






Infections Mimicking Malignancy in Kano, Nigeria: A Teaching Hospital Experience

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Abstract

Objective: This study aimed to evaluate the pattern of presentation of infectious lesions mimicking malignancy. This will serve to heighten clinical indices of suspicion and prevent unwarranted aggressive management. **Methods:** This is a 19-year (1999-2017) audit review of all morphologically diagnosed infection-related lesions in which malignancy was primarily clinically suspected. **Results:** Fifty-six cases of infection-related mimics of malignancy were diagnosed in the study period: schistosomiasis related, 22 (39.2%); actinomycosis, 21(37.5%); tuberculosis-related, 10 (17.9%); fungi-related, 3(5.4%). Twenty-one cases of actinomycosis of the lower limbs and oropharynx were mistaken for melanoma, squamous cell carcinoma, sarcoma, and oropharyngeal carcinoma. The mean age was 33±17years. The 10 patients with atypical *Mycobacterium tuberculosis*-mimicking malignancy had mean age of 37±14 years and included three in the testes, testicular cases, one from the jaw, and two cases

each from ovary, breast, and uterus. Of the three fungal lesions, there was a case each from the brain, skin, and bone. All were males with mean age of 21±7 years. **Conclusion:** For accurate diagnosis of infection-related mimics of malignancy, a high index of clinical suspicion, knowledge of and attention to characteristic radiological signs, and obtaining representative tissues for histopathologic and cytopathologic diagnoses are paramount.

Keywords: Schistosomiasis, Tuberculosis, Actinomycetoma, Fungal, Malignancy, Mimics

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Introduction

Mimics of malignancy pose diagnostic challenges clinically, radiologically, and sometimes, morphologically. Incorrect diagnosis of these entities

may lead to patient anxiety, delayed diagnosis, disease progression, unnecessary intervention, increased hospital costs and exposure of patients to risks (1-5).

These mimics, which include infections (bacterial, fungal, and parasitic infections) and benign neoplastic lesions, have varied pathological entities with uncommon presentations similar to malignancy (1,3-5). Inadequate clinical evaluation, history of cancer in a patient with swelling, similarities in radiological features, overlapping symptoms, and unusual clinical presentation appear to underlie misdiagnosis in these cases (1-5). Infections mimicking malignancy have geographical variation base on their patterns and prevalence and hence the need for this study in our locality(1-5). This study aimed to present an audit of infections that mimic malignancy in a bid to improve clinical index of suspicion in such cases.

Materials and methods

This is a 19-year (January 1999 to December 2017) retrospective hospital-based descriptive study carried out in the Department of Histopathology and Surgery of Aminu Kano Teaching Hospital (AKTH), Kano, Nigeria. The study conforms to the Health and Research Ethical committee of AKTH (ethical review reference number: AKTH/MAC/SUB/12A/P-3/VI/3190).

AKTH is a tertiary hospital with a bed capacity >700 and receives referrals and histological samples (with an annual average of 5500 samples) from cities and rural areas of Kano state (population, >13.4 million) and neighboring areas of Jigawa, Bauchi, Kaduna, and Katsina states. The study included all cases of infection in which malignancies were the sole clinical or radiological assessments during the study period. The point of data collection is from the time samples were received in Histopathology Department. Detailed clinical information was sought from clinicians, and cases with inadequate clinical information and other lesions in which non-malignancies were also suspected were excluded. A total of 56 cases were analyzed. The data, including clinical history, examination, clinical and radiological assessment, and histological diagnosis, were obtained from hospital request forms (histopathological request forms), patients' case notes, and duplicate copies of histopathology reports, reviewed slides, and electronic records of the Histopathology Department. The histopathological request forms were well archived

upon receipt, and the information they contain has been electronically converted in the past 15 years. This information includes pre-analytical diagnosis, detailed findings, including imaging, and contacts of physician. The keywords searched in histopathological electronic records and request forms were *clinical assessment* and *sole clinical/radiological assessment of malignancy*.

The collected information was tabulated and analyzed by descriptive statistics using the SPSS for Windows version 23.0 (IBM Corp., Armonk, NY, USA). The limitations of this study include missing data and large number of samples received from other hospitals with insufficient clinical information.

Results

A total of 77 cases were initially identified in the study period, but after evaluation, 21 did not meet the inclusion criteria due to insufficient information, and 18 (86%) of the excluded cases were samples received from hospital outside Kano.

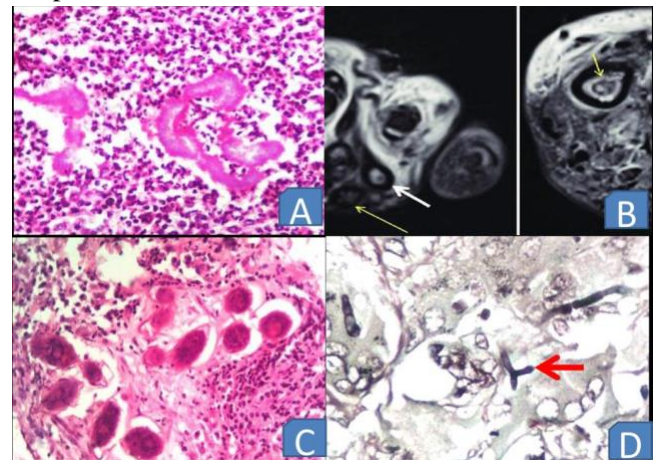


Figure 1. (A) Section of skin tissue shows filaments of Actinomyces spp surrounded by neutrophilic infiltrates. Hematoxylin & Eosin (H&E) x400. (B) Magnetic Resonance imaging of Eumycetoma showing 'Dot in a Circle' feature.²⁸ (white arrow). (C) Viable Schistosoma ova surrounded by inflamed fibrotic stroma (H&E) x400. (D) Non-septate hyphae of Aspergillus with right-angle branching (red arrow). Grocott Methenamine x400.

Fifty-six cases of infection in which malignancies were solely clinical and radiological suspicions were histologically diagnosed in the study period, and this represents 0.06% of all cases in the study period. These

comprised 22(39.2%) cases of schistosomiasis, 21(37.5%) cases of actinomycosis, 10(17.9%) cases related to tuberculosis (TB), and 3(5.4%) related to fungi. Malesex predominated, with a male/female ratio of 1.4:1.

Table 1. Characteristics of schistosomiasis-related mimics of malignancy

Sites involved/ clinical suspicion	n	%	Clinical findings	n	%
Prostate/ adenocarcinoma	3	13.7	High PSA	3	100
			Abnormal DRE	3	100
Ovarian/ Malignancy	1	4.5	Abdominal pain	1	100
			Abnormal USS	1	100
Gastric/ adenocarcinoma	1	4.5	Weight loss	1	100
			Gastric outlet obstruction	1	100
Colonic/ adenocarcinoma	8	36.4	Weight loss	8	100
			Mucoid (±bloody) stool	2	25
			Polyp on endoscopy	2	25
Rectal/ adenocarcinoma	8	36.4	Bloody mucoid stools	8	100
			Weight loss	8	100
Inguinal lymph node/lymphoma	1	4.5	Fever	1	100
			Rubbery, enlarged	1	100
		22	100		

The mean age of the schistosomiasis-related cases was 35±18years. Of the 22 cases,16(72.8%) were suspected as colorectal cancer and presented with weight loss, mucoid (±bloody) stools, and endoscopic polyps seen in 100%, 59%, and 25% respectively; 3(13.7%) were suspected as prostatic adenocarcinomas and had prostate

specific antigen (PSA) ranging from 8.0 to 9.3ng/mL, and digital rectal examination revealed hard contours; 1(4.5%) was suspected as ovarian malignancy and presented with hyper-echoic abdominal mass and pain in a 30-year-old female; 1(4.5%) was suspected as gastric cancer and presented with weight loss and gastric outlet obstruction in a 30-year-old male. The last schistosomiasis case was suspected to be lymphoma and presented with fever and rubbery and enlarged inguinal lymphadenopathy (Table 1).

The mean age was 33±17years for the 21 cases of actinomycetoma-related mimics of malignancy, and 20(95.2%) involved the lower limbs, whereas the remaining case involved the oropharynx. These frequently presented with swelling and ulceration of lower limbs and oropharynx and were mistaken for melanoma, squamous cell cancer, sarcoma, and oropharyngeal cancer (Table 2).

Table 2. Characteristics of actinomycosis-related mimics of malignancy

Sites involved/clinical suspicion	n	%	Clinical findings	n	%
Lower limb/ melanoma	11	11	Dusky swelling	11	55
Squamous cell carcinoma	8		With ulceration	19	95
Sarcoma	1	95.2			
Oropharynx/ carcinoma	1	4.8	Mass in the oropharynx	1	100
		21	100		

Ten cases of atypical *Mycobacterium tuberculosis*-related lesions mimicking malignancies commonly presented with swelling, ulceration, and abnormal bleeding. These included 3(30%) cases suspected to be testicular germ cell tumors, 2(20%) each were suspected to be ovarian germ cell tumors, breast cancer, and endometrial cancer, and 1(10%) was suspected jaw to be

Burkitt lymphoma (Table 3). The mean age of the cases was 37±14 years.

Table 3. Characteristics of tuberculosis-related mimics of malignancy

Sites involved/clinical suspicion	n	%	Clinical findings	n	%
Testicular/germ cell tumor	3	30	Firm swelling	3	100
Ovary/germ cell tumor	2	20	Minimal pain	2	67
Uterus/endometrial carcinoma	2	20	Abnormal echogenicity	2	100
Breast/carcinoma	2	20	Abnormal bleeding	2	100
Jaw/Burkitt lymphoma	1	10	Perimenopausal Enlarged and fungating Ulceration	2	100
			Ulceration	1	100
			Young age	1	100
	10	100			

Table 4. Characteristics of fungi-related mimics of malignancy

Sites involved	n	%	Clinical findings	n	%
Brain: astrocytic tumor	1	33	Space-occupying lesion	1	100
Skin: sarcoma	1	33	Young age	1	100
Bone: osteosarcoma	1	34	Ulceration	1	100
			Fungating lesion	1	100
			Young age	1	100
			Rapidly enlarged mass	1	100
			Ulcerated	1	100
			Short duration	1	100
	3	100			

Fungating, ulcerating, and space-occupying lesions, younger age, and short clinical courses marked the three

fungal lesions, one each from the brain (mimicking astrocytic tumor), skin (mimicking a sarcoma), and bone (mimicking osteosarcoma) (Table 4). All were males and had a mean age of 21±7 years.

Discussion

The preponderance of schistosomiasis-related mimics, their tissue distribution (predominantly gastrointestinal), and mean age of 35±18 years found in this study were similar to the preponderance of schistosomiasis, its site distribution, and age characteristics (mean 38.8years) of helminthic infections mimicking malignancy described by Pilszczek (1) in a systematic review. The preponderance of schistosomiasis may be related to the high prevalence (34.7%) of the disease in Nigeria (2). Preponderant presentation of gastrointestinal cases with weight loss and mucoid (±bloody) stools and occasionally as polyps on endoscopy have been described by Elbatee et al. (3) and Issa et al. (4). The polyps are usually recto-sigmoid but may affect any part of the gastrointestinal tract, including the stomach, where it caused antral fibrosis and consequent gastric outlet obstruction in our affected patient.

Presentations such as ovarian masses and enlarged rubbery lymphadenopathy have also been reported by Efareed et al. (5) and Lima et al. (6). PSA elevation in cases of prostatic schistosomiasis due to prostatitis and a hard craggy feel on digital rectal examination due to fibrosis increase suspicion of malignancy. Ultrasonography may also show nodularity (7). However, a relatively younger age at presentation may be helpful, as was the case in these reported patients who were in their mid- to late forties. In addition, adequate histological sampling must be done to ensure a small focus of malignancy is not missed.

Actinomyces is a chronic bacterial infection often affecting the cervico-facial, abdomino-pelvic and pulmono-thoracic regions of the body. The rarity of this lesion in the lower extremities and its usually ulcerative nature may underlie their greater likelihood of labeling it as malignancy, particularly squamous cell cancer, because of long-standing duration, or as melanoma, because of the dusky nature of the overlying skin and

location on the plantar surface of the foot, the most common location of melanomas in the study locality (8). Although detailed clinical history, including comorbidity, with immunosuppressive risk factors was unavailable in most of the actinomycosis cases, the hospitals from which the laboratory request forms originated showed that these were from rural areas where trauma during farming is an important risk factor. Prevalence among males and all age groups have also been described (9), both in keeping with characteristics of the cases in our index study (male/female ratio, 5:1; age range, 17-70years). Although actinomycetes are commensals in the oropharynx, when the organism proliferates and forms a nodulo-ulcerative lesion, as seen in one of our reported cases, the lesion is suspected to be oropharyngeal carcinoma (10).

In the northern region of Nigeria, where this study was conducted, approximately 14.4% of TB cases are extra-pulmonary (11). The testicular TB cases mimicking malignancy in our study were firm on palpation and hypo- and hyper-echoic on ultrasonography. Similar ultrasonographic findings, including diffuse and mixed patterns, have also been reported by Nepal et al. (12). The two ovarian masses were also hyper-echoic and the characteristics, i.e., similarity to the testicular lesions and the young age of the patients, underlined the clinical suspicion of germ cell tumors. In differentiating cases of gonadal TB from true malignancies, Nepal et al. (12) have suggested that the increased internal vascularity and homogeneity, which is more common with tumors, are less frequently seen in cases of gonadal TB.

Primary tuberculous mastitis, as found in two 23- and 25-year-old women, has also been reported by Goni et al. (11) and Baharoon (13). The ulcerative lesions, as seen in our cases, usually follow tuberculous abscesses. These may easily be suspected as malignant lesions following non-response to culture-guided antibiotics and the high incidence of breast cancer in young women in Nigeria, where a frequency of up to 12.2% has been reported in women 30years and younger (14). Similar background clinical knowledge of endometrial cancer in perimenopausal women, irregular per vagina bleeding, and foul-smelling discharge underlined the clinical presentations in our endometrial TB cases.

Hysteroscopy, although not done in our patients, typically show adhesions and atrophic and irregular endometrial lining with whitish deposits (15).

Primary TB of the orofacial region, particularly in TB-endemic areas, is more common in the young (16). The 15-year-old boy with jaw TB had destroyed maxillary bone suggestive of Burkitt lymphoma (endemic type). This would qualify as a type I (of types I-V) of Andrade's classification of orofacial TB (17). Although the patient presented with a history of long duration of over 6months, in the study region, late presentation of Burkitt lymphoma is more common, with patients usually presenting in stages C and D.

Cases of primary extra-pulmonary TB, irrespective of the site, have been frequently associated with immunosuppression, but this is present in only approximately 51.5% of cases (11). Similarly, studies have also shown that only approximately 53.6% of patients with extra-pulmonary disease have concomitant chest involvement and abnormal chest X-rays(18). Thus, a high index of suspicion is required in diagnosing these TB-related mimics of malignancy.

Blurring of vision, headaches, and seizures were the clinical presentation of frontal cerebral aspergillosis (Figure 1) in a patient who was suspected to have astrocytic brain tumor. Similar features were described in a 22-year-old patient by Neyazet al. (19). Although the magnetic resonance imaging findings were not available for review in our case, Neyazet al. (19) described T2 hypo-intensity, absence of choline peak, and irregular frond-like margins of the lesion as possible indicators of a fungal lesion. Although multiplicity and cavitation of the lesions may also be seen in the immunocompromised, there is a need to exclude nasal and pulmonary primaries.

For evaluation of eumycetoma, Yadav et al. (20), in a series of cases, have described the utility of "dot-in-a-circle" sign in the radiologic diagnosis of these lesions (Figure 1). This is characterized by fungi (dots) surrounded by a clear radiolucent region (containing giant and inflammatory cells histologically) and a fibrotic capsule (circle). Abd El Bagi(21) further classified the radiographic features of pedal bone mycetoma into stages 0 to VI. Our case falls in stage III,

which is characterized by localized bone invasion. It was suspected as osteosarcoma, among other possible malignancies described (22).

The case of sporotrichosis in a 12-year-old malnourished homeless boy presented as a nodulo-ulcerative fungating right subscapular mass. This is in keeping with other reports that have reported these lesions at unusual sites (23). Unlike the most common lymphocutaneous variant, fixed cutaneous and systemic sporotrichosis are more difficult to diagnose. The fixed cutaneous form more likely mimics malignancy, including nodulo-ulcerative basal cell carcinoma especially when located on the face (24).

The 56 cases evaluated in this study may have been fewer than the actual cases because some cases were omitted due to insufficient clinical information and missing data.

Conclusions and recommendations

This report on infectious lesions mimicking malignancy emphasizes the need for a high index of clinical suspicion (for their unusual manifestations) and the need to obtain representative tissues for histopathologic and cytopathologic diagnoses.

Declaration of interests

The authors declare no conflict of interest.

Author contributions

AJA led in writing the original draft. All other authors contributed to editing and reviewing the manuscript.

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