

# Primary Gastric Localization of Diffuse Large Cell Lymphoma and Viral Hepatitis C. A Case Report at the Department of Clinical Hematology of University Hospital of Yopougon, Abidjan (Côte d'Ivoire)

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Non-Hodgkin's lymphomas are characterized by its clinical and pathological polymorphism. In the stomach, MALT lymphomas are common and mostly associated with *Helicobacter Pylori* infection. We report a case of 76-year old woman with a medical history of chronic stomach pain, addressed for the investigation of normochromic normocytic anemia. The clinical picture included signs of digestive hemorrhage and stomach pain. Gastrointestinal endoscopy and histology noted an unspecified ulcer-budding tumor without signs of *Helicobacter pylori* infection. Immunohistochemistry concluded to diffuse large B cell lymphoma with CD79b +, BCL10 +/-, BCL2+, BCL6 +, MUM1+. The Ann Arbor classification was stage IE. The serology of *Helicobacter pylori* was negative. Pre-treatment investigation noted a comorbidity with Hepatitis C infection. This study has two interests. Firstly the rarity of the localization of this lymphoma, and secondly, the etiopathological interest because of association with hepatitis C virus.

**KEYWORDS:** Diffuse Large Cell Lymphoma, Stomach, Hepatitis C Virus

## INTRODUCTION

Non-Hodgkin's malignant lymphomas are malignant haemopathies characterized with clinical and anatomy diversity.<sup>1,2</sup> Extra-ganglionic forms are less frequent and represent 1/3<sup>rd</sup> of the sites, which 36% are gastrointestinal locations. The most common is gastric lymphoma of MALT.<sup>3,4</sup> Among the exposure factors, there are infectious agents including *Helicobacter pylori* in 80% of Gastric lymphoma<sup>5,6</sup>, the hepatitis C virus in 38.4% of low grade lymphomas.<sup>7</sup> Diffuse Large B cell lymphoma (DLBCL) is aggressive lymphoma. It accounts for about 40% of all Non-Hodgkin Lymphomas. Localized forms are infrequent and represent 35 to 45% of cases, and disseminated forms 55 to 65% of cases.<sup>8</sup> The primary localization of Diffuse Large B cell lymphoma in the stomach is a unusual situation. We report in this study a case of diffuse Large B cell lymphoma of the stomach without secondary dissemination associated with hepatitis C virus. The interest of this study was the rarity of this localization and the etiopathological interest because of association with hepatitis C virus.

## CASE REPORT

Mrs. G.B, 76 years old, with a medical history of chronic stomach pain, was referred for the investigation of normochromic normochromic anemia. According to the anamnesis the symptoms started about three (03) months ago with a permanent stomach pain associated with three episodes of the hematemesis and melena. Context of fever, weight loss, night sweats was noted. She consulted to the general hospital of her locality where

blood cell count exam discovered the anemia with 7g/dl of hemoglobin. Then she was addressed for investigation in our department. The clinical examination found the stage I of performance status of WHO, with the temperature of the fever being 38° C. The rest of the examinations are without particularities. The paraclinical examination found in blood cell count: Leukocytes at 9800/mm<sup>3</sup>, Neutrophils at 1500/mm<sup>3</sup>, hemoglobin at 9g/dl, reticulocytes at 60000/mm<sup>3</sup>, lymphocyte at 1800 /mm<sup>3</sup>, blood platelets at 170000 /mm<sup>3</sup>. The marrow bone examination was normal. We had requested a gastric endoscopy which noted budding gastric lesions of malignant appearance. Anatomopathology exam found a tumor proliferation consisting of lymphoid cells whose diameter was medium to large. Immunohistochemistry noted the expression of CD79b and it did not have a significant expression of CD10. These cells expressed BCL2, BCL6, MUM1. They didn't express CD5 and CD3. The proliferative activity was variable in places. There was the presence of some positivity of tumor elements for C-myc gene. The body scan, entero-scan and the colonoscopy were normal. The inflammatory assessment noted CRP <6 mg, fibrinemia 4.6 g/l, beta 2 microglobulin 3.74 mg / l, the LDH level was 383 IU and albumin 30 g/l with a gammaglobulinemia at 20 g/l. The bone marrow biopsy didn't show the infiltration. The serology of *Helicobacter pylori* was negative. The serology of viral hepatitis C had positive with viral charge significant. Other viral serologies were negative (HIV, HVB, HTLV1). We conclude at the DLBCL located to

the stomach without secondary localization (an Ann Arbor IE stage) associated with hepatitis C infection. We treated the patient with chemotherapy including Rituximab- Cyclophosphamide- Vincristine- Prednisolone associated the hepatitis viral C treatment and the symptoms disappeared.

## DISCUSSION

Stomach is the most site of localization of extra-ganglionic non-Hodgkin lymphoma.<sup>3,4,8</sup> In the stomach, we have two forms of lymphoma: MALT lymphomas which is low grade lymphoma with indolent evolution and whose evolution can be towards the aggressive lymphoma. Then there is an aggressive form such as the Diffuse Large Cell Lymphoma (DLCL) that are infrequent.<sup>8,9</sup> They are uncommon in children, but more common in adults patients<sup>10,11</sup> concurring the age of our patient. Etiopathologically, many advances have been made in understanding the mechanism of carcinogenesis of lymphomas. Some incriminated the infectious agents, other incriminated the genetic factors and toxic agents. The role of *Helicobacter pylori* has been described as an etiopathogenic model of gastric lymphomas. This bacterium is found in 80% of diagnosed patients.<sup>5,6</sup> In 1991, Parsonnet et al. on a cohort including several thousand patients who had serum samples as part of a systematic review, found the presence of anti-*Helicobacter pylori* antibodies in 90.9% of cases in patients with gastric lymphoma.<sup>12</sup> Several studies outside of Parsonnet et al. suggest the existence of a relationship between *Helicobacter pylori* and Gastric lymphoma.<sup>13,14</sup> The mechanism by which this bacterium provoke a lymphomatous proliferation remains controversial. According to Delchevier JC,<sup>15</sup> the chorion of the gastric mucosa is devoid of any B-lymphocytes in absence of infection with *Helicobacter pylori*. The inflammatory reaction induced by this bacterium causes the appearance of a B-lymphocyte population, then of gastric lymphoid nodules. The repeated antigen stimulation by this bacterium induces a monoclonal proliferation of B-lymphocytes, serving as a platform for Lymphomatous processes.

Hussel et al, in another study, have recently described the possible mechanism of the mode of action of *Helicobacter pylori*.<sup>16</sup> According to them, the proliferation of malignant B-lymphocyte in gastric lymphoma in culture would be dependent on a specific strain of *Helicobacter pylori*, the stimulation being in fact carried out by the activated T-

lymphocyte, specific for the *Helicobacter pylori* strain and their cytokines, and not by the bacterium itself. However, the direct responsibility of the bacterium in the genesis of Gastric Lymphoma remains to be proven, especially since there is a discrepancy between this hypothesis and the fact that more than half of the world population has or has had an infection with *Helicobacter pylori* without developing a lymphoma. Other factors could indeed intervene: environmental, nutritional, viral infections, dysregulation of immunity.

In addition, the type of strain of the bacterium involved is certainly an element to consider that could partly explain the discrepancy mentioned above. In our study, gastrointestinal endoscopy and serology did not show *Helicobacter Pylori*. On the other hand, there was a viral hepatitis C virus, a virus that is common in low-grade of Non-Hodgkin Lymphoma.<sup>7,17</sup> In this context, it would be understandable if the clinical findings of our patient was secondary to a gastric MALT lymphoma. The short duration of symptomatology revealed in the anamnesis, the endoscopic and immunohistochemical data excluded this possibility. Our observation could thus complete these last arguments that in addition to the *Helicobacter Pylori*, other factors are incriminated in the genesis of Gastric lymphoma. However by what mechanism would he obey the etiopathogenic model as a factor incriminating the hepatitis C virus? Does the chronic stimulation of the immune system by hepatitis C virus in particular as described in the study of Besson C et al.<sup>18</sup> serve as a basis for a lymphomatous stage as localized as seen in our study? Is it an interlinked process without there being a cause-and-effect phenomenon between gastric lymphoma and this hepatitis C virus?

## CONCLUSION

The case present could add to current literature suggesting that apart from infection with *Helicobacter Pylori*, other factors are implicated in the occurrence of gastric lymphomas. It also raises the problem of the link between the hepatitis C virus and the aggressive lymphomas located in the stomach.

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