDS. The specimen was removed by midline exploratory laparotomy along with removal of nine lymph nodes near the site of intussusception and appendix as well. Post-operative course was uneventful.

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Grossly, the resected specimen (Figure 3) was congested and gangrenous. Histologically, the tumor was arising from submucosa arranged in diffuse loosely cohesive sheets and nodules. The tumor cells were medium to large with scant cytoplasm, vesicular nuclei with prominent nucleoli. Eosinophils and eosinophilic precursors were noted admixed with tumor cells. Nuclear pleomorphism seen. Mitotic activity (2-3/10 high power field) and areas of necrosis were present. The tumor was reaching up to the serosa and both resection margins were free of tumor. Two out of 9 removed lymph nodes were involved by the tumor and showed similar histomorphology

suggesting high grade hemato-lymphoid malignancy - possibilities of: i) high grade non-Hodgkin's lymphoma (diffuse large B-cell lymphoma); or ii) granulocytic sarcoma. Immunohistochemistry is mandatory for confirmation and typing.

Immunohistochemistry showed tumor cells were positive for CD20, CD 3, CD 5, CD 10. In contrast, immunostaining for CD30, BCL 2, cMYC, CD23 and cyclin D1 was negative. Ki-67 showed high proliferative index. These findings led to a diagnosis of *Germinal center* type of diffuse large B-cell lymphoma (DLBCL) of the terminal ileum.

Patient came from a remote area therefore he was referred to the oncology unit near his hometown for adjuvant chemotherapy. Patient was instructed to follow up regularly and strictly adhere to the treatment. Patient received a total of 6 cycles R-CHOP regimen with frequency of every 21 days. Patient endured the chemotherapy with no complications. Whole body PET-CT done 1-month post-chemotherapy to evaluate the disease status concluded that there was no evidence of any FDG avid residual/recurrent lymphomatous nodal lesions or any other FDG avid extra nodal lymphomatous deposits proved complete resolution of the disease.

Discussion

Intussusception occurs when a segment of bowel and its associated mesentery (the intussusceptum) invaginates into the lumen of an adjacent bowel segment (the intussuscipiens). While intussusception is a leading cause of intestinal obstruction in children, it adds only 1%-5% of all obstructions in adults.

Intussusception in both pediatric and adult patients may be caused by an intraluminal, mural, or extraluminal process. The most easily understood mechanism by which intussusception occurs is when an intraluminal mass is pulled forward by peristalsis and drags the attached bowel wall segment with it (*e.g.*, pedunculated tumors, such as adenomatous polyps or lipomas). In trans-mural process, a focal area of bowel wall does not contract normally. Peristaltic forces in the adjacent or opposite bowel wall are then able to rotate the abnormal segment inward, causing a kink, which subsequently acts as a lead point (*e.g.*, sessile malignancies, local inflammation, surgical suture lines, flaccidity associated with gluten enteropathy and lymphoid hyperplasia). Extraluminal factors cause an adhesion that binds one side of the bowel and causes a focal area of abnormal peristalsis or kinking, which then acts as a lead point (*e.g.*, inflamed Meckel's diverticulum or appendix).[6]

Adult intussusceptions are classified into three major types according to their site in the alimentary tract: entero-enteric which is limited to the small bowel, ileo-colic or ileo-cecal in which ileum invaginated through the ileo-cecal valve and colon-colic which is confined to the colon.[7] The presenting symptoms are nonspecific, and the majority of cases in adults have been reported as chronic, consistent with partial obstruction. Colicky abdominal pain (85%-100%) is the most common presenting symptom in patients with intussusception, followed by nausea (41%-75%), vomiting (35%-70%), bleeding (16.4%-27.3%), and diarrhea and constipation (22.5%-69%). In contrast to intussusceptions in children, palpation of an abdominal mass during clinical examination is reported in 9.1% to 62.5% of adult patients with intussusception. The most common age of presentation is around the fifth and sixth decades of life with a slight male preponderance.[8]

As opposed to children, adult intussusception is idiopathic only in 10% and associated with identifiable cause in 90% individuals. Adult intussusceptions mostly arise from the small bowel, about 50%-75% are caused by benign lesions. Up to 90% of adult cases have a well-definable pathological lead point. Most lead points in the gastrointestinal tract involve primary or metastatic malignancy, lipomas, leiomyomas, adenomas, neurofibromas, postoperative adhesions, Meckel's diverticulum, foreign bodies, vascular anomalies, lymphoid hyperplasia, trauma, celiac disease, cytomegalovirus colitis, lymphoid hyperplasia secondary to lupus, Henoch-Schönlein purpura, Wiskott-Aldrich syndrome, appendiceal stump, or inflammatory fibroid polyps (IFP).[9] Less commonly, malignant lesions may act as lead points with metastases being the most common. Malignant intraluminal causes of small bowel intussusception include primary leiomyosarcomas, adenocarcinoma, GIST tumors, carcinoid tumors, neuroendocrine tumors, and lymphomas.[10]

Most common extra-nodal site involved by lymphoma is gastro-intestinal tract accounting for 5%-20% of all cases.[11] Gastrointestinal lymphoma is usually secondary to the widespread nodal diseases. Primary gastrointestinal lymphoma, consti-

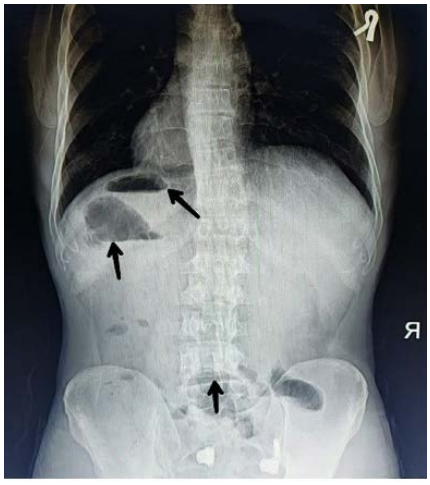

Figure 1. Plain radiograph of abdomen showing atypical air fluid levels (black

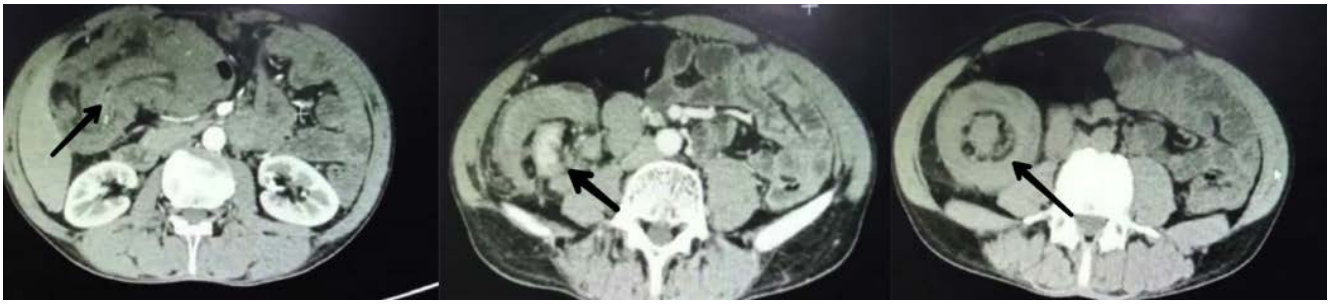

Figure 2. Axial images of contrast enhance computed tomography showing the caecum and ascending colon showing the intramural small bowel segment (black arrows), giving the typical 'target' sign appearance.

tutes only about 1%-4% of all gastrointestinal malignancies. Almost 90% of the primary gastrointestinal lymphomas are, histopathologically B cell tumors. Most common primary gastro-intestinal lymphomas are non-Hodgkin's lymphoma followed by Most common non-Hodgkin's lymphoma is diffuse large B-cell lymphoma contributes around 30-40%.Certain risk factors have been implicated in the pathogenesis of gastrointestinal lymphoma including *Helicobacter pylori* (*H. pylori*), human immunodeficiency virus (HIV), coeliac disease, *Campylobacter jejuni* (*C. jejuni*), Epstein-Barr virus (EBV), hepatitis-B virus (HBV), human T-cell lymphotropic virus-1 (HTLV-1), inflammatory bowel disease and immunosuppression.[12]

Primary malignant tumors of the small intestine accounts for less than 2% of all gastrointestinal malignancies. Lymphoma represents 15%-20% of all small intestine tumors and 20%-30% of all primary gastrointestinal lymphomas. Stomach is the most commonly involved site followed by small intestine and rectum.[13] Most common site involving in lymphoma of small intestine is ileum (60%-65%) followed by jejunum (20%-25%), duodenum (6%-8%).[14] The clinical presentation of small intestinal lymphoma is non-specific symptoms, such as colicky abdominal pain, nausea, vomiting, weight loss and rarely acute obstructive symptoms, such as intussusceptions, perforation or diarrhoea.[15] Although intussusception is a rare condition, most common lymphoma causing intussusception is diffuse large B-cell lymphoma.[16]

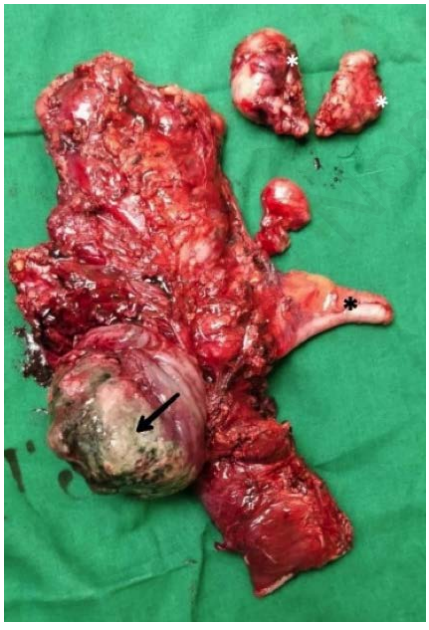

Figure 3. Resected specimen showing the gross findings of ileo-colic intussusception (black arrow) along with excised lymph nodes (white asterisks) and appendix (black asterisk).

The pre-operative diagnosis of adult intussusception is challenging because the clinical presentation is often vague and the condition is rare. An exact diagnosis can be made by detailed history and clinical examination and certain imaging modalities such as X-rays, ultrasonography (US), computed tomography (CT), magnetic resonance imaging (MRI), enteroclysis, endoscopic procedures, diagnostic laparoscopy, scintigraphy, angiography, capsule endoscopy, and FDG-PET/CT. Abdominal radiographs are the first diagnostic tool as obstructive symptoms dominate the clinical picture in most cases. Ultrasonography is considered as an important tool for the diagnosis of intussusception in both adults and children. Typical imaging features include the target or doughnut sign in the transverse view and the *pseudo-kidney*, *sandwich*, or *hayfork sign* in the longitudinal view. Overall, the sensitivity of US is 98% to 100% and specificity is 88%. Computed tomography is currently considered as the gold standard tool in confirming intussusception, with the reported sensitivity of 58% to 100% and specificity of 57%-71%. Computed tomography showing *Bowel-within-bowel* configuration suggested by mesenteric vessels and fat compressed between the walls of the small bowel is pathognomonic of intussusception. MRI is reserved for selected candidates in whom inconclusive CT findings or an atypical sonographic appearance suggests pathological lead point, such as lymphoma.[17]

Treatment of choice in adults is surgical resection of the involved bowel segment, since the lead point could be malignancy, which could not only metastasize but also attenuates blood flow, leading to necrosis of the involved bowel. Some significant clinical conditions and findings on imaging can assist the surgeon faced with adult intussusception to confidently proceed with surgical exploration: i) intussusception with associated signs or symptoms of clinical obstruction, ii) intussusception with a lead point mass appreciated on cross-sectional imaging studies, and iii) colon-colic or ileocolic intussusception given the high association with malignancy in many of these cases, particularly ileocolic. In the setting of colon-colic or ileocolic intussusception, preoperative colonoscopy can frequently be pursued to confirm the presence of pathology and/or malignancy. When indicated, surgery may be performed laparoscopically or open, depending on the skill and experience of the surgeon. Regardless of the approach, the intussusception must be successfully identified and then carefully reduced (in children) or resected (adults).

In contrast to pediatric patients, where intussusception is primary and benign, preoperative reduction with barium or air is not suggested as a definite treatment for adults The hypothetical risks of primary manipulation and reduction of the affected bowel include: i) intraluminal seeding and hemorrhagic tumor spreading; ii) perforation and seeding of microorganisms and tumor cells to the peritoneal cavity; and iii) increased risk of anastomotic complications. Azar *et al.*[10] report that, for left-sided or rectosigmoid cases resection with construction of a colostomy and a Hartmann's pouch with reanastomosis at a second stage is counted securer, particularly in the emergency setting whereas for right-sided colonic intussusceptions, resection and primary anastomosis can be carried out even in unprepared bowels.

Compared to surgery alone, adjuvant chemotherapy or radiotherapy can significantly improve event-free survival. The Danish lymphoma study group[18] found that surgery in combination with chemotherapy is superior to any other treatment combinations in localized disease. The use of chemotherapy for localized disease is unclear, but it is offered under the assumption that lymphoma is a systemic disease requiring systemic therapy. The current chemotherapeutic standard of care is cyclophosphamide, doxorubicin, vincristine, and prednisone, with or without rituximab. Surgical resection combined with this chemotherapy has been shown to independently improve overall survival for intestinal large B-cell lymphoma.[19] Salemis *et al.* reported a case of jejuno-jejunal intussusception caused by a primary B-cell non-Hodgkin's lymphoma for that resection without reduction was performed. But the patient refused the post-operative adjuvant chemotherapy. Seven months later, he came with upper gastro-intestinal bleeding, and the diagnostic assessment disclosed gastric infiltration of large B-cell non-Hodgkin's lymphoma. Despite chemotherapy he died of disseminated progressive disease 7 months later.[20] However, we counselled and instructed our patient about the significance of adjuvant chemotherapy post-operatively and educated him to adhere to strict follow-up. We referred the patient to the cancer institute near his hometown, and kept tracing him frequently. We made sure our patient completed 6 cycles of R-CHOP regimen without fail. After successful completion of chemotherapy, one month later whole body FDG-PET/CT was done. The scan revealed no evidence of residual lym-

phoma or recurrence and complete eradication of malignancy. Hence, surgical resection along with chemotherapy is the best modality of treatment for localized lymphoma causing intussusception.

Conclusions

Adult intussusception is a rare entity where history and clinical examination are imprecise. Imaging modalities are needed to arrive at the diagnosis. Once suspected, surgical intervention is needed to prevent the complications such as obstruction, ischemia, and necrosis of bowel. Besides surgical therapy, adjuvant chemotherapy plays a pivotal role in the treatment of gastro-intestinal NHL for the abolition of the tumor. We appeal to all the surgeons to be judicious in the intervention of all adult intussusceptions as almost always the cause is found and to do aggressive monitoring of adjuvant chemotherapy received by the patients. This will significantly reduce the number of patients presenting later with disseminated disease and subsequently reduces mortality caused by widespread involvement of the disease.

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