Biopsy case mix and diagnostic yield at a Malawian central hospital

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Abstract

Cancer is a major disease burden worldwide resulting in high morbidity and mortality. It is the leading cause of mortality in developed countries and is one of the three leading causes of death for adults in developing countries. Pathological examination of tissue biopsies with histological confirmation of a correct cancer diagnosis is central to cancer care. Without an accurate and specific pathologic diagnosis, effective treatment cannot be planned or delivered. In addition, there are marked geographical variations in incidence of cancer overall, and of the specific cancers seen. Much of the published literature on cancer incidence in developing countries reflects gross estimates and may not reflect reality. Performing baseline studies to understand these distributions lays the groundwork for further research in this area of cancer epidemiology. Our current study surveys and ranks cancer diagnoses by individual anatomical site at Queen Elizabeth Central Hospital (QECH) which is the largest teaching and referral hospital in Malawi. A retrospective study was conducted reviewing available pathology reports over a period of one full year from January 2010 to December 2010 for biopsies from patients suspected clinically of having cancer. There were 544 biopsies of suspected cancer, taken from 96 anatomical sites. The oesophagus was the most common biopsied site followed by breast, bladder, bone, prostate, bowel, and cervical lymph node. Malignancies were found in biopsies of the oesophagus biopsies (squamous cell carcinoma, 65.1%; adenocarcinoma, 11.6%), breast (57.5%), bladder (squamous cell carcinoma, 53.1%) and stomach (37.6%). Our study demonstrates that the yield of biopsy for clinically suspected malignancy was greater than 50% for the 11 most common sites and provides a current survey of cancer types by site present in the population reporting to our hospital.

Introduction

Histological confirmation by a qualified pathologist is central to cancer diagnosis and required to create informed cancer treatment plans. Cancer causes a major disease burden worldwide with significant associated mortality and morbidity. It is the leading cause of death in developed countries and is one of the three leading causes of death for adults in developing countries[1,2].Cancer is currently responsible for more than 7 million deaths per year worldwide, more than malaria, tuberculosis and HIV/AIDS combined[1]. In the developing world, the number of new cancer cases will increase significantly over the next 10 years[3]. By 2020 there are expected to be 15 million new cases of cancer every year, 70% of which will be in developing countries, where governments are least prepared to address the growing cancer burden and where survival rates are often less than half those in more developed countries[3]. African countries will account for over a million new cancer cases a year and they are the least able of all developing countries to cope, having fewest cancer care services[3]. Limitations of resources and basic infrastructure in Malawi result in most Malawians having no access to cancer screening, early diagnosis, treatment, or palliative care. In order to improve this situation, data on cancer incidence is desperately needed to create strategic goals and focused treatment approaches to maximize lives saved.

There are over 200 different types of cancer, but four cancers (i.e., lung, breast, prostate, and large bowel) account for more than half of all cases where data are available [1]. However, there are marked geographical variations in incidence of cancer overall and in the specific cancers seen. Such differences reflect exposure to distinct causative environmental factors such as toxins, infection, and may also represent differences in inherited predisposition. In addition to providing data on neoplastic disease, descriptive epidemiology provides the basis for prevention, health service planning and allocation of resources.[4]

In Malawi and many other developing countries there are limited studies in the field of cancer epidemiology and cancer in general which impact negatively on the allocation of resources to its management. Few studies have been carried out in Africa to determine the variations or ranking of cancer in the specific organ sites leading to the inequitable distribution of resources mostly used to combat the spread of HIV, TB and malaria, which are all acknowledged to be major killers in the developing world[3]. However, in Malawi no similar study, according to our knowledge, has been conducted.

This study therefore will stand as an initial audit upon which large scale epidemiology studies can be based and incorporate all cancer types common in the country. It would also help allocate appropriate health care resources to cancer following increased levels of understanding of distribution of different cancer types in particular sites.

The main aim of this study was to rank current cancer diagnoses by individual anatomical site in the year 2010 at QECH, which is the largest teaching and referral hospital in Malawi.

Additional objectives of the study were:

1. To determine the yield (% cancer) of biopsies suspected of malignancy clinically.

2. To determine the distribution of anatomic sites commonly biopsied.

3. To rank histological cancer diagnosis according to individual biopsied sites.

Method

Study oversight

The study was approved by the Institutional ethical board at the Malawi College of Medicine.

Study design and population: We conducted a retrospective study at QECH and the College of Medicine Histopathology Laboratory, which is the main pathology laboratory for the hospital. The two institutions are next to each other in the city of Blantyre. This study enrolled cases that either had excision or incision biopsies from the departments of surgery,

adult oncology and pediatric oncology from January 2010 to December 2010 with confirmed histological diagnosis. All gynaecological cases were excluded in the study. This was because of frequent use of cytology and visual inspection using acetic acid in our setting and we thought histological reports would grossly under-estimate lesions from this site relative to other sites.

Data collection and analysis

The recruited cases and diagnoses from the wards were verified at the College of Medicine Histopathology Laboratory. The individual diagnosis and site of biopsy was verified at the pathology department using the laboratory reference number. The data was retrospectively collected on a standardized structured questionnaire that captured age and gender of patient, site of biopsy and diagnosis from clinical records and pathology records. Data was entered and analysed using proportions and frequency tables using Microsoft excel and Epiinfo software packages. Frequencies of all biopsied sites were calculated and all diagnoses per individual biopsied site, stratified by gender and age were ranked.

Study limitations

This is a retrospective, hospital based audit, however there were no missing set of records. Since the study is hospital based it fails to capture other cases that did not report to our hospital from within its catchment area.

Results

There were 544 biopsies that fulfilled our inclusion criteria of the total 1481 specimens sent to COM histopathology for histology in 2010. The remaining samples were those from other hospitals and gyaenecological biopsies. Of the 544, 50% were from males, 49.6% from females, and in 0.4% gender was unrecorded. The median age was 37 years with an interquartile range of 24 to 52 years. There were 244 cancer diagnoses out of the 544 biopsies taken which represents a yield of 44.9%. The 544 biopsies came from 96 anatomical sites. The oesophagus was the most common site (n=43;8.3%) followed by the breast (n =40; 7.6%), bladder (n=32; 6%), bone (n= 32;6%), prostate (n= 26; 4.9%), large bowel (n=18; 3.4%), cervical lymph nodes (n= 16:3%), nose (n=16;3%) , stomach (n= 16;3%), skin (n=15;2.8%), liver (n= 8:1.5%).

Squamous cell carcinoma accounted for 64% of oesophageal biopsies, followed by adenocarcinoma in 11%. The median age for patients with adenocarcinoma was 65 years whilst that of squamous cell carcinoma was 45 years. There was a female predominance in squamous cell carcinoma with 17 females and 11 males.

Of the 40 breast biopsies 47.5% were reported either as adenocarcinoma or ductal carcinoma. The age range of the breast cancer cases were 24 to 87 years with a mean of 50.7 and median of 46 years. Small numbers of other related malignancies, including fibroadenomas and other benign diseases accounted for the rest.

Thirty-two specimens from the bladder were obtained, and more than half (53%) were squamous cell carcinomas, 9.4% were adenocarcinoma whilst 9.4% were transitional cell carcinoma. The median age for the squamous cell carcinoma was 47 years and the majority was female (67.4%). Transitional cell carcinoma median age was 16 years whilst adenocarcinoma was 50 years.

The stomach site had 16 specimens reported, the majority of the cases 9 (56.3%) were benign, 5 (31.3%) were adenocarcinoma. The median age of the five patients with malignancy was 68 years.

More than half of the 15 cervical lymph node biopsies were malignant. Three were Kaposi's sarcoma (median age of 30years), and 2 (13.3%) were reported as invasive squamous cell carcinoma. The squamous cell carcinoma group had a median age of 48 years. Other diagnoses were 2 non-Hodgkin's lymphoma (13.4%) and 1 (6.7%) metastatic carcinoma, with unspecified histology.

In the prostate 2 (7.7%) were adenocarcinoma and the rest 24 (92.3%) showed benign prostate hypertrophy (BPH).

Of the 8 liver biopsies, 4 were hepatocellular carcinoma, 1 was an adenocarcinoma (median age of 38 years) and one hepatoblastoma was reported from a 9 year old. The remaining 25% percent of the biopsies of the liver were non-malignant (Figure 2).

Discussion

The most commonly biopsied sites had oesophagus, bladder and liver yielding cancer diagnoses in over 75% of biopsies. The breast cancer yield of 57.5% demonstrates that a suspicious breast mass or lesions is likely to be cancerous. Overall, these findings highlight the importance of histological confirmation as a requirement for treatment since cancer is common and varied.

Cancer of the prostate is the fifth most common cancer in the world and the second most common in men[5]. The relative low yield of prostatic cancer in our study can be explained by the younger age of our patients (average 65 years) who had prostate biopsies compared to other studies. The average age was 67 years in the SEER data of 2004 to 2008 and 73 years in SEER-Medicare data of 1991 to 2007[6,7]. The ranking (5th) of this cancer in the National Cancer Registry is low. However, a report from Zimbabwe indicates prostate cancer as the commonest cancer in males.[12] The majority of the cases in our study (92.3%) were benign prostate hypertrophy. Another reason for the low cancer yield in this group may reflect the fact that there was no pre-biopsy PSA determination. The rate of invasive prostatic adenocarcinoma was 58.2% in a study where the average pre-biopsy PSA level was 8.7μg/L.[8] Our data may suggest prostate cancer is missed or misdiagnosed.

The relatively low yields of cancer from the gastrointestinal tract - stomach 37.6% and large bowel 44.4% - may be explained by frequent occurrence of other benign lesions in these sites such as ulceration and polyps respectively. However these yields are still high enough to argue for a high index of suspicion for cancer and biopsy in these sites.

The oesophagus was the most commonly biopsied site. This is not surprising, considering it is the second reported cancer in males and third in Malawi if both sexes are considered according to the National Cancer Registry (NCR)[9]. The most common histological diagnosis on this site was squamous cell carcinoma (65.1%) which is consistent with the global findings but opposite to Western trends where adenocarcinomas predominate[5]. This underlies the fact that Barrett's esophagus is not the main risk factor in Malawian cases of oesophageal cancer. The predominance of squamous histology suggests that smoking, alcohol and aflatoxin B may be important aetiological factors.

In Malawi Kaposi sarcoma is thought to be the most common

malignancy in adults, but in this study, skin is not the most biopsies were not taken commonly. This may be because it is assumed that clinical diagnoses of Kaposi sarcoma are made. Apart from these two cancers other malginanices are likely to get biopsied due to difficulty in making a definite diagnosis clinically. For this reason, we believe the data for the cancers other than Kaposi sarcoma and skin do represent the distribution of cancers that present at our hospital.

Cervical cancer is the commonest cancer in females and the second most frequent when both sexes are combined (NCR)[9]. However, our study did not include gynaecologic cancers.

Breast cancer is by far the most frequent cancer of women in the world ranking second overall when both sexes are considered together, and fifth in women according to the Malawi National Cancer Registry[5,9]. The ease in tissue procurement, as well as the difficulty in distinguishing benign from malignant breast disease contributes to the frequency of these biopsies.

Bladder biopsies had a high yield of squamous cell carcinoma histology (53.1%) which is different from the findings in developed countries where transitional cell carcinoma as the most common histology. This finding is consistent with reports from neighbouring countries where squamous cell carcinoma predominates. A study in north west Tanzania reported squamous cell carcinoma histology in 55.1% of cases. These were found to be associated with schistosomiasis compared to the non squamous cancers.[13]It has been suggested that such high prevalence of squamous cell carcinoma in parts of Africa is linked to chronic infection with Schistosoma hematobium.[5]

Samples from the 15 cervical node biopsies yielded cancers in 53.4% but infections represented only 33.3%. The most common cancer was Kaposi's sarcoma, unlike the squamous cell carcinoma reported in Western literature. This may be due to the high HIV prevalence in Malawi and argues strongly against the practice of diagnosing TB clinically based on the repsence of enlarged nodes without taking a biopsy. Our data shows that the occurrence of malignancies at this site is not rare.

Conclusion and recommendations

Our study demonstrated that the yield of malignancy in most of the sites clinically suspected to have cancer was very high and gives histological ranking for different biopsied sites. This supports the practice of using histology as a gold standard to diagnose cancer. The histological trends as well as the findings of malignancy rather than TB in cervical lymph nodes re-enforces this. It also demonstrates differences in prevalence of cancer histology in particular sites which suggests differences in risk factors between our Centre, located in Sub-Saharan Africa, and the West.[10,11] More studies on cancer epidemiology in this region should be encouraged to fully understand the incidence and risk factors for the different cancers in Sub-Saharan Africa.

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Author contributions

The study was conceived by LM, the proposal was written by PM, RN, and KM but critiqued by LM. The analysis and first draft of write-up was done by PM and reviewed by all authors; LM wrote the discussion. DM and LS did the final critique and proof-reading of final draft.

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