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Intussusception as clinical presentation of primary non-Hodgkin lymphoma of the colon in a HIV-patient

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ABSTRACT
Intestinal intussusception rarely occurs in the adult population and accounts only for 1% to 5% of all the causes of intestinal obstruction. This complication is more frequent in the small bowel and can be due to different aetiologies, including inflammatory, infectious or neoplastic diseases. Malignancies account for 50% to 60% of all cases of colon invagination. The gastrointestinal (GI) tract is the most common site for extra-nodal non-Hodgkin lymphomas (NHL), representing 5% to 20% of all the cases. However, primary NHL of the GI tract is a very infrequent clinic-pathological entity and accounts only for 1% to 4% of all the neoplasms of the GI tract. Primary NHL of the colon is a rare disease and it comprises only 0.2% to 1.2% of all colonic malignancies. Here we describe a case of an AIDS adult patient who developed an intussusception secondary to a primary large B cell lymphoma of the transverse colon. English and Spanish literature was reviewed.
Key words: Primary non-Hodgkin lymphoma of the colon. Intestinal intussusception. HIV. AIDS.

INTRODUCTION
Intestinal intussusception or invagination is defined as the introduction or telescoping of a segment of the GI tract within the lumen of the adjacent segment. Generally, this complication is associated with the obstruction to the passage of the intestinal content as well as the reduction of the vascular flow with ischemia and necrosis of the intestinal wall (1). Intestinal intussusception is a frequent complication in the pediatric population but is very rare in adults, where intussusception represents only 1% to 5% of the cases of intestinal occlusion. Aetiologies also differ in comparison to pediatric cases (2,3).

Patients infected with human immunodeficiency virus (HIV) present a high risk to develop non-Hodgkin lymphomas (NHL). HIV associated NHL is characterized by the frequent extra-nodal involvement as the primary clinical manifestation of the neoplasm (70% to 80% of cases), “B” phenotype and high grade histopathological subtype. Here we describe the case of a HIV positive patient who developed a colonic intussusception as clinical presentation of primary NHL.

CASE REPORT
A 44-year-old man with a history of HIV infection diagnosed 20 years before, anti-hepatitis C antibodies and inhaled drug abuse was admitted to our hospital with a 20 day history of intermittent abdominal colicky pain, predominantly on the periumbilical region and in the left flank, and fever, night sweats and weight loss (5 kg) during. He was receiving highly active antiretroviral therapy (HAART) based on tenofovir, emtricitabine and ritonavir-boosted lopinavir.

One day before hospital admission, the patient reported worsening abdominal pain, nausea and vomiting. Physical examination revealed painful abdominal distention without signs of peritoneal irritation. Bowel sounds were present. The rest of the physical examination was unremarkable. Chest-X-ray was normal.
Relevant laboratory findings included: red blood cell count 5.2 x 10^6/L, haematocrit 46% haemoglobin 14.9 g%, white blood cell count 6.2 x 10^9/L, platelets 142 x 10^3, erythrocyte sedimentation rate 110 mm/h, lactate dehydrogenase (LDH) 450 U/L, renal and liver functions were normal. The CD4 T-lymphocyte count was 150 cells/µL and the plasma viral load was undetectable (less than 50 copies/mL). Abdominal X-ray showed the dilatation of the cecum, ascending and transverse colon ahead of the invagination. Abdominal ultrasound revealed an image compatible with intestinal intussusception and hypoechoic lesions on the colon wall consistent with diffuse lymphomatous infiltration of mucosa and submucosa. On the transverse plane, “target sign” or “doughnut sign” with the invaginated intestinal loop (Fig. 1, arrows) was observed. Diagnosis of intestinal intussusception was made and the patient underwent a laparotomy. It confirmed the intussusception of the transverse colon caused by an infiltrative tumor. A transverse hemicolecction with resection of 18 cm of the colon with a termino-terminal anastomosis was made. There were no postoperative complications. Histopathology of the surgical piece showed a serosa without relevant changes; adjacent to the serosa, an exophytic tumoral lesion of 6.3 x 6 cm that occluded 80% of the intestinal diameter and 95% of the lumen, 5.2 cm of margin of resection, was detected. Microscopy examination of the biopsy smears showed a dense proliferation of atypical lymphoid cells, of median and large-sized, eosinophilic cytoplasm and one or various nucleoli next to the basal membrane, underlying a transmural infiltrate of atypical lymphocytes with extensive areas of ulceration and necrosis (Fig. 2). Histopathology of 15 lymph regional nodes was normal. Immunohistochemistry revealed that neoplastic cells were positive for CD20 (Fig. 3), partial expression of leukocyte common antigen (LCA) and BCL6 with co-expression of BCL2 and MUM1 in 60% of the overall cellularity. Ki67 proliferation index was high (> 90%). A computed tomography (CT) scan of the thorax, abdomen and pelvis was normal and a bone marrow biopsy was negative for atypical neoplastic infiltration. Final histopathological diagnosis was primary diffuse large B cell lymphoma (DLBCL) of the colon (WHO).

DISCUSSION
GI tract is the most common site of extra-nodal NHL, accounting for 5% to 20% of all the cases. However, primary NHL of the gastrointestinal tract is a rare clinical-pathological entity comprising only 1% to 4% of all the gastrointestinal malignancies (4). Although NHL can affect any region of the GI tract, oral cavity, stomach, small intestine and ileocecal region are the most commonly involved sites (5). Primary NHL of the colon is a rare tumor representing only 0.2% to 1.2% of all colonic malignancies (6). These tumors are more frequent in men with a median age of 55 years at diagnosis (6).

Clinical presentation includes insidious abdominal pain, nausea, vomiting, “B” symptoms (fever, night sweats and weight loss), abdominal mass and, most rarely, rectal bleeding (6,7). The most common locations are the cecum and the left colon; colonoscopy, ultrasound and computed tomography scan findings are similar to those of epithelial tumors (6). Only histopathological examination and immunohistochemistry techniques confirm the diagnosis (8). Histologically, 85% of cases are B-cell lymphomas and the most frequent histopathological subtypes, according to the REAL/WHO (Revised European-American Classification of Lymphoid Neoplasms/World Health Organization) are DLBCL, as in our patient, mucosa-associated lymphoid tissue (MALT) lymphoma, mantle-cell lymphoma and Burkitt’s lymphoma (6).

In adults, intussusceptions with acute or subacute intestinal obstruction represents only 5% of cases and the small bowel is the most common site of the invagination (3). Intussusceptions can be classified according to the anatomical location into entero-enteric, ileocecal, ileo-colic and colo-colonic (9). In the ileocecal location, the valve acts as the initial point of the invagination (10).

In the last years, a significant number of adult intussusceptions have been reported in AIDS patients, the majority of cases due to Kaposi’s sarcoma and NHL of the GI tract (11). Malignancies are the most common causes for adult intussusceptions of the large bowel, especially adenocarcinoma and secondary NHL. Miscellaneous causes include post-operative adhesions, benign lesions (lipoma, leiomyoma and adenomatous polyps), endometriosis and tuberculosis (9,10).

In a recent review of adult intussusceptions, Kaval et al. (12) analyzed 17 patients assisted between 1998 and 2012. In this series, the median age was 35 years old, the majority of patients were males (11 cases) and intussusception involved the small bowel in 70.5% of
cases. In 29.4% of the cases the large bowel was affected. Malignancies were the only cause of intussusceptions of the large bowel, as in the present case.

Abdominal ultrasound is a low cost, non-invasive method with similar sensitivity and specificity to CT scan (10,13). Typical ultra-sonographic features associated with intussusception include the “target sign” or “doughnut sign” on transverse plane and “pseudo-kidney sign” or “hayfork sign” on longitudinal view. In the study carried out by Kaval et al. (12), abdominal ultrasound revealed the diagnosis in 58.8% of cases (10 of 17 patients), and in all cases diagnosis was confirmed by CT scan. In the other 5 cases, diagnosis was only suspected by CT scan. CT scan aided in the pre-surgical diagnosis of intussusception in 15 (88.2%) patients. Enhancement surrounding the intussusception can be seen after the injection of contrast. CT scan may also contribute to define the location, characteristics of the tumor and its relationship to the surrounding tissues. Additionally, it may help to establish the stage of the neoplasm (9).

In our patient, IHQ was positive for CD20 and LCA and negative for cytokeratins, confirming the diagnosis of DLBCL (WHO). The patient had a tumor of the transverse colon without regional lymph nodes or bone marrow infiltration. Laboratory findings and CT scan of the thorax, abdomen and pelvis were also normal. In consequence, our case filled the criteria of Dawson and Richard for the diagnosis of primary NHL of the colon (14).

Primary NHL of the colon is an uncommon disease with a few number of cases published in the medical literature. The optimal treatment of this neoplasm is yet to be established. Surgical treatment is necessary in adult patients, as in our case, due to the frequency of organic lesions. Surgery is the treatment of choice to resolve the intussusception and the obstruction in case of ileocecal or colonic involvement. Surgery is also necessary to obtain a biopsy to establish the diagnosis and to assess the regional extension of the neoplasm. Surgery is the first-line therapy in complications such as perforation (15).

Currently, chemotherapy alone is the gold standard treatment and is complementary to surgery, as in our patient (10). CHOP (cyclophosphamide, doxorubicine, vincristine and prednisone), with or without rituximab, is the most used regimen in both immunocompetent and immunocompromised patients (6).
In conclusion, intussusception is an infrequent cause of mechanical intestinal obstruction in adult patients that should be included in the differential diagnosis of abdominal pain in HIV/AIDS patients. In those cases of colonic involvement, NHL should be considered as a probable diagnosis due to the high frequency of these tumors in the HIV population.

REFERENCES
Fig. 1. Ultrasonographic image, transverse plane: “doughnut sign” (arrows).
Fig. 2. H/E 40x: Transmural infiltration by atypical lymphoid cells with extensive areas of ulceration and necrosis.

![Image of transmural infiltration by atypical lymphoid cells with extensive areas of ulceration and necrosis.]

Fig. 3. Expression of CD20 for the majority of atypical lymphoid cells.