

BURKITT LYMPHOMA – CLINICIANS’S PERSEVERANCE IN ESTABLISHING THE DIAGNOSIS

Lorena Elena Melit¹, Oana Cristina Marginean¹, Mihaela Chincesan¹,
Andreea Dinca¹, Raluca Damian², Maria Oana Marginean¹

¹*Pediatrics Clinic 1, University of Medicine and Pharmacy, Targu-Mures*

²*Neonatology Clinic 1, Emergency Clinical County Hospital of Targu-Mures*

ABSTRACT

Burkitt lymphoma, a subtype of non-Hodgkin lymphomas, appears especially in small ages and it presents the most rapid tumor growth encountered in the human beings. We present the case of a 5 year-old child who presents diffuse, abdominal pain, abdominal distension and decreased consistency stools, and who is transferred in the Pediatrics Clinic 1 Targu-Mures, with the diagnosis of severe malnutrition and hypoproteinemia edema of unknown etiology. The laboratory investigations performed showed leukocytosis, mildly increased erythrocyte sedimentation rate, anemia, decreased level of serum proteins, and also an increased level of LDH. The abdominal ultrasound revealed intraperitoneal fluid, and the abdominal CT exam showed free fluid between the intestinal loops, 2 fistulas, one between the duodenum and the colon, and the other one between the jejunum and the colon, but also enlarged lymph nodes. The surprise during the surgery is the discovery of a tumor mass which involves the duodenum, the jejunum and the colon, and the pathological exam establishes the diagnosis of Burkitt lymphoma, extranodal type, with evolution after surgery burdened by multiple complications. After the third surgical intervention, the chemotherapy is initiated. Even though in some cases, the clinical picture is not suggestive for the severity of the pathology, the clinician’s perseverance is the one that finally leads to the establishment of the diagnosis.

Keywords: Burkitt lymphoma, child, diagnosis

INTRODUCTION

Burkitt lymphoma is a type of B cells non-Hodgkin lymphoma, with an incidence of approximately 5%, which was described for the first time in children from Africa between the years 1958-1962 (1). More than half of this children presented jaw tumors, but then it was proved that this type of tumor can affect other organs too, such as the ileum, cecum, ovaries, kidney and breast. Non-Hodgkin lymphoma is the most frequent malignant tumor of the bowel, which affects the children over the age of 5, whose etiology was initially related with Epstein-Barr virus (EBV) infection (2,3). The degree of malignancy of these tumors is very high and with the most rapid tumor growth encountered in human beings (4,5). In case of a Burkitt lymphoma suspicion, especially in developing countries, it is mandatory for the physician to perform

an abdominal ultrasound or a CT exam, that can establish the possible malignant character of the tumor (6,7). In order to establish the extension of the disease, it is also necessary to perform a thorax radiography and, or a thorax CT, medullary and spinal fluid examinations. The sites of appearance for Burkitt lymphoma are different, being able to affect lymph nodes, thus leading to a lymph node type, or it can involve different organs, type called extranodal. The clinical symptoms and signs that appear in case of patients suffering from Burkitt lymphoma of the gastrointestinal system, can be: abdominal pain, abdominal distension, gastro-intestinal bleeding, obstruction by compression, bowel occlusion, bowel perforation, or even peritonitis. Due to the very fast growth and to the high degree of malignancy of this type of non-Hodgkin lymphoma, in the lack of early treatment or diagnosis, these patients die very quickly because of the tumor spread-

Corresponding author:

Oana Cristina Marginean, University of Medicine and Pharmacy, 38 Gh. Marinescu Street, Targu-Mures

E-mail: marginean.oana@gmail.com

ing with liver metastases, kidney ones or metastases in other organs. The differential diagnosis implies other types of abdominal tumors, peritoneal carcinomatosis, TBC of the gastrointestinal tract, etc. The positive is established by the pathological exam and immunohistochemistry. The treatment of Burkitt lymphoma consists in surgical resection and intensive chemotherapy. Usually are used combinations like cyclophosphamide, cytarabine, doxorubicine, etoposide, methotrexate, vincristine, etc. In some particular cases, the intensive chemotherapy can be combined with Rituximab (monoclonal antibody), radiotherapy, stem cells autologous transplantation or steroids therapy.

CASE PRESENTATION

We present the case of a 5 year-old boy, known from birth with a brachial plexus paresis of obstetrical etiology, with personal history of epilepsy diagnosed at the age of 3 years, under antiepileptic treatment, who from approximately half a year presents modified consistency stools, even diarrheic, and abdominal pain. Due to these reasons, the child was admitted at the regional hospital with the diagnosis of severe malnutrition, low protein edema, whose etiology could not be established, therefore he was transferred in the Pediatrics Clinic 1 Targu-Mures, compartment of Gastroenterology, in order to perform supplementary investigations.

The clinical exam performed at the moment of admission reveals influenced general status, weight deficit (14 kg), ailing facies, pale/sallow skin, edema of the inferior limbs, burn mark on the anterior thorax, multiple dental caries, conjunctive-adipose tissue very weak represented, especially on the superior and inferior limbs and the thorax, hypotonia of the right superior limb (brachial plexus paresis), thorax with large base, systolic murmur second degree, distended abdomen, above the xiphopubic level, with the presence of abdominal meteorism, without spontaneous contraction of the abdominal muscles, elastic, diffuse abdominal pain on palpation, bowel movements present, decreased consistency of the stools, physiological micturition, without meningeal irritation signs.

The laboratory investigations revealed a mildly increased erythrocyte sedimentation rate (25 mm/h), leukocytosis (Leu 15,500/mm³), and hypochromic microcytic anemia (Hb 7.76 g/dL, Htc 23.5%, MCV 64.6 fL, MCH 21.4 pg). The biochemical parameters pointed a value of LDH above the upper normal limit (300 U/L), hypoproteinemia (total proteins 5.76 g/dL) and decreased level of serum

iron (Fe 3.23 μmol/L), normal liver and kidney function. The culture from the stools, the parasitological exam and the digestion probes did not show any pathological aspects. The abdominal ultrasound revealed liquid in the abdominal cavity: near the gall bladder and the liver, between the bowel loops, in the Douglas space, and increased abdominal meteorism (Fig 1, 2). Raising the suspicion of megacolon, we performed irigography, which showed distension of the entire colic frame, at the level of the jejunum loops and also enlarged sigmoid. The colonoscopy did not revealed any pathological elements macroscopically, only a dilated intestinal lumen. Because the gastrointestinal symptoms persisted, the abdominal pains became more intense, the hemoglobin decreases after 5 days to 6.9 g/dL, and the abdominal ultrasound shows an increased quantity of intraperitoneal liquid, we decided to repeat the CT examination of the abdomen and pelvis, even though the CT performed initially in the regional hospital did not show any pathological aspects. The abdominal and pelvic CT performed in our clinic revealed intense stasis at the gastro-duodenal level, fistula between the proximal jejunum loops and the descendent colon, ischemia of the bowel walls of the involved loops, mesenteric enlarged lymph nodes and minimal adjacent fluid collections.

Raising the suspicion of a peritonitis with fistula between the jejunum and the colon, we decide to transfer the patient in Pediatrics Surgery Clinic, where it is performed exploratory laparotomy, which reveals a tumor mass that interests the left colic angle, the terminal part of the duodenum, the angle between the duodenum and the jejunum, with perforation of the duodenum, jejunum, colon, covered perforations. It was removed the terminal part of



FIGURE 1. Ascites in the hepato-renal Morrison space

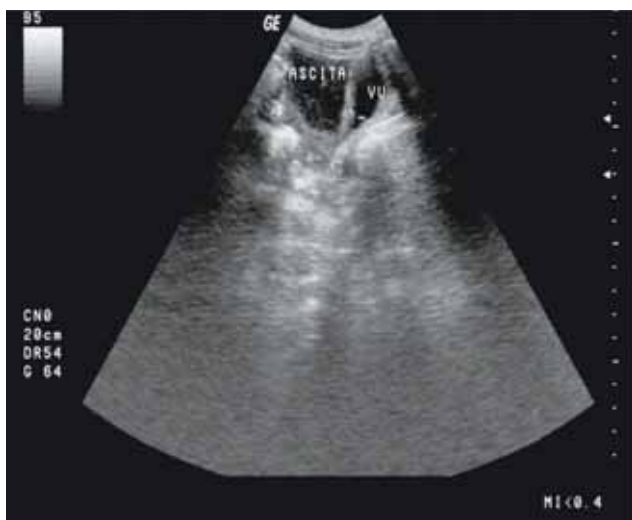


FIGURE 2. Ascites in the Douglas space

the duodenum, the angle between the duodenum and the jejunum and the left colic angle, and it is performed an anterior anastomosis between the stomach and the duodenum and colostomy. The evolution after surgery was not favorable, the general status worsened, with the appearance of biliary liquid on the drainage tubes, and during the surgical re-intervention, it was noticed a distal duodenal fistula and also a left colonic one. These were sutured and it was performed an anastomosis between the jejunum and duodenum, with initially favorable evolution. After another week, the general status altered again, the patient presented vomiting, abdominal meteorism and the absence of stools in the colostomy bag, reason for which, thus during the third re-intervention, there were noticed multiple adhesions between the intestinal loops. In the end the evolution after surgery was favorable, the patient started to eat by mouth, intestinal bowel movements present, with stool elimination in the colostomy bag.

The pathological exam of the removed operator specimens (duodenum, jejunum and colon) reveals a lymphoproliferative malignant process that infiltrates the entire colonic wall and partially the duodenum and the jejunum. The morphological aspect and the immunophenotype of the tumor cells and the localization of the lesion pleads for high malignancy degree lymphoma, extranodal Burkitt lymphoma. The 5 lymph nodes examined that did not present tumor involvement.

The diagnosis of Burkitt lymphoma is established. The patient is transferred again in the Pediatric Clinic 1, compartment of Hemato-Oncology, in order to initiate the chemotherapy after surgery. After completing the paraclinical and imagistic exams in view of staging (normal bottom eye exam,

negative cranial and thoracic CT, negative medullary exam), the case is labeled as Burkitt lymphoma, third stage. It is decided the initiation of chemotherapy according to B-NHL BFM 04 protocol that comprises cytoreductive prephase (V), followed by 6 cycles of chemotherapy (A²⁴; B²⁴- 3 cycles of each). Until now, the patient received prephase V and the first cycle A²⁴ associated with supportive treatment, with favorable evolution.

DISCUSSIONS

Burkitt lymphoma is part of the non-Hodgkin lymphoma class that are on the 4th place as incidence of the malignant tumors in the children from United States (8). The surgical treatment remains essential; the resection of the tumor preventing the complications and increasing the effect of chemotherapy. This type of is often present as extranodal type, as in the case we presented, where it appears the intestinal involvement, or as an acute type leukemia (9). The clinical presenting picture of the patients with Burkitt lymphoma of the gastrointestinal tract comprises: diffuse, persistent, abdominal pain, abdominal distension, constipation, gastrointestinal bleeding, etc. Part of these symptoms were present also in the case of our patient, but he presented modified consistency stools (even diarrheic, 1-2/day) due to the 2 fistulas between the intestinal loops, through which it was created a type of shunt of the intestinal transit. The ileo-cecal localization of the tumor can lead to repeated invaginations or repeated episodes of bleeding (10). The latter one being also met in the case of our patient, the progressive decreasing of the hemoglobin was a sign of occult bleeding at the level of the gastrointestinal tract. There are also unusual cases of presentation of Burkitt lymphoma, such as acute pancreatitis, described in a 13 year-old child, who presented infiltration of the gastric and duodenal wall (11). The advantage of this type of presentation is that it leads to an early establishment of the diagnosis, and thus to a better prognosis. The appendix is another extranodal situs, being maybe the most indicated organ to be explored in the case of Burkitt lymphoma suspicion because it is a lymphoid organ. Thus, this type of lymphoma can mimic an acute appendicitis, though with low incidence, as in the two cases described by Weledji et al, two female patients, one 13 years old and the other one 18 years old (12). Another rare situs for the localization of Burkitt lymphoma is the peritoneum that can lead to a delay in establishing the diagnosis, as in the case of the 61 year-old patient described by

Oliveira et al, who presented due to an increase in volume of the abdomen, from approximately 3 days, without any associated symptoms (13). Burkitt lymphoma can be localized also in other organs, such as the kidney, the ovary, the breast, etc. In very rare cases, there can appear the synchronous involvement of two different organs, being described in the specialty literature the case of a 15 year-old teenager, with the involvement of the stomach and the ovary, mimicking a Krukenberg tumor, not only implants of the Burkitt lymphoma in these two organs, fact that is often encountered (14). The diagnosis can also be difficult to establish in case of pregnant women, due to increased frequency of gastrointestinal symptoms during pregnancy, such as nausea, vomiting, and also due to the hesitation to perform paraclinical examinations

during pregnancy, such as digestive endoscopy (18), as in the case of a 26 year-old pregnant woman, diagnosed in the last month of pregnancy with gastric Burkitt lymphoma (15).

CONCLUSIONS

The particularity of our case presented by us underlines the difficulties encountered by the clinician in establishing the diagnosis when the clinical signs and the laboratory investigations are in contradiction with the imagistic investigations. The early establishment of the diagnosis in order to initiate the chemotherapy remains a crucial factor for the surviving of these patients, which needs perseverance in order to surpass the provocation of the diagnosis.

REFERENCES

1. **Burkitt D.** A sarcoma involving the jaws in African children. *Br J Surg* 1958; 46: 218-223.
2. **Brady G., MacArthur G.J., Farrel P.J.** Epstein-Barr virus and Burkitt lymphoma. *J Clin Path* 2007; 60(12): 1397-1402.
3. **Mulima N., Molyneux E., Jaffe H. et al.** Association between Burkitt lymphoma among children in Malawi and infection with HIV, EBV and malaria: results from a case-control study. *PLoS One* 2008; 3e: 2505.
4. **De Leval L., Hasserjan R.P.** Diffuse large B-cell lymphoma and Burkitt lymphoma. *Hematol Oncol Clin North Am* 2009; 23: 791-827.
5. **Klein E., Klein G.** Burkitt lymphoma. *Semin Cancer Biol* 2009; 19: 345-346.
6. **Bissen L., Brassen L., Azagra J.S., Deirie P.** Burkitt's lymphoma of the appendix. *JBR-BTR* 2002; 85: 257-259.
7. **Biswas S.** Report of a case of abdominal Burkitt's lymphoma presenting as a localised right iliac fossa pain mimicking acute appendicitis. *Interneer J Surgery* 2007; 9: 1.
8. **Ward E., DeSantis C., Robbins A. et al.** A Childhood and adolescent cancer statistics, 2014. *CA Cancer J Clin* 2014; 64: 83-103.
9. **Swerdlow S.H., Campo E., Harris N.L. et al.** World Health Organization Classification of Tumors of Haematopoietic and Lymphoid Tissues. Lyon, France: IARC Press, 2008: 262-264.
10. **Grajo J.R., Kayton M.L., Steffensen T.S. et al.** Presentation of Ileal Burkitt Lymphoma in Children. *Radiology Care* 2013; 6(8): 27-38.
11. **Silva Gloria F., Paiva M., Tavares A. et al.** Pediatric Burkitt lymphoma presenting as acute pancreatitis. *Acta Med Port* 2008; 21: 515-520.
12. **Weledji E.P., Ngowe M.N., Abba J.S.** Burkitt's lymphoma masquerading as appendicitis – two case reports and review of the literature. *World Journal of Surgical Oncology* 2014; 12: 187.
13. **Oliveira C., Matos H., Serra P. et al.** Adult abdominal Burkitt lymphoma with isolated peritoneal involvement. *Radiology Care* 2014; 8(1): 27-33.
14. **Ziade F., Von der Weid N., Popovic-Beck M., Nydegger A.** Burkitt's lymphoma – an atypical presentation. *BMC Pediatrics* 2012; 12: 113.
15. **Tazi I., Nafil H., Mahmal L.** Epigastric discomfort during pregnancy presenting as gastric Burkitt lymphoma. *African Health Sciences* 2011; 11(2): 288-289.