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HISTOLOGIC ANALYSIS OF GYNAECOLOGIC LESIONS IN NIGERIANS
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HISTOLOGIC ANALYSIS OF GYNAECOLOGIC LESIONS IN NIGERIANS

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ABSTRACT

***Background*: Gynaecological neoplasms are a cause of significant morbidity and mortality in females all over the world.**
***Objective*: To determine the pattern of gynaecological lesions seen in Me Cure Healthcare, Lagos Nigeria.**
***Design*: A descriptive retrospective study.**
***Setting*: Histopathology section of Me Cure Healthcare Limited from August 2009 to August 2014.**
***Subjects*: Histopathological reports and paraffin sections of gynaecologic lesions/ specimens which were diagnosed by Me Cure Healthcare.**
***Results*: A total of 691 gynaecologic specimens were received. The youngest patient was 14 years, while the oldest patient was 79 years with a mean age of 40.47 years and Std of ± 10.59. Eighty three percent of specimens were benign neoplastic lesions, while 5.9% of specimens were malignant neoplastic lesions. Uterine leiomyomas were the most common lesions and majority of them were seen in age groups 30-39 and 40-49 years. Simple endometrial hyperplasia without atypia accounted for most endometrial lesions (52,3%) and were seen more in age groups 30-39 and 40-49 years. Most ovarian lesions (45.9%) were non neoplastic cysts and seen more in age groups 20-29 and 30-39 years. The cancers seen were those of the cervix (56.1%), endometrium (22%), ovary (14.6%), uterus (4.9%) and choriocarcinoma (2.4%) in that order. Cervical cancer was seen in 36.5% of cervical lesions and involved mainly age groups; 30-39 years, 50-59 years and 60-69 years (each of these age groups had five cases). The mean age for cases of cancer of the cervix was 50 years Std ± 13.0 and all the age groups except 10-19 years were involved.**
***Conclusion*: Benign lesions were the most common with uterine leiomyoma accounting for most of them, while cervical carcinoma was the the common gynaecological cancer. Endometrial cancer cases were noted to be on the rise.**

INTRODUCTION

Gynaecological neoplasms are a cause of significant morbidity and mortality in females all over the world. Gynaecological cancers encompass a diverse group of tumours with different epidemiological and pathological features, clinical presentations and treatment strategies (1). Gynaecological cancers include cancers of the ovary, fallopian tube, uterine body (corpus uteri), cervix, vagina and vulva as well as choriocarcinoma which primarily come under the care of gynaecologists and gynaecological oncologists (2). Epidemiologically, gynaecological cancers are grouped into two based on etiology; those associated with chronic viral infections and have known premalignant stages before the development of invasive cancer (uterine cervix, vagina and vulva) and those not associated with chronic infections (ovary, fallopian tube and uterine corpus) (2). Incidence has been increasing in most regions of the world, but there are huge inequalities between rich and poor countries. Incidence rates remain highest in more

Histologic analysis.indd 245 9/25/15 10:01 PM

developed regions, but mortality is relatively much higher in less developed countries due to a lack of early detection and access to treatment facilities (3). Studies from different countries show different pattern and frequency of gynaecological malignancies (4-12). Most of the studies from African and Asian countries, reported cervical cancer as the most common gynaecologic malignancy, with rates varying from 48.6 to 85.2% and the mean age of affected patients been in a range of 43.7 to 54.5 years. However studies from Pakistan reported ovarian carcinoma as the most common cause of gynaecologic malignancy in that environment (13). There are conflicting reports on the second most common gynaecological cancer (4-13). Almost all the foreign studies and all the Nigerian studies were hospital based studies conducted in tertiary healthcare facilities. No research has been done on gynaecological lesions seen from a private laboratory, despite the fact that many Nigerians utilise the services of private hospitals that most times send their histological samples to private laboratories for histological diagnosis. We set out to review our data base with respect to gynaecological lesions to see the pattern in relation to those from government owned tertiary hospitals and to add to the growing database of gynaecological lesions so as to help to combat gynaecological cancer menace through actions like health education, screening programmes, and appropriate resource allocation of scarce resources.

MATERIALS AND METHODS

This retrospective study included histopathological reports of all gynaecologic specimens which were received and processed by histopathology section of Me Cure Health Limited (a modern large privately owned diagnostic establishment), from August 2009 to December 2013. This histopathology section renders services to many privately owned hospitals within Lagos State and few neighboring states. These gynaecologic specimens were received in 10% buffered formalin and processed with auto processors. Paraffin embedded sections (at 2-3μm) were routinely stained with hematoxylin and eosin stains while special stains and immunohistochemistry were applied when needed. Data were extracted from the establishment computer database and entered into an Excel sheet. Data were analyzed using predictive analytical software, version 17 (IBM, SPSS Inc, Chicago, IL, USA). The research was approved by review board of the establishment.

RESULTS

A total of 691 gynaecologic specimens were received and formed 14.9% of 4,642 histologic specimens processed during the period. The youngest patient was 14 years, while the oldest patient was 79 years with a mean age of 40.47 years ± 10.59. Age group 30-39 years accounted for 41% of cases, while age groups 40-49 years and 50-59 years accounted for 27.8%and 12.4% of cases respectively. Age group 70-79 accounted for 0.7% of cases, Table 1.

Myometrium (body of the uterus) was the most common site and responsible for 56% of cases. A distant second common site was specimens from the endometrium (18.4%), followed by ovarian lesions which accounted for 15.8% of cases. The least common site was the vulva, which accounted for 0.3% of cases, Table 2. Eighty three percent of specimens were benign neoplastic lesions, while 5.9% of specimens turned out to be malignant neoplastic lesions, Table 2.

Malignant cervical neoplasm was seen in 36.5% of cervical lesions and involved mainly age groups; 30-39 years, 50-59 years and 60-69 years (each of these age groups had five cases). Endocervical polyp and nabothian cyst were responsible for 30.2% of cervical lesions, while 14.3% of cervical lesions was due to cervical intra-epithelial neoplasm and was seen most in age group 30-39 years, Table 3.

Most of the myometrial lesions were uterine leiomyoma, which was seen in 90.6% of cases. Majority of the leiomyomas were seen in age groups 30-39 and 40-49 years. Leiomyosarcomas were seen in only 0.5% of cases, Table 4.

Table 5, shows various endometrial lesions. Simple endometrial hyperplasia without atypia accounted for most (52.3%) and seen more in age groups 30-39 and 40-49 years. Endometrial adenocarcinoma, mixed mullerian tumour and choriocarcinoma, each accounted for 3.8%, 3.1% and 0.8% respectively. Most of the endometrial adenocarcinoma and mixed mullerian tumour were seen in age group 60-69 years, while the only case of choriocarcinoma was seen in age group 30-39 years.

Non neoplastic cysts were responsible for most ovarian lesions (45.9%) and were seen more in age groups 20-29 and 30-39 years. Germ cell ovarian lesions accounted for a distant second, with age groups 20-29 and 30-39 years been responsible for most cases as, Table 6.

The cancers seen were those of the cervix (56.1%), endometrium (22%), ovary (14.6%), uterine corpus (4.9%) and choriocarcinoma (2.4%) in that order. The mean age for cases of cancer of the cervix was 50 years ± 13.0 and all the age groups except 10-19 years were involved. Age groups 20-29 and 70-79 years had the least number of cases. Endometrial cancers were seen in only three age groups (50-59, 60-69 and 70-79) with 55.6% of cases occurring in age group 60-69 years. The mean age for cases was 62.5 years ± 6.4. The ovarian cancers were seen in three age groups, with majority seen in age group 60-69 years. Two cases of leiomyosarcoma were seen and the mean age was 49.5 years ± 21.9. The only case of choriocarcinoma was seen in age group 30-39 with a mean age of 31 ± 1 as shown in Table 7.

Histologic analysis.indd 246 9/25/15 10:01 PM

Table 1
Age distribution of cases

Age group	Frequency (Percentage)
10-19	4 (6)
20-29	82 (11.9)
30-39	283 (41)
40-49	192 (27.8)
50-59	86 (12.4)
60-69	39 (5.6)
70-79	5 (0.7)
Total	691 (100)

Table 2
Site and histologic type of lesions

Sites	Malignant	Borderline	Benign	Cystic	Inflammatory	Normal	Total	P (%)
Vulva	0	-	2	-	-	-	2	0.3
Cervix	23	-	33	-	7	-	63	9
Myom	2	-	384	-	-	-	386	56
Endo	10	-	106	-	3	8	127	18.4
Ovary	6	1	48	48	5	1	109	15.7
Fallo	0	-	-	-	1	3	4	0.6
Total	41 (5.9)	1 (0.1)	573 (83)	48 (7)	16 (2.3)	12 (1.7)	691	100

P= Percentage, Myom= Myometrium, Endo= Endometrium, Fallo= Fallopian tube

Table 3
Frequency of cervical lesions in relation to age

Diagnosis	20-29	30-39	40-49	50-59	60-69	70-79	Total (%)
Naboth C	1	2	5	1	1	-	10(15.9)
Endo Cx P	2	4	1	1	1	-	9 (14.3)
Cervicitis	-	3	4	-	-	-	7 (11.1)
Leiomyoma	-	3	1	1	-	-	5 (7.9)
CIN	-	4	2	1	2	-	9 (14.3)
Sq Cell Ca	1	5	3	5	5	1	20 (31.7)
Adeno Ca	-	-	1	-	1	-	2 (3.2)
Adeno Sq	-	-	-	-	-	1	1 (1.6)

Endo Cx P = Endocervical polyp, Naboth C= Nabothian cyst, CIN = Cervical intra epithelial neoplasia, Sq Cell Ca = Squamous cell carcinoma, Adeno Ca = Adenocarcinoma, Adeno Sq= Adeno squamous carcinoma.

Histologic analysis.indd 247 9/25/15 10:01 PM

Table 4
Frequency of myometrial lesions in relation to age

Diagnosis	20-29	30-39	40-49	50-59	60-69	70-79	Total (%)
Leiomyoma	33	157	113	37	8	1	349 (90.6)
Adenomyosis	-	9	10	1	-	-	20 (5.2)
Adenomyomata	1	5	6	1	-	-	13 (3.4)
Atypical Leio	-	-	-	1	-	-	1 (0.3)
Leiomyo Sa	-	1	-	-	1	-	2 (0.5)

Atypical Leio = Atypical leiomyoma, Leiomyo Sa = Leiomyosarcoma

Table 5
Frequency of endometrial lesions in relation to age

Diagnosis	20-29	30-39	40-49	50-59	60-69	70-79	Total (%)
Normal P	2	4	1	-	-	-	7 (5.5)
Arias S R	1	-	1	-	-	-	2 (1.6)
Endometritis	-	2	1	-	-	-	3 (2.3)
Endo P	2	6	5	7	4	-	24 (18.8)
Simple Hyp	7	21	21	16	2	-	67 (52.3)
Complex Hyp	-	2	1	2	1	-	6 (4.7)
Atypical Sim	-	6	-	-	1	-	7 (5.5)
Atypical Com	-	1	1	-	-	-	2 (1.6)
Adenocarcinoma	-	-	-	1	3	1	5 (3.8)
MMMT	-	-	-	1	2	1	4 (3.1)
Choriocrcinoma	-	1	-	-	-	-	1 (0.8)

Normal P = Normal placental tissue, Arias S R = Arias stella reaction of pregnancy, Endo P = Endometrial polyp, Simple Hyp = Simple hyperplasia, Complex Hyp = Complex hyperplasia, Atypical Sim = Atypical simple hyperplasia, Atypical Com = Atypical complex hyperplasia, MMMT = Malignant mixed mullerian tumour

Table 6
Frequency of ovarian lesions in relation to age

Diagnosis	10-19	20-29	30-39	40-49	50-59	60-69	70-79	Total (%)
N N C	2	16	22	9	1	-	-	50(45.9)
Ophoritis	-	1	4	-	-	-	-	5 (4.7)
Endometriosis	-	1	1	-	-	-	-	2 (1.8)
Ovarian G	-	1	-	-	-	-	-	1 (0.9)
Surf Epith T	-	1	4	1	2	6	-	14(12.8)
Stromal T	1	1	3	-	2	-	-	7 (6.4)
Germ cell T	1	9	9	4	3	1	-	27 (24.8)
Krukenberg T	-	-	1	-	-	-	-	1 (0.9)
Metastatic(N)	-	1	1	-	-	-	-	2 (1.8)

NNC = Non neoplastic cyst, Ovarian G = Ovarian gestation, Surf Epith T = Surface epithelial tumour, Stromal T = Stromal Tumour, Germ cell T = Germ cell tumour, Krukenberg T = Krukenberg tumour, Metastatic (N) = Metastatic (non specific).

Histologic analysis.indd 248 9/25/15 10:01 PM

Table 7
Age distribution of cancer cases

Age group	Cervix	Endometrium	Ovary	Uterus	Choriocarcinoma
20-29	1	-	1	-	-
30-39	5	-	2	1	1
40-49	4	-	-	-	-
50-59	5	2	-	-	-
60-69	6	5	3	1	-
70-79	2	2	-	-	-
Total	23(56.1)	9 (22)	6 (14.6)	2 (4.9)	1 (2.4)
Mean Age (SD)	50 (13.0)	62.5 (6.4)	62.5 (3.5)	49.5 (21.9)	31 (1)

DISCUSSION

There are a lot of privately owned hospitals with specialist services in Nigeria. Whenever they do surgeries or any medical procedure that generates a biopsy or a specimen, they usually send them to privately operated histopathological laboratories, like Me Cure Health Limited. In recent times, prolonged industrial strikes by various hospital workers union in the government owned facilities and deteriorating infrastructures have made the privately owned facilities to be the preferred choice to render health related services including histological diagnosis of tissue and surgical specimens. Invariably the need to include information from these privately owned health facilities to the national data base has become apparent.

Benign neoplastic lesions, accounted for 83% of all gynaecological cases seen during the period under review. This agrees with findings by Ozumba *et al* that reported a rate of 82.6% (12). This shows that benign neoplasms are by far the most common gynaecological neoplasms. Uterine leiomyoma (UL) accounted for 50.5% of all gynaecological lesions and the mean age of cases was 39.6 years. This is far higher than 25.9% reported by Ozumba *et al* (12), however UL was still the most common lesion seen in that study. UL is the most common benign tumour of the female genital tract in the reproductive age group, occurring in more than 50% of women (14,15). The risk factors for clinically significant UL are nulliparity, obesity, African racial origin and a positive family history (15). The great majority of UL are asymptomatic, however common presenting symptoms are menstrual disturbances and pressure symptoms depending on the size of the tumour and the location (15). Other symptoms include subfertility, abortion, abnormal lie and post partum haemorrhage (14,15). Due to the fact that it is mainly seen in women of child bearing age and could be implicated in subfertility, it makes surgical intervention a necessity.

Nabothian cysts and endocervical cysts each accounted for 15.9 and 14.3% of cervical lesions respectively and together form 2.7% of all the cases. This rate is less than 8.4% reported by Ozumba *et al* (12). Nabothian cysts (also called mucinous retention cysts or epithelial cysts) are common and benign and are considered a normal feature of adult cervix (16). It usually occurs in the transformation zone of the cervix, when a gland orifice is blocked due to inflammation and squamous metaplasia (16). Endocervical polyps have an unclear etiology, are more often found incidentally at pelvic examination and rarely may present as postcoital, instrumental or postmenopausal bleeding (16). These symptoms are usually what necessitates visitation to a gynecologist and the subsequent removal.

Endometrial hyperplasias of different types were responsible for 64.1% of endometrial lesions and 11.9% of all lesions and majority of them were due to simple endometrial hyperplasia without atypia. Only atypical endometrial hyperplasias are clearly associated with subsequent development of adenocarcinoma (17). If left untreated, approximately 8% of patient with atypical hyperplasia will progress to carcinoma, whereas the progression rate in women with complex hyperplasia could be as high as 30% (17,18). Complex atypical hyperplasias cases may have co-existent cancers in as high as 20-50% of situations which have lead to the suggestion that whenever there is complex atypical hyperplasia, that the woman should have full surgical management (17).

Over 50% of the ovarian lesions were non neoplastic cyst and ovarian inflammatory disorders. They were mainly seen in the younger age groups and none was seen in age groups 60-69 and 70-79 years. These ovarian cysts were mainly solitary follicular cysts and corpus luteal cysts. This finding agrees with previous findings that non neoplastic ovarian lesions are very common (19,20). These cysts usually occur due to failure of ovulation and studies have shown that majority (about 90%) of them resolve spontaneously (21). Because some of these non neoplastic lesions of

Histologic analysis.indd 249 9/25/15 10:01 PM

the ovary form a pelvic mass and potentially mimic an ovarian neoplasm, their proper recognition and classification are important to allow for appropriate therapy (22).

Benign ovarian neoplasm accounted for 44% of all ovarian lesions and 6.9% of all cases. This is higher than 4.3% reported in Enugu (12). All the germ cell tumours and sex cord stromal tumours were benign and most of the cases were seen in people in second and third decades of life. The peak age incidence for all the benign cases was the third decade. This is similar to findings by Forae *et al*, Kanthikar *et al* and Mendal *et al* (19,20,23). However while the germ cell tumours were the most common in this study and in keeping with findings in Benin City; Nigeria, benign surface epithelial tumours were the most common in Dhule, India (19,20).

Cancers of the cervix, endometrium and ovary in this other were the most common female genital malignancies seen in our series. Cervical cancer accounted for 56.1% of all gynaecological malignancies and the mean age of cases was 50 years. This is similar to the rate of 57.8% reported in Ghana (8). This study rate of 56.1% is higher than 23.9% reported in Pakistan, 13 and 48.6% reported in Kano; 10 Nigeria, but less than 63.1% in Port Harcourt, 11 far less than 81.5% in Enugu, 12 82.4% in Benin 25 (both in Nigeria) and 85.2% in Nepal, 6 80.6% in Botswana 7 and 78% in Zimbabwe (9). The reason for the slightly lower rate in Kano was due to improved efforts at cervical screening and early detection of cervical dysplasia in the last 10-15 years in that centre(10). The lower rate in this series in respect to other studies, may be due to a little increase in awareness, because Lagos; Nigeria (where this study was conducted) is probably the city with most enlightened people in Nigeria and generally its citizens tend to be a bit more informed than the rest of the populace. However much more still needs to be done to further reduce the rate. Breast cancer is the most prevalent cancer in women in most countries globally, although cervical cancer is the most prevalent in much of sub-Saharan Africa and South Asia (3). With 528 000 new cases every year, cervical cancer is the fourth most common cancer affecting women worldwide, after breast, colorectal, and lung cancers; it is most notable in the lower-resource countries of sub-Saharan Africa (3). Cervical cancer can have devastating effects with a very high human, social, and economic cost, affecting women in their prime (3). In sub-Saharan Africa, 34.8 new cases of cervical cancer are diagnosed per 100 000 women annually, and 22.5 per 100 000 women die from the disease. These figures compare with 6.6 and 2.5 per 100 000 women, respectively, in North America. The drastic differences can be explained by lack of access to effective screening and to services that facilitate early detection and treatment (3). In this study, women in the productive age groups (30-39,40-49, 50-59 and 60-69) were mostly involved, causing loss of workforce with its economic consequences and the disastrous effects on children when they lose their mothers early. These findings bring into sharp focus the need to implement the tools already available for cervical cancer, notably HPV vaccination combined with well-organised national programmes for screening and treatment (3). The major risk factors for cervical cancer include; early age at first intercourse (16 years and younger), history of multiple sexual partners, genital human papilloma virus infection and prior squamous intra-epithelial lesion/cervical intra-epithelial neoplasm (4). Cervical cancer of squamous cell carcinoma histologic pattern, which is usually the most common pattern (87% in this study) has well known and documented pre-cancer stage called cervical intra-epithelial lesion (CIN) (4). Cancer of the cervix is a preventable disease and a key aspect of its prevention is the detection of the premalignant form by cervical screening (4). In this study, CIN accounted for 14.3% of cervical lesions and 66.7% of them were seen in 30-39 and 40-49 age groups at least two decades before the mean age of cervical cancer in this series. This emphasis the point that cervical smears (papanicolaou stained cervical smear) with colposcopic biopsies when done early, goes a long way to reduce morbidity and mortality associated with cervical cancer. In developed countries where routine mass screening and Human papilloma virus vaccination are available, the incidence and mortality of cervical cancer is much reduced (4). In Nigeria however, cervical smear is not routinely done. Cost is a major hindrance and usually when NGO provides the services, it is usually for a limited number of women and period. Even after the initial screening, those that have abnormal or positive smears are not followed up; rather they are advised to see a gynecologist which they women usually do not do. Although the vaccine for the prevention of human papilloma virus 16 and 18 induced cervical cancer has been approved and is currently been administered in developed countries, in low resource countries where the end user is required to pay for it, it is largely unaffordable to the average woman (24). Emphasis to increase awareness must be encouraged, especially in the local communities and there is great need for health policy makers to ensure that routine cervical cancer screening and HPV vaccine are placed on top priority list so as to save our females at their productive age.

Endometrial cancer is the second commonest cancer and accounted for 22% of gynaecological cancers in this study. All the cases were seen in age group 50-79 years with the peak at 60-69 years with a mean of 62.5 years. Endometrial cancer was also the second commonest female genital tract cancer in Port Harcourt and Botswana (7, 11) but this is different with

Histologic analysis.indd 250 9/25/15 10:01 PM

the other studies where it ranked third (5,8,9,10,13,24) or even fifth (6). The reason for this is not known or it may be a changing pattern. Since endometrial cancer is usually seen in post menopausal women (age at diagnosis is usually in the sixth decade), increasing life expectancy and improving access to diagnostic facilities for those living in urban centres in Nigeria may be the reasons (11,25). Endometrial cancer is a hormone dependent cancer and mainly affects post-menopausal women in developed countries, with 188,000 new cases diagnosed annually and obesity is a major risk factor (4). The strongest and most consistent association with body mass has so far been seen for endometrial cancer, the risk of which is increased two- to six-fold in obese compared to lean women, both before and after menopause (4). After menopause, obesity promotes endometrial cancer by enhancing the peripheral (as opposed to gonadal and adrenal) production of estrogens. Other associated epidemiological risk factors, include unopposed estrogen and sedentary lifestyle (26). Endometrial cancer is thought to evolve through a premalignant stage called endometrial hyperplasia but the natural course of progression from endometrial hyperplasia to endometrial cancer is not clearly understood (2). With westernisation of lifestyle and increase life expectancy in Nigeria, endometrial cancer may be on the rise, hence the need to increase public awareness of the dangers of weight increase.

Ovarian cancers were the third most common gynaecological cancers and had two age group peaks (30-39 and 60-69) and accounted for 14.6% of gynaecological cancers. This rate is higher than 6.4% in Nepal, 6 3.4% in Botswana, 7 5% in Zimbabwe, 9 10% in Port Harcourt,11 but far less than 25.3% in Ghana, 8 30.5% in Kano 10 and 42.5% in Pakistan (13). No reason was given for the high rate in Pakistan except that the finding was in keeping with previous findings in that country while the high rate in Kano, was alluded to the fact that It may probably be due to awareness of various gynaecological conditions created by Muslim Medical Women Association of Kano State, which was making their women present at their Teaching Hospital with such conditions (10). Most cases of ovarian cancer occur spontaneously although genetic predisposition is responsible for ovarian cancer in 10% of cases (27). These hereditary ovarian cancers are associated with inherited germ line mutations in the BRCA-1 and BRCA-2 genes as well as the Lynch type 2 gene associated with hereditary nonpolyposis colorectal cancer (27). Such genetic ovarian cancers are histologically serous adenocarcinoma (28). Histologic sub-typing is necessary for the treatment decision as germ cell tumours of the ovary are potentially curable at all stages and for prognostcation (29,30). Serous and undifferentiated cancer of the ovary have worse prognosis compared to other cancers (30).

Choriocarcinoma accounted for 2.4% of cancers and was seen in the 30-39 years age group. This is not surprising since, being a disease associated with pregnancy, it is more likely to occur in active reproductive life (8). Low rates were reported in most studies except Zimbabwe and Kano (6,9,10,11). This is because while this study like many others was based on tissue diagnosis only, choriocarcinoma is diagnosed on clinical grounds using biochemical levels of human chorionic gonadotropin. No case of vaginal or vulval cancer was seen.

In conclusion, benign lesions were the most common with uterine leiomyoma accounting for most of them, while cervical carcinoma was the most common gynaecological cancer. Endometrial cancer cases were noticed to be on the rise.

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Histologic analysis.indd 251 9/25/15 10:01 PM

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Histologic analysis.indd 252 9/25/15 10:01 PM