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Manuscript Accepted Early View Article

TYPE OF ARTICLE: Case Report

TITLE: Primary DLBCL of the cervix presenting as bilateral hydronephrosis

AUTHORS:

Joel Alcid[1], Christian Fidler[2]

AFFILIATIONS:

[1]MD, Resident, Internal Medicine, Drexel, Philadelphia, PA, USA, joelalcidmd@gmail.com

[2]MD, Attending, Hematology Oncology, Abington-Jefferson Health, Abington, PA, USA, Christian.fidler@jefferson,edu

CORRESPONDING AUTHOR DETAILS

Joel Alcid

Hahnemann University Hospital / Drexel Medicine, 239 N Broad St, Philadelphia PA, USA, 19102

Email: joelalcidmd@gmail.com

Short Running Title: Primary DLBCL of the Cervix Presenting as Bilateral Hydronephrosis

Guarantor of Submission: The corresponding author is the guarantor of submission.

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ABSTRACT

We present a case of a 66-year-old postmenopausal woman who presented with a 1 month history of fatigue, dysuria and hematuria. A 7-9cm mass of the lower uterine segment/cervix was seen. Biopsy revealed it to be a CD 20 positive diffuse large B-cell type NHL. She was diagnosed as stage IE and started on R-CHOP chemotherapy (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone).

Case Report

A 66-year-old postmenopausal woman presented with a 1 month history of fatigue, dysuria and hematuria. She received multiple courses of antibiotics as an outpatient without improvement. On admission labs, she was found to have a creatinine of 6.92 (baseline ~1.2). A retroperitoneal ultrasound was obtained and revealed bilateral moderate to severe hydronephrosis. A non-contrast CT abdomen and pelvis revealed a large ~7-9cm mass involving the lower uterine segment/cervix displacing the rectosigmoid colon. She underwent further examination under anesthesia and multiple biopsies of the cervical mass were obtained. Histological examination of the biopsy specimen revealed diffuse large B-Cell Lymphoma (DLBCL). Immunohistochemical staining tested positive for CD 20, MYC, CD 10, and BCL 6. After complete diagnostic workup, she was diagnosed with diffuse large B-Cell Lymphoma stage IE. Patient was started on R-CHOP chemotherapy (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone). After 6 cycles of chemotherapy, a PET scan for restaging was obtained and revealed a significant decrease in SUV. However, only a minimal decrease in tumor size was visualized. A ~7-8cm bulky mass remains, and consolidation radiation therapy is being considered.

Conclusion

Primary Diffuse Large B-cell Lymphoma of the female genital tract is a rare diagnosis and must be diagnosed early due to the aggressiveness of the tumor. There is no standard treatment regimen. Patients are often treated with chemotherapy as the first line of treatment, which has provided promising results.

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65 **Keywords:** Diffuse Large B Cell Lymphoma, cervix, uterus, Non-Hodgkin's
66 lymphoma

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97 **INTRODUCTION**

98 Non-Hodgkin's lymphoma (NHL) arises most frequently in lymph nodes or other
99 lymphatic tissue. Primary extra nodal lymphoma accounts for one-third of cases. The
100 most commonly affected extra nodal sites are the gastrointestinal tract and skin, but
101 may affect any organ. The most common extra nodal lymphoid neoplasm is the
102 diffuse large B-cell Lymphoma, which comprises 25% of NHL. Primary lymphomas of
103 the female reproductive tract are extremely rare, less than 1% of extra nodal NHL
104 and <0.5% of gynecologic malignancies. The cervix is the most commonly affected
105 pelvic site, but may also occur in the ovary, uterus, vagina, vulva, and regional lymph
106 nodes. We present a case of primary diffuse large B-cell Lymphoma involving the
107 cervix and uterus [1].

108

109 **CASE REPORT**

110 A 66-year-old postmenopausal woman presented with a 1 month history of fatigue,
111 dysuria and hematuria. She received multiple courses of antibiotics as an outpatient
112 without improvement. On admission labs, she was found to have a creatinine of 6.92
113 (baseline ~1.2). A retroperitoneal ultrasound was obtained and revealed bilateral
114 moderate to severe hydronephrosis. A non-contrast CT abdomen and pelvis
115 revealed a large ~7-9cm mass involving the lower uterine segment/cervix displacing
116 the rectosigmoid colon, likely representing the site of obstruction (Figure 1) (Figure
117 2) and (Figure 3). An enlarged multi-fibroid uterus was also noted. There was no
118 hepatosplenomegaly or adenopathy. On pelvic examination, a diffuse thickening was
119 noted between the vagina and bladder. There was a firm mass wrapping around the
120 cervix with thickening of the rectovaginal wall. She underwent further examination
121 under anesthesia and multiple biopsies of the cervical mass were obtained. Patient
122 also had bilateral percutaneuos nephrostomy tubes placed to treat the obstruction.
123 Histological examination of the biopsy specimen revealed diffuse large B-Cell
124 Lymphoma (DLBCL). Immunohistochemical staining tested positive for CD 20, MYC,
125 CD 10, and BCL 6. Staging workup with bone marrow aspirate and biopsy was
126 negative for any monoclonal B-Cell or T-Cell population. PET scan revealed mild
127 metabolic activity at the lower uterine segment/cervix and upper vagina. Findings
128 would correspond to a Deauville score of 3 to 4. Viral serologies for HIV, hepatitis B

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129 surface antigen, and hepatitis C were negative. After complete diagnostic workup,
130 she was diagnosed with diffuse large B-Cell Lymphoma stage IE. Patient was started
131 on R-CHOP chemotherapy (rituximab, cyclophosphamide, doxorubicin, vincristine,
132 and prednisone). After 6 cycles of chemotherapy, a PET scan for restaging was
133 obtained and revealed a significant decrease in SUV. However, only a minimal
134 decrease in tumor size was visualized. A ~7-8cm bulky mass remains, and
135 consolidation radiation therapy is being considered.
136

137 **DISCUSSION**

138 DLBCL is the most common extranodal NHL neoplasm (30-58%). Median age of
139 onset of patients affected by this neoplasm is 40 years old. Primary lymphoma of the
140 female reproductive tract is extremely rare. Clinical symptoms are usually non-
141 specific and can include vaginal bleeding (70%), bilateral hydronephrosis, perineal
142 discomfort (40%), persistent vaginal discharge (20%), abdominal pain, however,
143 some patients are asymptomatic. The classic B symptoms of lymphoma (fever, night
144 sweats, and weight loss) are rarely seen. Our patient presented outside the median
145 age range, but had the corroborative symptoms of hydronephrosis. Few cases have
146 been reported of DLBCL of the cervix presenting with hydronephrosis [2].
147 Diagnosing lymphoma of the cervix or uterus can present challenges. A
148 papanicolaou smear has limited diagnostic value and is usually negative, because
149 these tumors infiltrate the cervical stroma, and the squamous and glandular lining is
150 initially preserved. Deep cervical biopsies are needed along with histopathologic
151 evaluation for definitive diagnosis. In a study of women with primary cervical
152 lymphoma, 41% had an abnormal cervical cytology [3] [4].
153 The study of choice for detection and staging of DLBCL is computerized tomography
154 scans. Also included in the workup for staging are bone marrow biopsy and positron
155 emission tomography scan (PET). It is important to distinguish the etiology of the
156 tumor, adenocarcinoma vs squamous cell carcinoma vs lymphoma, as these tumors
157 have different mainstays of treatment. Surgery and radiation are used for
158 adenocarcinoma and squamous cell carcinoma, and chemotherapy/immunotherapy
159 is used for lymphoma [5].

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Another important aspect in the diagnosis of lymphoma is immunohistochemical staining, as this can determine the type and subtype of lymphoma. Expression of CD 20, CD 10, BCL 6, and MUM 1 negative are suggestive of germinal center B-type lymphoma (DLBCL). Our patient expressed CD 20, CD 10 and BCL 6, consistent with DLBCL [6].

Due to the rarity of this malignancy, optimal treatment has never been standardized and therapy is still under discussion. DLBCL of the cervix/uterus has been managed with chemotherapy, radiation therapy and surgery. The most commonly used and preferred regimen is R-CHOP. With this therapy, it has been reported that up to 70-80% of patients achieve complete remission with 6 cycles of R-CHOP. Other regimens that have been used are MACOPB (methotrexate, cytarabine, cyclophosphamide, vincristine, prednisolone, and bleomycin, CHOP-bleo (cyclophosphamide, doxorubacin, vincristine, prednisolone, and bleomycin), and ASAP (doxorubacin, methylprednisolone, cytarabine, and cisplatin). For large bulky tumors (>10cm), residual lesions, or tumors with incomplete response, radiation therapy can be considered. According to a review of cases by Anagnostopoulos et. al. 118 cases were reviewed, and revealed 16.8% had chemotherapy only, 10.9% had radiation therapy only, and 9.2% had surgery only and the remaining patients had multiple modalities of treatment [7] [8].

The overall survival rate of for patients for DLBCL of the cervix, uterus, and vagina is 89% with a relapse free survival rate of 70% [2] [6] [11].

CONCLUSION

Primary Diffuse Large B-cell Lymphoma of the female genital tract is a rare diagnosis and must be diagnosed early due to the aggressiveness of the tumor. There is no standard treatment regimen. Patients are often treated with chemotherapy as the first line of treatment, which has provided promising results.

CONFLICT OF INTEREST

I declare no conflict of interest

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192 **AUTHOR'S CONTRIBUTIONS**
193 Joel Alcid, M.D.
194 Group 1- substantial contributions to conception and design, acquisition of data
195 Group 2- drafting the article, revising it critically for important intellectual content
196 Group 3- final approval of version to be published
197
198 Christian Fidler, M.D.
199 Group 1- substantial contributions to conception and design, acquisition of data
200 Group 2- drafting the article, revising it critically for important intellectual content
201 Group 3- final approval of version to be published
202
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233 treatment of primary uterine B-cell Lymphoma with rituximab-chop
234 immunocheotherapy. Haematologica 92:e26-e27
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236 **FIGURE LEGENDS**
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238 Figure 1: CT Abdomen and Pelvis. 7x9cm mass involving the lower uterine segment
239 and cervix
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241 Figure 2: CT Abdomen and Pelvis. 7x9cm mass involving the lower uterine segment
242 and cervix
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244 Figure 3: CT Abdomen and Pelvis. 7x9cm mass involving the lower uterine segment
245 and cervix
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FIGURES

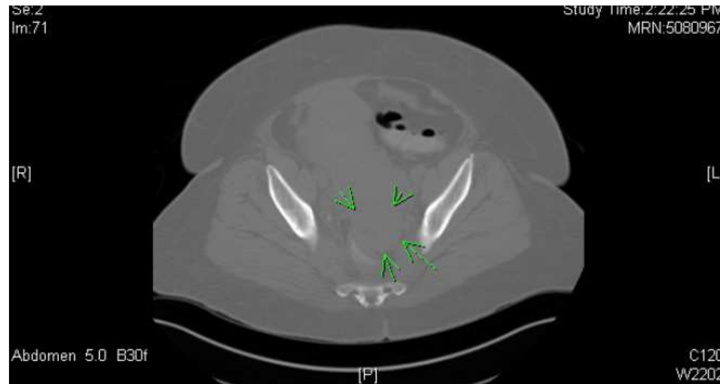


Figure 1: CT Abdomen and Pelvis. 7x9cm mass involving the lower uterine segment and cervix

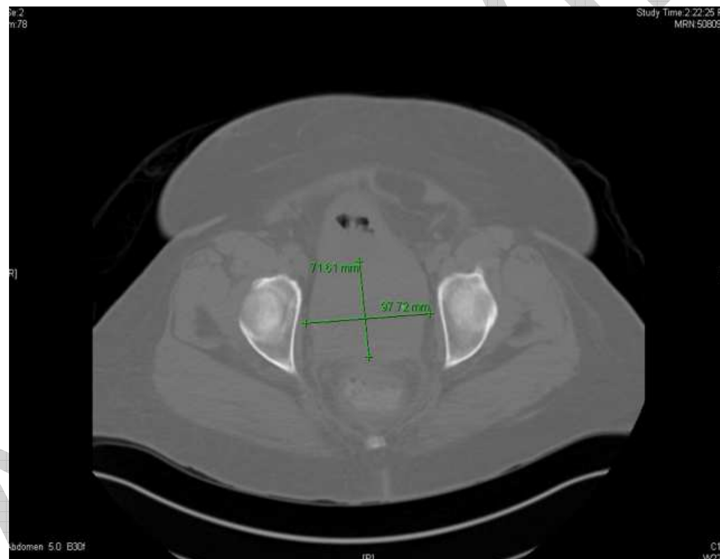
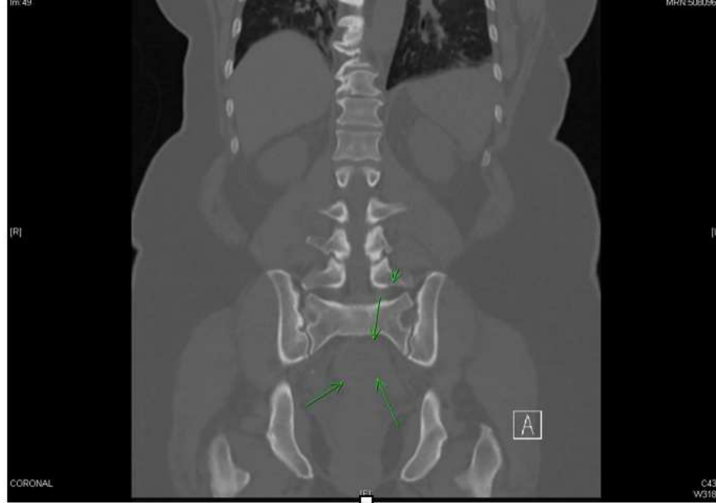


Figure 2: CT Abdomen and Pelvis. 7x9cm mass involving the lower uterine segment and cervix

265 

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267 Figure 3: CT Abdomen and Pelvis. 7x9cm mass involving the lower uterine segment
268 and cervix

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