LYMPHOMAS OF THE FEMALE GENITAL TRACT IN IBADAN

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ABSTRACT

Context: Female genital tract cancers are second only to breast malignancies. Cervical cancer is the commonest while epithelial cancers constitute the major histologic type. Lymphoid neoplasms are extremely rare, with the Burkitt's variety accounting for majority of cases seen in the African female.

Objective: This is a review of the obstetric/gynaecological patients seen at the University College Hospital, Ibadan between 1976 and 2005, predating the commencement of a nationwide research into non – Hodgkin's lymphoma funded by the Aboderin Foundation.

Study Design: Records of subjects were analysed for their sociodemographic and clinicopathological characteristics, recruiting only those who satisfy the criteria for diagnosing genital tract lymphomas according to Kosari et al[1]. Retrievable archival paraffin blocks of subjects were also analysed using immunophenotyping.

Results: Fifteen cases were identified within the study period; the highest yearly incidence rate being 3 in 1977. In eighteen of the years studied no cases were seen. Most cases (80.0%) occurred in the ovaries. Eighty percent (12) of patients were 25 years or below and nulliparas and grandmultiparas formed 46.7 and 13.4% respectively. Unilateral or bilateral oophorectomy was the commonest surgical procedure (53.3%) while 20.0% had total abdominal hysterectomy with or without bilateral salpingoophorectomy. Data were unavailable concerning use of adjuvant therapy and outcome of treatment.

Four archival paraffin blocks were available for immunophenotyping using the affordable panel of CD20, CD10 and Bcl – 2 antibodies; all were Burkitt's lymphoma.

Conclusion: Female genital lymphomas are very rare, affecting the young and nulliparous. The Burkitt's type is commonest.

INTRODUCTION

Malignancies of the female genital tract account for 30.6% of cancers in the Nigerian female, being second only to breast cancer in incidence[2]. Worldwide, cancers of the cervix are the most common and those of the fallopian tubes have the least incidence and prevalence rates amongst gynaecological cancers. Epithelial neoplasms are the predominant histological types, whereas lymphoid neoplasms are extremely rare, being among the least common female genital tract malignancies[3].

The majority of female genital tract lymphomas arise from systemic involvement in patients with primarily extragenital lymphomas, and only about 1% of primary extranodal lymphomas originate in the female genital tract[4]. The ovaries and adnexa are the most common locations of female genital tract lymphomas, followed by the uterus and cervix, vagina and vulva[1,3].

About 73% of all previously reported female genital tract lymphomas are non – Hodgkin's lymphomas[3]. However, in the series of Kosari et al[1], less than 1% of all female genital tract lymphomas were due to Hodgkin's lymphoma. In African children and young adult women, the majority of these cases are Burkitt's lymphomas[5,6]. In a large Caucasian series of female genital tract lymphomas, the most common morphological variants were diffuse large B cell lymphoma, follicular lymphoma and Burkitt's lymphoma, in descending order of frequency[1].

The diagnosis of genital tract lymphomas is hampered by their rarity and the fact that the primary sites are usually outside of the pelvis. If not clinically considered, they can pose a diagnostic challenge[7]. The treatment of these lymphomas is usually by surgical resection followed by radiotherapy and or

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chemotherapy.

The present study is a review of the characteristics of patients with genital tract lymphomas and their tumours over the thirty year period from 1976 to 2005, diagnosed at the University College Hospital (UCH), Ibadan, Nigeria. This period preceded somewhat the nationwide commencement of research into non – Hodgkin's lymphomas funded by the ABODERIN FOUNDATION.

MATERIALS AND METHODS

Methodology

This is a retrospective study of the case records and surgical pathology materials of subjects managed at University College Hospital (UCH), Ibadan within the thirty year period from January 1976 to December 2005. The records of the Pathology and Medical Records Departments were analysed to extract information about these patients and their tumours. These data include their sociodemographic and clinicopathological details.

According to the criteria of Kosari et al[1], genital tract lymphomas recruited in the present study were considered as primary only if:

1. The disease process was confined to the female genital tract at the time of diagnosis, irrespective of involvement of one or more genital tract sites.
2. Full investigation did not reveal evidence of extragenital lymphoma.
3. The peripheral blood and bone marrow did not contain leukemic cells.
4. No remote organs were involved within a time lapse of 6 months.

Fresh tissue sections were prepared from all available archival paraffin blocks of all eligible cases for immunophenotyping of the malignant lymphoma subtypes.

MATERIALS

The subjects studied were those either managed at the various clinical departments in UCH, Ibadan or those whose histological specimens were sent to the Pathology Department of UCH, Ibadan, for review.

RESULTS

Fifteen cases of gynaecological lymphomas were identified between 1976 and 2005, giving an estimated incidence rate of 1 case every two years. However in eighteen of the thirty years no cases were seen while in 1977 and 2000 the highest yearly figures of 3 and 2 were seen respectively.

Time trend and location of cases

The five yearly trends showed that the highest number of cases occurred in the time frame of 1976 to 1980, while no cases were seen in that of 1991 to 1995. Most of the cases, 12 (80%) occurred in the ovaries, followed by 2 (13.3%) in the pelvic retroperitoneal space and 1 (6.7%) in the vagina respectively. Table 1 shows these trends.

Age and parity distribution

Most cases, 12 (80%) occurred in women who were 25 years or younger, with more than half of these, 7 (58.3%) aged less than 15 years. The stated parity ranged between 0 and 12. Nulliparas constituted half of the cases, 7 (46.7%), while the grandmultiparas – defined as parity of 5 and above – were 2 (13.3%). The parity was not stated in 5 (33.3%) of the cases. The age and parity trends are depicted in Table 2.

MODE OF MANAGEMENT

Unilateral or bilateral oophorectomy was done in 8 cases (53.3%), while total abdominal hysterectomy with or without bilateral salpingoophorectomy was carried out in 3 patients (20%). Biopsy of the retroperitoneal and vaginal masses was the only stated procedure in one case each. In two cases, the type of procedure done could not be ascertained.

Data could not be retrieved about the adjuvant therapy instituted or the outcome of treatment in terms of survival percentages.

Immunophenotyping

Archival paraffin blocks were available for immunophenotyping in only 4 of all 15 (26.7%) cases of female genital tract malignant lymphomas. All the four were histologically diagnosed as Burkitt`s lymphoma of the ovary. Their ages were 10, 18, 21 and 58 years respectively. The immunohistochemical panel of antibodies applied to confirm these diagnoses included CD20, CD10 and Bcl-2. All cases showed immune-positivity for CD20 which is consistent with its B – cell lineage and all cases also showed immunonegativity for Bcl-2 which is characteristic of most cases of Burkitt`s lymphoma. However only the case seen in the 10 year old girl showed immunoreactivity with CD10, a feature classical of childhood Burkitt`s lymphoma. The lack of positivity seen in the older patients is remarkable as this pattern suggests that these may be cases of adult Burkitt-like lymphoma. Additional immunological markers such as CD23, Bcl-6 and p53 (which are not presently available at our facility) are useful in further differentiation and confirmation of these histological subtypes of malignant

lymphomas.

DISCUSSION

Primary malignant lymphomas of the female genital tract are very rare diseases which require very stringent diagnostic criteria and laboratory facilities like immunohistochemistry[8, 9, 10] that are difficult to obtain in low resource settings[6]. This is compatible with our finding of only 15 cases of such malignant lymphomas in 30 years at our teaching and referral hospital in Ibadan.

The ovary, like in this study is the commonest site that is affected[8]. Although diseases limited to the vagina and cervix were highlighted in a case series reported by Cohn et al in 2007[11], and other parts of the female genitalia including the uterus and vulva. Apart from the ovary, only two other sites – the vagina and the pelvic retroperitoneal space – were represented in the patients we studied.

There is controversy whether indeed these are sites of primary tumours or they represent secondaries from extra genital lesions. But the demonstration of B and T lymphocytes within the normal ovary[12, 13] has been taken as supportive evidence of tumours arising primarily from the genitalia, even though they are very rare. Primary ovarian lymphoma (POL) is thus said to constitute 0.5% of all cases of non – Hodgkins lymphomas (NHL) and to occur in 1.5% of all ovarian malignancies[14] with the commonest type being the diffuse large B-cell lymphoma[8].

Burkitt's lymphoma of the ovary which was confirmed in this study by immunohistochemical reactions to CD20, CD10 and Bcl – 2 antibodies by all the available archival paraffin blocks is the commonest type of ovarian non-Hodgkin's lymphoma, as confirmed by a similar study at our centre in 1981[5]. It is a disease of children and young adults. Indeed, eighty per cent of our patients were aged 25 years and under. Most were also nulliparous.

Chishima et al (2006)[9] described the case of a 25 year old nulligravida with Burkitt's lymphoma who had unilateral salpingoophorectomy and adjuvant chemotherapy. She was disease free at the time of their reporting, which was 30 months after the initial diagnosis. This highlights the possibility that the prognosis for ovarian non-Hodgkin's lymphomas is likely to be better than previously thought[14, 15, 16].

The implication of all these for practice, apart from cure or long term remission is the possibility of conservation of fertility when these diseases with their predilection for younger women are diagnosed early and treated promptly and effectively with minimal surgery. It is in this light that the ongoing nationwide research efforts into non-Hodgkin's lymphomas are being viewed to have the following prospects:

1. There will be heightened awareness about the diseases. The Ibadan arm of the study for example organised workshops involving health care workers which sensitized them to develop a higher index of suspicion when faced with atypical cases in their various areas of medical practice.
2. This will be associated with better screening of likely cases through radiological and other laboratory investigations and biopsies.
3. The availability of immunohistochemical means to determine immunoreactivity to lymphoma-specific antigens will ensure more definitive diagnoses.
4. The increasing expertise with managing gynaecologic oncology cases highlighted by Odukogbe et al[17] coupled with easier availability of chemotherapeutic agents will translate into more patients surviving to adulthood and able to retain the much desired fertility.

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Table 1: Five – yearly trend and locations of gynaecological lymphomas at Ibadan (1976 – 2005).

	1976-1980		1981-1985		1986-1990		1991-1995		1996-2000		2000-2005		Total	
Number and frequency	No	%	No	%	No	%	No	%	No	%	No	%	No	%
	5	33.3	1	6.7	2	13.3	-	0.0	3	20.0	4	26.7	15	100
Location:														
Ovary	4	33.3	-	0.0	1	8.3	-	0.0	3	25.0	4	33.3	12	100
Retroperitoneal	1	50.0	-	0.0	1	50.0	-	0.0	-	0.0	-	0.0	2	100
Vagina	-	0.0	1	100	-	0.0	-	0.0	-	0.0	-	0.0	1	100

Table 2. Age and parity distribution of patients.

Age and parity distribution	Para 0		Para 1–4		Para ≥ 5		Parity not stated		Total	
	No	%	No	%	No	%	No	%	No	%
≤ 15 years	7	100	-	0.0	-	0.0	-	0.0	7	46.7
16 – 25 years	-	0.0	1	20.0	-	0.0	4	80.0	5	33.3
26 – 35 years	-	0.0	-	0.0	-	0.0	1	100	1	6.7
36 – 45 years	-	0.0	-	0.0	-	0.0	-	0.0	-	0.0
> 45 years	-	0.0	-	0.0	2	100	-	0.0	2	13.3
Total	7	46.7	1	6.7	2	13.3	5	33.3	15	100

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