Cancer Treatment Communications 7 (2016) 62–66

Contents lists available at ScienceDirect

Cancer Treatment Communications

journal homepage: www.elsevier.com/locate/ctrc

Adult intussusception in diffuse large B-cell lymphoma following chemotherapy: A case report and literature review

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ARTICLE INFO

Article history:
Received 6 November 2015
Received in revised form
13 January 2016
Accepted 4 April 2016

Keywords:
Intussusception
Diffuse large B-cell lymphoma
Chemotherapy

ABSTRACT

Secondary adult intussusception is associated with a pathological condition involving a lead point, including malignant tumors such as a primary or metastatic adenocarcinoma, GIST, leukemia, lymphoma, or carcinoid tumor. Thirty percent of small intestine intussusception was caused by malignancy. Most of these malignancies were metastases, while primary small intestinal malignancy were rare. Intussusception in lymphoma patients has been reported, with predominant location of intussusception in the ileo-colica region. Intussusception occuring after chemotherapy has been reported in four cancer patient following chemotherapy, but no report about this condition in lymphoma patient. A 44-year-old female patient with DLBCL was diagnosed of intussusception eight days after the initiation of chemotherapy. Plain abdominal radiology and CT scan confirmed intussusception on the ileo-colica region. No surgical intervention was done due to the condition of the patient. This is the first reported case of inssusception in a DLBCL patient that had undergone chemotherapy for the lymphoma.

1. Introduction

Intussusception is the telescoping of a proximal segment of the gastrointestinal tract within the lumen of the adjacent segment [1], and rarely occurred in adults [2]. Secondary adult intussusception is associated with a pathological condition involving a lead point, including malignant tumors such as a primary or metastatic adenocarcinoma, gastro intestinal stromal tumor (GIST), leukemia, lymphoma, or carcinoid tumor. Malignant lesions was found in 30% of small intestine intussusception. They are predominantly metastases, while primary small intestinal malignancy such as adenocarcinoma, carcinoid, GIST, or lymphoma are rare [1,3,4].

1.1. Presentation of case

A 44-year-old female was admitted with complaints of nausea, vomit, and abdominal pain a week prior to admission. She vomited every time she ate, containing food, no blood or faeces. Her abdominal pain was diffuse with colicky characteristic. She had not defecated for three days and her bowel movement decreased. She had history of right axillary lymphadenopathy since a year ago, that was diagnosed from diffuse large B-cell lymphoma (DLBCL) non germinal center B-cell subtype Ann Arbor stage 1 four weeks prior to admission. Biopsy of the lymph node revealed diffusely distributed dense tumor cell with prominent large round nucleoli. There were also abnormal mitoses. The immunochemistry staining of the biopsy was positive for CD 20, Ki-67 and LCA, negative for CD 3, CD5, CD 10, CD 15, CD 30, BCL 6, Cyclin D1 and FISH for t (11;14). Her human immunodeficiency virus (HIV) serology examination was negative. She had undergone chemotherapy a week before admission with rituximab 500 mg, vincristine 2 mg, doxorubicin 70 mg, cyclophosphamide 1200 mg on the first day and prednisone 40 mg q.i.d in 5 days. On physical examination, the patient was fully alert, with blood pressure of 120/80 mmHg, and pulse of 110 beat per minute. Abdominal examination found distended abdomen with no tenderness on palpation and decreased bowel movement. Laboratory examination on the day of admission found white blood cell count of 2750/μL with segment neutrophil and lymphocyte count of 84% and 10%. Other laboratory results were within normal limit. Ultrasound examination done four weeks before admission found no signs of intussusception, or paraaortic or parailiac lymphadenopathy.

On the second day of admission, abdominal examination found distended abdomen with tenderness on palpation and absence of bowel movement. Plain abdominal radiology found high obstructive ileus (Fig. 1), computed tomography (CT) scan found intussusception with a leading point on the ileo-colica region

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http://dx.doi.org/10.1016/j.ctrc.2016.04.002
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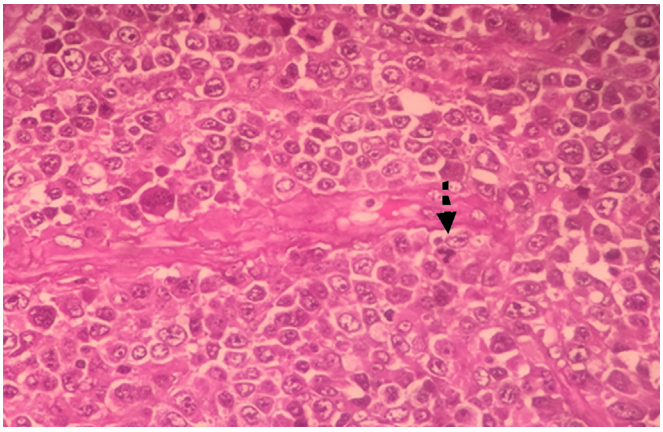

Fig. 1. Biopsy of the lymph node revealed diffusely distributed dense tumor cell with prominent large round nucleoli. There were also abnormal mitoses (dashed arrow). (100 ×, HE).

(Fig. 2). There was no evidence of perforation on plain abdominal radiology and CT scan. The white blood cell count was 540/μL with segment neutrophil and lymphocyte count of 52% and 35%. The patient was assessed as sepsis due to intra abdominal infection caused by intussusception. Patient was given granulocyte colony stimulating factor (G-CSF) of filgrastim 300 micrograms, ceftazidime 1 g t.i.d and amikacin 500 miligrams o.d., parenteral nutrition and a nasogastric tube to release the distention. Surgical intervention was postponed to optimize the patient's condition. The low neutrophil count due to the chemotherapy in this septic patient would render her condition to deteriorated if surgical intervention was done immediately. On the 5th day the patient defecated, the abdominal distention improved and bowel movement was present. Laboratory examination of the faeces showed no blood. There was no nasogastric production and she began to be fed through nasogastric tube with enteral nutrition. On the 7th day, she had septic shock, with blood pressure decreased to 80/60 mmHg and pulse increased to 130 beat per minute. Despite fluid resuscitation, vasopressor agents and antibiotics, her condition kept deteriorated and the patient passed away on the 8th day with cause of death irreversible septic shock due to intra abdominal infection caused by intussusception. Fig. 3.

2. Discussion

Intussusception is the telescoping of a proximal segment of the gastrointestinal tract within the lumen of the adjacent segment [1]. Adult intussusception is not common [2]. Adult intussusception can be classified as primary or idiopathic and secondary. Primary intussusception accounts for 8–20% cases and is more likely to occur in the small intestine, while secondary intussusception is associated with a pathological condition involving a lead point. The pathological condition includes a benign polyp, lipoma, appendix, Meckel's diverticulum, or a malignant tumor such as a primary or metastatic adenocarcinoma, gastro intestinal stromal tumor (GIST), leukemia, lymphoma, or carcinoid tumor [1,3,4]. A study found that location of adult intussusception is the small intestine that accounts for 50–88% cases and the large intestine that accounts for 12–50% cases. Malignant lesions as the pathological condition was found in 30% of cases that occur small intestine, and in 30–68% of cases that occur in large intestine. Malignant lesions as cause of large intestine intussusception are colon adecocarcinoma, lymphoma, lymphosarcoma, and leiomyosarcoma. Malignant lesions as cause of small intestine intussusception are predominantly metastases. Primary small intestinal malignancy such as adenocarcinoma, carcinoid, GIST, or lymphoma rarely cause this condition [5].

The diagnosis of the patient in this case report was DLBCL, a varian of non-Hodgkin's lymphoma (NHL). She had no abdominal pathology found on history, physical or ultrasound examination at the time of diagnosis of lymphoma. She had nausea, vomit, and abdominal pain a week prior to admission, at the same time she had undergone chemotherapy. Thus the complaints were thought to be side effects of her chemotherapy. On the second day the patient's abdomen was distended with tenderness on palpation and absence of bowel movement. Her plain abdominal radiology and CT scan confirmed an intussusception on the ileo-colica region.

The gastrointestinal tract is one of the most common extranodal sites of non-Hodgkin lymphoma (NHL). Approximately 80–90% of primary gastrointestinal tract lymphomas are of B-cell origin [6]. Gastrointestinal lymphoma could be a lead point of intussusception [7]. A review study found 36 cases of intussusception due to lymphoma. According to the location of intussusception, 24 were in the ileo-colica region, 10 were in the enteric region, and 2 were in the colica region. Thirty four were diagnosed with various types of NHL and two were diagnosed with Hodgkin's lymphoma (HL) [8]. None of the reports found intussusception after chemotherapy. The location of intussusception in this patient was in the ileo-colica region, a location of most intussusception due to lymphoma. The unusual finding in this case report was the intussusception occurred eight days after the initiation of chemotherapy, which was the first to be reported.

The summary of cases of intussusception following chemotherapy is described in Table 1. Intussusception occuring after chemotherapy were reported in an acute myeloblastic leukemia patient, 16 days after induction chemotherapy with daunorubicin and cytarabine[9] and a sigmoid colon cancer patient after 28 days (2 courses) of chemotherapy with oxaliplatin, leucovorin, fluorouracil (mFOLFOX6) [10]. The leading point of intussusception could be a cancer metastatic mass in the intestine [13]. This mass occurred due to cancer infiltration and hyperplasia of a polypoid nature or by intramural extravasation of blood that formed a hematoma [14]. A hematoma could also occurred as the result of thrombocytopenia at presentation or after chemotherapy. Enlarged lymph nodes that were common in patients with colon cancer or acute leukemia, especially the lymphoblastic type could be the leading point of intussusception [13]. Intussusception that occurred after chemotherapy might had a leading point formed by leukemic infiltrate, edema or necrosis [15].

Other 2 cases of intussusception occurred in patients with stomach cancer [11] and glioblastoma multiforme [12], after the chemotherapies had been completed. In the case of stomach cancer, 4 years after completion of chemotherapy, intussusception occurred in the descending colon thought to be the recurrence of the stomach cancer. In the case of glioblastoma, 2 years after completion of chemotherapy, intussusception occurred in the ileo-colica region thought to be secondary malignancy in the form of therapy-related non-Hodgkin lymphoma after treatment with temozolomide.

The possible explanation for the intussusception in this patient could be the same as the first two cases. Intussusception in this case occurred in the time when the chemotherapy began to take effect. The effect might formed a leading point of edema or necrosis of the cancer, lymphoma or leukemic mass or the metastatic mass in the intestine. Recurrence of cancer or secondary malignancy as in the last to cases of intussusception would be unlikely in this patient. The possibility of second malignancy in the intestine would also be unlikely, as there were no findings in history, physical examination and abdominal ultrasound of it before the chemotherapy. The definite cause of intussusception in this patient

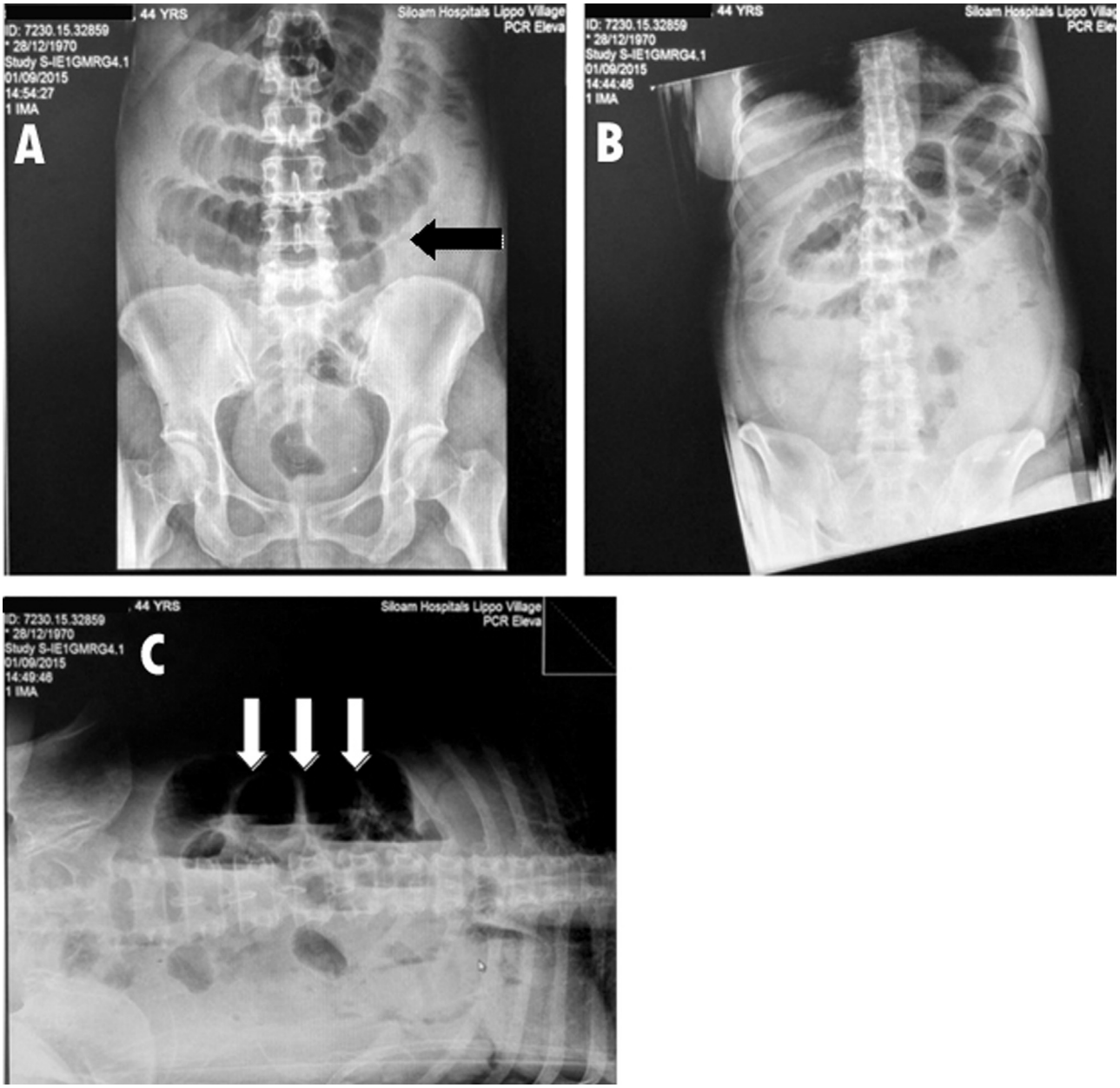

Fig. 2. Plain abdominal radiology. A. Supine position showed that the intestines in the middle of abdomen were dilated (black arrow). B. Up-right position showed no free air beneath the diaphragm. C. Left lateral decubitus position showed with multiple air fluid level (white arrow), and no free air in the abdominal cavity.

could not be determined, as no surgical intervention or autopsy were done.

The diagnosis of adult intussusception is difficult because the rarity of case and the nonspecific symptoms and signs. Diagnosis is made based on history, physical examination, and imaging examination, such as radiology, ultrasound, or CT scan. Plain abdominal radiology shows the obstructive signs that is present in most cases of intussusception. Ultrasound signs of intussusception include the target or doughnut sign in the transverse view and the pseudokidney, sandwich, or hayfork sign in the longitudinal view were not found in the patient at the time of diagnosis of lymphoma. The sensitivity and specificity of ultrasound are 98–100% and 88% consecutively, so it could rule out the presence of intussusception in this patient before the chemotherapy. Signs of intussusception on CT scan is image of bowel-within-bowel which is a picture of mesenteric fat and vessels compressed between walls of the intestines were found on the second day of admission [16,17] that was found in this patient.

A review study stated that there was still controversy about the appropriate treatment modalities for primary gastrointestinal lymphomas. Some studies implied that surgical procedures according to oncological principles are sufficient, while others support the addition of chemotherapy to surgery to increase survival. In general, chemotherapy is added to surgery in cases with poor prognostic factors, such as high LDH level, T-cell phenotype, extranodal involvement of ≥ 2, Ann Arbor stage oIII to IV, age above 60 year-old, ECOG performance status of above 1 and high positive rate of the Ki67 proliferation index immunochemically. For secondary gastrointestinal lymphomas, chemotherapy was performed first, followed by surgery in accordance to the status of intestinal involvement. The size of the surgical procedure should be determined intraoperatively in cases of intestinal obstruction requiring urgent surgery [8]. In this case, the gastrointestinal involvement of DLBCL before the initiation of chemotherapy was not clear. Intussusception occurred when the chemotherapy began to take effect. As there was axillary lymphadenopathy before

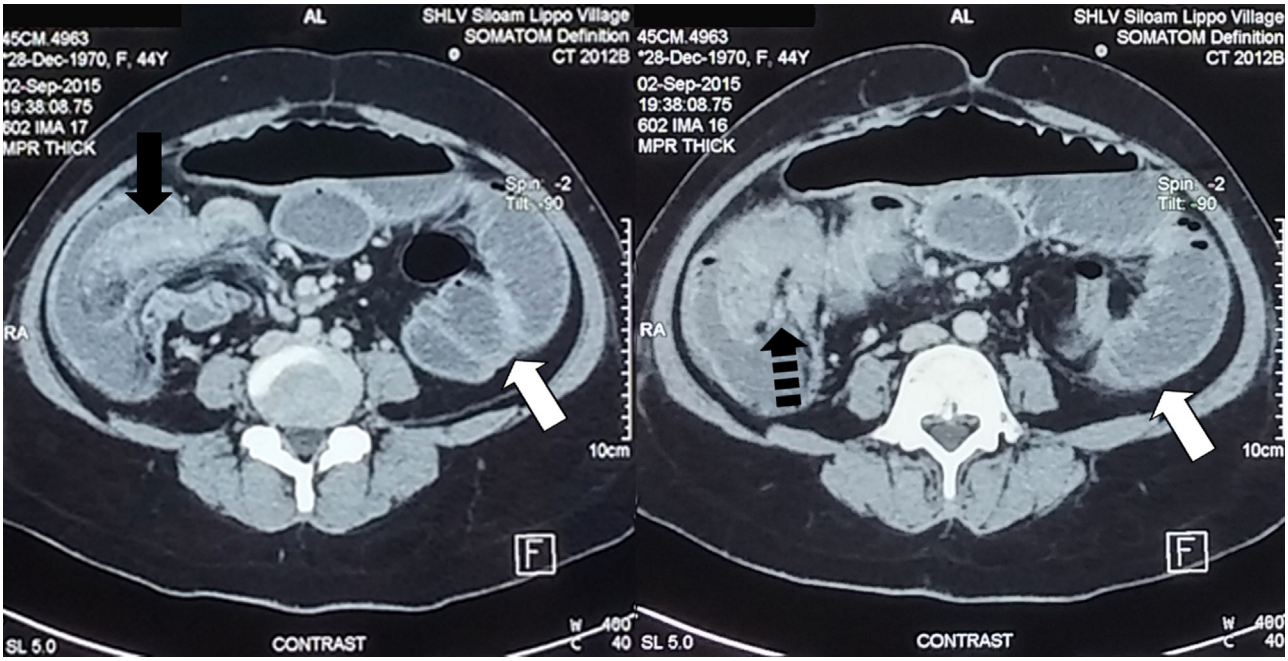

Fig. 3. Computed tomography scan of the abdomen showed dilated small intestines with no thickening of the walls (white arrow), with image of intestine within intestine (black arrow) and a leading point (dashed arrow) on the region of ileo-colica, suggestive of intussusception. No signs of ischemia and lymphadenopathy of the intestines were found.

Table 1
A summary of cases of intussusception following chemotherapy.

	Year	Age, sex	Cancer	Chemotherapy	Time (after the first course of chemotherapy)	Location	Management
Law MF, et al. [9]	2015	29, F	Acute myeloid leukemia	Daunorubicin, cytarabine	16 days	Ileo-colica	Right hemicolectomy
Kida K, et al. [10]	2012	62, F	Sigmoid colon cancer	Oxaliplatin, leucovorin, fluorouracil (mFOLFOX6)	28 days (2 courses)	Sigmoid colon	Sigmoidectomy
Fukuchi M, et al. [11]	2011	74, M	Stomach cancer	Irinotecan, S-1, paclitaxel	4 years 2 months	Descending colon	Left hemicolectomy
Raman V, et al. [12]	2014	6, M	Glioblastoma multiforme	Temozolomide	2 year	Ileo-colica	Right hemicolectomy

chemotherapy and gastrointestinal involvement after chemotherapy, the gastrointestinal lymphoma in this case was thought to be secondary. In secondary gastrointestinal lymphoma, chemotherapy is the first line of treatment followed by surgery. There would not be any difference in the management had the gastrointestinal lymphoma had been identified before chemotherapy.

Management of adult intussusception is surgical intervention [18]. Surgical intervention which is a resection of the segment of the intestine with lymphoma is recomended because it may relieves obstruction, eliminates the risk of perforation, and reduces the likelihood of hemorrhage [19]. This patient had intussusception in the ileo-colica region after chemotherapy for lymphoma, so infiltration was suspected thus resection of the involved intestine should be performed.

The timing of surgical intervention in neutropenic patients is still a dilemma. A study on surgical conditions in neutropenic cancer patients found that neutrophil counts should be improved to prevent serious comorbidities and that surgery should be delayed, when possible, to allow for neutrophil to recover [20]. Other study recommended conservative, nonsurgical approach based on bowel rest, nasogastric suction, total parental nutrition and broad-spectrum antibiotic therapy in neutropenic enterocolitis patients without complications such as peritonitis, perforation or bleeding [21]. The patient showed no evidence of peritonitis, perforation or bleeding. On the 5th day the patient defecated, there was no nasogastric production, the abdominal distention improved, bowel movement was present and there was no blood on faeces examination. Based on these findings, surgical intervention in this patient was postponed to optimize her condition. The low neutrophil count due to the chemotherapy in this septic patient could deteriorated her condition if surgical intervention was done immediately. But her condition deteriorated before surgical intervention could be done.

In conclusion, this is the first reported case of inssusception in a DLBCL patient that had undergone chemotherapy for the lymphoma. The nature of the post chemotherapy patient with sepsis presented dilemmatic situation on the management of the intussusception.

Conflict of interest statement

All authors have no conflict of interest to be declared.

Acknowledgments

This study received no grants or funds from any source.

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