

GLOBAL HEALTH

Addressing the Growing Cancer Burden in the Wake of the AIDS Epidemic in Botswana: The BOTSOGO Collaborative Partnership



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Botswana has experienced a dramatic increase in HIV-related malignancies over the past decade. The BOTSOGO collaboration sought to establish a sustainable partnership with the Botswana oncology community to improve cancer care. This collaboration is anchored by regular tumor boards and on-site visits that have resulted in the introduction of new approaches to treatment and perceived improvements in care, providing a model for partnership between academic oncology centers and high-burden countries with limited resources. © 2014 Elsevier Inc.

Introduction

The global burden of cancer is considerable. The majority of cancer cases and over 70% of cancer deaths occur in low-income and middle-income countries (1-3). On the basis of current population trends, global cancer mortality is expected to double by the year 2030. In sub-Saharan Africa, the rising epidemic of cancer is coupled with a high prevalence of human immunodeficiency virus (HIV) infection, presenting unique challenges for patients, health care providers, and local governments.

The nation of Botswana (Fig. 1) sits at the crossroads of cancer and HIV infection. It has one of the most successful HIV treatment programs (4) and now faces a rising burden of malignancies, predominantly among HIV-infected persons receiving appropriate antiretroviral treatment. Massachusetts General Hospital (MGH) and Botswana Harvard AIDS Institute, along with the Botswana—University of Pennsylvania Partnership and Baylor College of Medicine, have partnered with the local oncology community and the government of Botswana with the goal of addressing this rising burden. Here we aim to describe the MGH and Botswana Harvard AIDS Institute efforts as a model of a partnership between academic medical centers and low-income and middle-income countries with limited oncology resources.

Health and Cancer Care in Botswana

At the time of independence in 1966, Botswana was one of the poorest countries in Africa and had very limited health care infrastructure. The development of stable democratic governance and the subsequent discovery of mineral wealth have permitted rapid and sustained economic expansion (5). Botswana is now among the most affluent countries in Africa and has invested heavily in health care with construction of over 300 health clinics and dozens of regional hospitals to care for a population of 2 million persons.

Despite an intense epidemic of HIV infection/acquired immune deficiency syndrome (AIDS) during which life expectancy dropped to less than 40 years by the early 2000s, the Botswana government's investment in health care (most notably HIV infection care) was able to reverse this decline with an increase in longevity to over 65 years

currently (6, 7). Botswana had one of the first public anti-retroviral treatment programs in Africa and has achieved remarkable coverage, with over 90% of citizens who require treatment currently receiving therapy, according to government estimates (8). Although the incidence of HIV infection may be declining in Botswana, the burden of chronic infection is immense, with an estimated 25% of adults living with HIV infection (4).

As AIDS-related mortality has plummeted the late sequelae of chronic HIV infection have risen, and cancer in particular has emerged as a public health challenge in Botswana. At 2 referral hospitals, wards previously full with HIV-infected patients with tuberculosis and other opportunistic conditions have been repurposed as oncology wards. Antiretroviral therapy has been associated with a decreased incidence of Kaposi sarcoma, but other AIDS-defining and non-AIDS-defining cancers have increased in incidence since treatment became available (9). Over 60% of patients with cancer have HIV infections (10). Cancer prevention and early detection by screening, aside from a growing program in cervical cancer, are not routine, leading to late diagnosis and presentation with advanced disease among both HIV-infected and HIV-uninfected patients (11). Leading malignancies in Botswana are Kaposi sarcoma; cervical, breast, head and neck, esophageal, and prostate cancer; and non-Hodgkin lymphoma (12).

One of the main challenges for cancer care in Botswana is the lack of human capital (ie trained specialists in many fields, including pathology, clinical oncology, radiology, surgical subspecialties, and medical physics and engineering). Botswana hopes to address this issue through developing efforts in postgraduate training at the University of Botswana School of Medicine, but a well-established oncology training program does not yet exist, resulting in a significant shortage of care providers and expertise in the country to cope with the rapidly growing cancer burden.

As recently reviewed (13), a core oncologic infrastructure does exist in Botswana. Limited specialized oncologic care is available in 3 government hospitals, Princess Marina Hospital in Gaborone, Nyangabgwe Referral Hospital in Francistown, and Letsholathebe II Memorial Hospital in Maun (Figs. 2 and 3), and 2 private facilities, Gaborone



Fig. 1. Map indicating Gaborone and Francistown, Botswana. The majority of cancer care is delivered in referral centers in these cities.

Private Hospital and Bokamoso Private Hospital in Gaborone, but this care is limited by human capital and unreliable access to medications and diagnostics. Expatriate oncologists, recruited to Botswana through a service program of the government of China or through a for-profit Indian medical staffing company, supervise care at the public oncology facilities, along with generalists (medical house officers). Since 2007, medical oncologists from the Texas Children's Hospital have provided specialized care for children with cancer. A few clinical oncologists, trained in both radiation and medical oncology at foreign institutions, practice in the private sector. At the government facilities and sometimes even private facilities, there are shortages of chemotherapeutic agents and other antineoplastic drugs, leading to interruptions in, or missing components of, multidrug regimens, and to shortages of drugs to manage the complications of therapy, including antiemetics, antibiotics, narcotics, and growth factors. There are also challenges with regard to cancer diagnosis, inasmuch as both the tools and the personnel to perform biopsies are in short supply, often delaying the start of treatment.

The National Health Laboratory (NHL), a government institution in Gaborone, and Nyangabgwe Referral Hospital in Francistown provide the majority of pathology services in Botswana. The Ministry of Health employs 4 anatomic pathologists to interpret specimens from throughout the country. The NHL alone receives approximately 35,000 specimens, including over 24,000 Papanicolaou smears, each year. The typical time from receipt of a specimen to reporting generally exceeds 1 month. This prolonged turnaround time is caused not only by a lack of human



Fig. 2. Princess Marina Hospital, Gaborone, (above) and Nyangabgwe Referral Hospital, Francistown (below). Long waits and crowded facilities are common in these referral hospitals.

capital but also by a lack of the necessary equipment to care for a population this large.¹ For the vast majority of specimens, histologic appearance alone is used for diagnosis and grading of malignancies.

Currently, radiation therapy is available only at Gaborone Private Hospital. Although radiation is administered in the private sector, the Botswana government has made it available for all citizens by fully supporting the costs of treatment for the 90% of patients without sufficient private medical insurance. A single linear accelerator and a high-dose-rate brachytherapy device are housed at GPH. With a population of 2 million, the International Atomic Energy Agency recommendations would indicate the need for up to 4 linear accelerators in Botswana (14), far more resources than currently available.

¹ Capacity is being expanded; meanwhile, the National Health Laboratory currently has 1 embedding station, 1 automated processor, and 1 microtome. It does not offer frozen sections, intraoperative cytology, electron microscopy, immunofluorescence, polymerase chain reaction, or fluorescence in situ hybridization on tissue blocks. A limited array of immunohistochemistry testing became available in early 2013; previously a small subset had been outsourced to South Africa for immunohistochemistry testing.



Fig. 3. Chemotherapy administration at Princess Marina Hospital.

Notably, however, other sub-Saharan countries with significantly larger populations (eg, Rwanda and Mozambique) have no such facility. A teaching hospital affiliated with the University of Botswana is under construction and plans to include radiation therapy services in the future.

The oncology department at GPH is staffed by 2 oncologists, a medical physicist, nurses, therapists, and a dosimetrist, and it treats approximately 60 patients per day, the majority for curative intent (80% radical, 20% palliative). The linear accelerator (Elekta Precise, Stockholm, Sweden) has independent jaws but no multileaf collimator. Customized Cerrobend blocking is used in up to 15% of cases. Verification imaging is performed with conventional radiographic films. A dedicated computed tomography simulator (Philips AcQSim, Amsterdam, the Netherlands), which also often serves as a source of diagnostic and staging imaging, is available, and 3-dimensional treatment planning is performed for both external beam radiation therapy and brachytherapy.

BOTSOGO Collaboration

After a year-long needs assessment in 2011 and to help improve cancer care in Botswana, the MGH/Harvard Medical School community has partnered with the oncology community and government of Botswana to form the BOTSOGO (BOTSwana Oncology Global Outreach) initiative (15). The name BOTSOGO, pronounced “bot-so-ho,” is taken from the Setswana (primary language for most Botswana) word for “health.” This collaborative effort in oncology care was spurred by existing relationships in HIV/AIDS research and care delivery developed within the Botswana-Harvard AIDS Institute Partnership (BHP). BHP, founded in 1996, is an independent not-for-profit research organization in Gaborone affiliated with the Harvard School of Public Health and the Botswana Ministry of Health.

The initial efforts of the BOTSOGO initiative have been organized around the following themes: (1) on-site visiting to share expertise in clinical cancer care for capacity-building purposes in identified areas of most need, impact or both; (2) developing a forum for multidisciplinary case discussions

and education; (3) identifying and conducting collaborative research initiatives; and (4) relationship building with local stakeholders for long-term sustainability and growth.

Clinical care and capacity building

Likely driven by prevalent HIV infection, Botswana has one of the highest rates of cervical cancer in the world, with an age-standardized incidence of 38 per 100,000 women (compared to less than 10/100,000 in developed countries) (9), and it is the leading cause of cancer-related mortality (16). The Botswana—University of Pennsylvania collaboration has pioneered capacity development in screening and early detection of cervical lesions (17). We sought to complement these activities by providing hands-on training and mentorship, with initial efforts focused on enhancing capacity for cervical cancer treatment.

Once diagnosed, cervical brachytherapy is a critical tool in disease management and, along with external beam radiation therapy, can be curative even for locally advanced disease (18). Before 2012, patients were sent to South Africa to receive brachytherapy. It was the consensus of local care providers and the government of Botswana that the development of local capacity for brachytherapy was a high priority. A modern high-dose-rate device (Nucletron/Elekta AB, Stockholm, Sweden) was purchased and installed at GPH in 2011, and insertions began in February 2012.

The first visit of the BOTSOGO team coincided with the initiation of cervical brachytherapy in Botswana. Hands-on, practice-changing guidance was provided for treatment planning, equipment selection, ultrasound image guidance, source insertion, and patient treatment. A follow-up visit occurred in September 2012, when approximately 25 cases were treated over a 1-week period (Fig. 4). This visit helped to alleviate a 3-month brachytherapy backlog. Of note, insertions were challenging because of fibrosed cervixes and delay-induced tumor recurrences. Titanium tandem and split ring (TSR) treatments were initiated with a donated applicator set (Mick Radio-Nuclear Instruments,



Fig. 4. Ultrasound-guided cervical brachytherapy insertion, Gaborone Private Hospital.

Inc., Mount Vernon, NY). These applicators provide ideal geometry for the advanced disease typically seen in Botswana. Further visits by our team in May and September 2013 and additional support from the Botswana—University of Pennsylvania collaboration have helped optimize the procedure. The oncologists at GPH have now developed significant expertise, and they treat 30 to 50 brachytherapy cases per month.

With the successful development of capacity in brachytherapy administration, the focus of visits has expanded to include patient care and treatment planning case discussions for external beam radiation therapy, including disease management with particular attention to pelvic malignancies and head and neck malignancies, and to quality and safety. A distance learning program for physicians, therapists, nurses, and physics staff is under development.

The BOTSOGO initiative has since grown to include all cancer-related disciplines. MGH medical and surgical oncologists visited Botswana in May 2013, focusing on lymphoma and breast cancer management and providing patient care and didactic teaching at Princess Marina Hospital in Gaborone and Nyangabgwe Referral Hospital in Francistown (15). In September 2013, a visit by an MGH pathologist looked to help address possible bottlenecks at NHL, including the donation of an additional microtome for processing of pathology slides. A full-time MGH faculty medical oncologist is now based in Botswana as of March 2014 to provide specialized clinical care, train medical students and residents, assist with quality improvement measures, and conduct research initiatives.

Multidisciplinary tumor board and educational initiatives

We have established the first sustainable multidisciplinary tumor board in Botswana, which connects the Botswana oncology community (including oncologists, surgeons, pathologists, infectious disease physicians, house officers,



Fig. 5. Botswana-Harvard multidisciplinary tumor board. Above, Gaborone. Below, Boston.

nurses, therapists, and students) with MGH/Harvard-based disease site experts (Fig. 5). Since its initiation during the first visit of the BOTSOGO team to Botswana in February 2012, the tumor board has met monthly to discuss specific patient management challenges. Attendees in Botswana and the United States have been able to conduct these meetings through an internet-based platform (WebEx, Santa Clara, CA). Thus, we have fostered relationships not only between care providers in Botswana and MGH/Harvard but also among care providers from different disciplines and different institutions within Botswana. In addition to providing a venue for education and constructive peer review, the conference provides a regular forum for discussion of relevant health systems issues.

The tumor board has covered a wide range of cases and topics selected by care providers of patients in Botswana, including common (eg, cervical, breast, head and neck, Kaposi sarcoma, non-Hodgkin lymphoma) and uncommon (eg, leiomyosarcoma, vaginal carcinoma, penile, gastrointestinal stromal tumor, pediatric) cancers (Table 1). Case presentations by the treating physicians in Botswana are followed by an open discussion of challenging diagnostic, treatment, or health system issues that affect the care of the patient. The conference concludes with a focused review of best practice by disease site experts and with possible strategies for adapting these to

Table 1 BOTSOGO multidisciplinary tumor board case summaries

Date	Title	Cancer type	HIV status
Feb 12	Woman with cervical cancer	Cervix	+
Apr 12	58-year-old man with lung mass	Lung	–
May 12	35-year-old woman with leiomyosarcoma	Leiomyosarcoma	+
Jul 12	20-year-old man with hepatocellular carcinoma	Hepatocellular carcinoma	–
Aug 12	65-year-old woman with dark heel mass	Melanoma	Declined test
Sep 12	39-year-old with non-Hodgkin lymphoma	Non-Hodgkin lymphoma	+
Nov 12	36-year-old woman with epigastric pain	GIST	–
Dec 12	29-year-old woman with a breast mass	Breast	–
Jan 13	39-year-old man with bilateral pleural effusion	Kaposi sarcoma	+
Feb 13	35-year-old woman with HIV infection and a tonsillar mass	Tonsillar SCC	+
Mar 13	47-year-old woman with postcoital bleeding	Vagina	+
Apr 13	2 men with breast masses	Breast	–
May 13	38-year-old woman and a 26-year-old man with neck and axillary masses	NHL	Pt 1 +; Pt 2 –
Jun 13	Oncologic management of a large neck mass	Malignant peripheral nerve sheath tumor	+
Jul 13	2 women with rectal masses	Rectal adenocarcinoma	–
Sep 13	29-year-old with vulvar cancer	Vulvar	+
Oct 13	5 children with lower extremity masses	Osteosarcoma	–
Nov 13	2 men with penile lesions	Penile	+
Dec 13	2 men with groin and neck swelling	Castleman disease	+
Feb 14	52-year old woman with an enlarging perineal mass	Myoepithelioma	–
Mar 14	A 51-year old woman with epigastric pain	Pancreas	–
Apr 14	A 41-year old female with pain and bleeding after treatment for breast cancer	Breast; Palliative Care	–

Abbreviations: GIST = gastrointestinal stromal tumor; HIV = human immunodeficiency virus; NHL = non-Hodgkin lymphoma; SCC = squamous cell carcinoma

clinical circumstances in Botswana and for HIV-infected patients (19).

A recurrent theme throughout the conferences is that barriers to diagnosis and care often result in advanced disease (Fig. 6). These barriers include long-distance travel to referral hospitals for individuals living in less accessible areas, a decreased awareness of the signs and symptoms of cancer, a tendency to seek opinions from traditional healers, processing delays for pathology specimens, limited access to appropriate drugs and therapies, and wait times associated with large patient numbers in a resource-limited setting.

In addition to enhancing the core activities of the tumor board, the BOTSOGO collaboration is conducting a 3-day oncology symposium (cosponsored with Botswana Ministry of Health, University of Botswana, Baylor College of Medicine, Texas Children's Hospital, and University of Pennsylvania) in Gaborone in May 2014 to further catalyze the development of a Botswana comprehensive cancer control plan, standardized cancer treatment guidelines, local engagement in oncology research, and improved provision of cancer care.

Research initiatives

Many facets of the cancer problem in sub-Saharan Africa remain poorly understood (20). The spectrum of disease, its

relationship to viral pathogens (eg, HIV, Epstein-Barr virus, human papilloma virus) and other exposures, and successful approaches to treatment with limited resources require further definition. Addressing these knowledge gaps to enable quality care and prevention has emerged as a priority of the BOTSOGO collaboration. Again leveraging the resources of the Botswana Harvard AIDS Institute, the collaboration has supported the development of research infrastructure, including support to the Botswana National Cancer Registry; sustained the Botswana Prospective Cancer Cohort; and promoted several collaborative research projects that build on these shared resources.

Stakeholder collaboration

Integrated oncologic care is complicated and demands a multidisciplinary and interdisciplinary process with many invested partners. In addition to building strong relationships with the oncology teams at GPH and on the wards of the 2 main referral hospitals, PMH and Nyangabgwe Referral Hospital, we have also actively collaborated with representatives from the Botswana Ministry of Health, Botswana-Harvard AIDS Institute Partnership, NHL, University of Botswana, the Cancer Association of Botswana, Botswana—University of Pennsylvania collaboration, Baylor College of Medicine, Texas Children's Hospital and the US embassy in Botswana. Through these

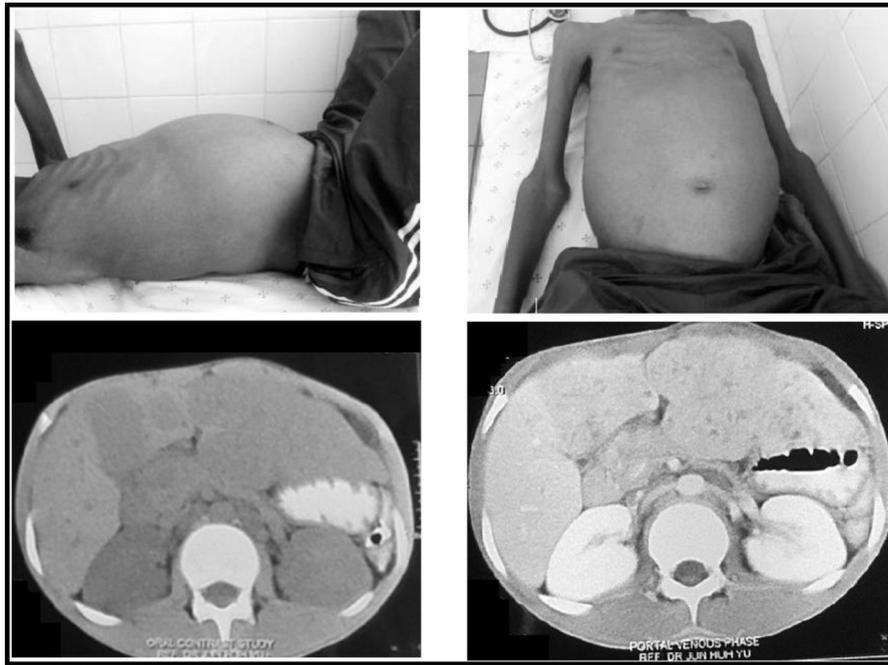


Fig. 6. Subject of Multidisciplinary Tumor Board. 20-year old man presenting with weight loss, vomiting, abdominal pain and distension, with a diagnosis of hepatocellular carcinoma. Computed tomography showing multinodulated masses within the left lobe of the liver and hilum, with dilated intrahepatic biliary ramifications in the region of the caudate and left lobes.

robust partnerships and a shared common goal of improving the care of cancer patients, Botswana is poised to build itself as a center of excellence in oncology for sub-Saharan Africa. Given the country's success in addressing the HIV/AIDS crisis, this goal seems achievable.

Future Goals and Conclusions

In conclusion, a collaborative and sustainable relationship in oncology care has been established between MGH/Harvard and Botswana, anchored by regular tumor boards and on-site visits and exchanges that have resulted in the introduction of new approaches to treatment and perceived improvements in patient care. In the future, we aim to expand our teaching and training efforts in the multiple oncologic specialties, further address issues of drug and equipment access, continue to promote public education about cancer, provide bidirectional exchange opportunities for faculty and trainees, and foster ongoing research links to study cancer in the setting of HIV infection. The BOTSOGO collaboration provides a model for partnership between academic oncology centers and high-burden countries with limited resources.

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