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CASE REPORT

Papillary Variant of Intestinal-Type Sinonasal Adenocarcinoma in an Elderly Female Nigerian: A Case Report

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Summary
Intestinal-type sinonasal adenocarcinomas (ITAC) are rare tumours accounting for about 1.4% of all neoplasms and less than 4% of all sinonasal malignancies. The papillary variant accounts for 18% of ITAC, with few cases reported worldwide and no known documented case in Nigeria. This variant has the best prognosis but can easily be misdiagnosed. Most ITAC occurs in men with a history of long-term exposure to sawdust. There are very few reported cases among farmers. This report describes a rare case of a papillary variant of ITAC in an 83-year-old Nigerian retired female farmer who presented with a 10-month history of recurrent nasal discharge and blockage. The diagnosis was made following a paranasal CT scan and histology with immunohistochemistry of the debulked nasal mass. ITAC should be suspected in patients with chronic unilateral nasal obstruction, rhinorrhea, epistaxis, and long-term exposure to sawdust or leather dust and agricultural produce or products.

Keywords: Adenocarcinoma, Epistaxis, Chronic nasal discharge, Papillary, Sinonasal, Intestinal-type.

Introduction

The sinonasal adenocarcinomas are categorised into intestinal-type and non-intestinal-type, depending on their resemblance to the intestine's mucosa. [1,2] The intestinal-type sinonasal adenocarcinoma (ITAC) is a rare tumour that accounts for less than 1% and 4% of all neoplasms and sinonasal malignancies, respectively. [3 -5] Its epidemiology is still emerging, though few cases have been reported worldwide. [3,4,6,7] Other types of sinonasal malignant tumours, including squamous cell carcinoma, salivary gland malignant tumours, and non-intestinal type adenocarcinoma, have been reported in Nigeria, but there has been no known report of papillary variant of ITAC in Nigeria as of the time of this publication. [8-10] ITAC commonly occurs in males between 55 and 60 years of age.[4] The age at the

time of diagnosis ranges from 12 to 86 years, with a mean of 58 years.[1]

There is a known strong association between ITAC and occupational exposure to sawdust and leather dust.[1] An association has also been reported for agricultural workers, food manufacturers, and motor vehicle drivers among men and a textile occupation among women.[1] Though ITAC is an aggressive tumour, it seldom metastasises.[1] It often occurs in the ethmoid sinus, nasal cavities, and maxillary sinus in about 40%, 27%, and 20% of cases respectively; however, it may be impossible to ascertain the exact site of origin of larger destructive lesions.[1] Advanced tumours invade the orbit, pterygopalatine, infratemporal tissues, and the cranial cavity. [1] Most present with unilateral nasal obstruction, rhinorrhea, and epistaxis.[1] Advanced tumours may cause pain, neurologic disturbances, exophthalmos, and visual disturbances.[1]

Radiological imaging, including computed tomography (CT), magnetic resonance imaging (MRI), and histology, are used to diagnose ITAC.[1] The five main morphologic categories include papillary, colonic, solid, mucinous, and mixed variants.[1,6] The papillary variant of ITAC constitutes 18% of all the types of ITAC, and it has the best prognosis with a three-year cumulative survival of 82%.[1] The solid and mucinous variants have the worst prognosis.[1,3] The most common histological types seen among woodworkers and in sporadic cases are the papillary and colonic types.[1] The papillary variant of ITAC is very rare and can easily be misdiagnosed.[1] Proper diagnosis of this tumour using radiological imaging, histology, and immunohistochemistry are essential for its management. Extensive tumours are treated with aggressive surgical resection with or without adjuvant radiotherapy or chemotherapy.[1] However, treatment failure and local recurrence are common.[3] Complete surgical resection of less extensive and well-differentiated tumours has also shown improved clinical outcomes.[3]

This report describes the clinical presentations, diagnosis, and management of a rare case of a papillary variant of intestinal-type sinonasal adenocarcinoma in an elderly Nigerian retired female farmer.

Case Description

The patient was an 83-year-old female farmer who presented to our facility with a 10-month history of recurrent nasal discharge and blockage. The discharge was initially watery but later turned mucoid and then bloody. There was associated nasal blockage necessitating mouth-breathing. It was also associated with noisy breathing, nasal pain, and poor sleep. She had no prior diagnosis of hypertension or diabetes. She did not smoke or drink alcohol. She had no previous history of frequent exposure to sawdust or leather dust. On clinical examination, she was conscious and alert. Her pulse rate was 74 beats/minute, her blood pressure was 139/82mmHg, her respiratory rate was 28 cycles/minute, her body temperature was 36.20 Celsius, and her oxygen saturation (SPO_2) in room air was 96%. Clinical examinations of her chest and abdomen were essentially normal.

The full blood count showed reduced haematocrit of 31.9% (35.0 - 54.0%), white blood cell count of 7.1 x 10^9/L (3.5 - 10.0 x 10^9/L), and elevated relative lymphocyte count of 66.2% (20.0 – 40.0%), with mildly elevated absolute lymphocyte count of 4.7 (0.6 - 4.1 x 10^9/L). The results of her serum electrolyte, urea, and creatinine showed mildly elevated serum sodium of 148mmol/L (135-145mmol/L), mildly elevated serum chloride of 111mmol/L (91-110mmol/L), and reduced serum urea of 2.1mmol/L (2.9-7.5mmol/L). A pre-operative serial 1.25mm axial and coronal computerised tomography (CT) of the paranasal sinuses

showed a large ill-defined iso-to-hypodense enhancing mass with a few small non-enhancing areas causing thinning of the right ethmoid sinus wall. The mass occupied the right maxillary sinus and extended into the right ethmoid, frontal, and sphenoid sinuses and the right nasal cavity. The right sphenoid sinus wall appeared mildly eroded. There were areas of cortical thickening involving the right maxillary and sphenoid sinuses with a deviation of the nasal septum to the left. The overall paranasal sinus CT features suggested a right sinonasal carcinoma (Figure 1). Her chest x-ray, abdominopelvic ultrasound, and colonoscopy findings were essentially normal.

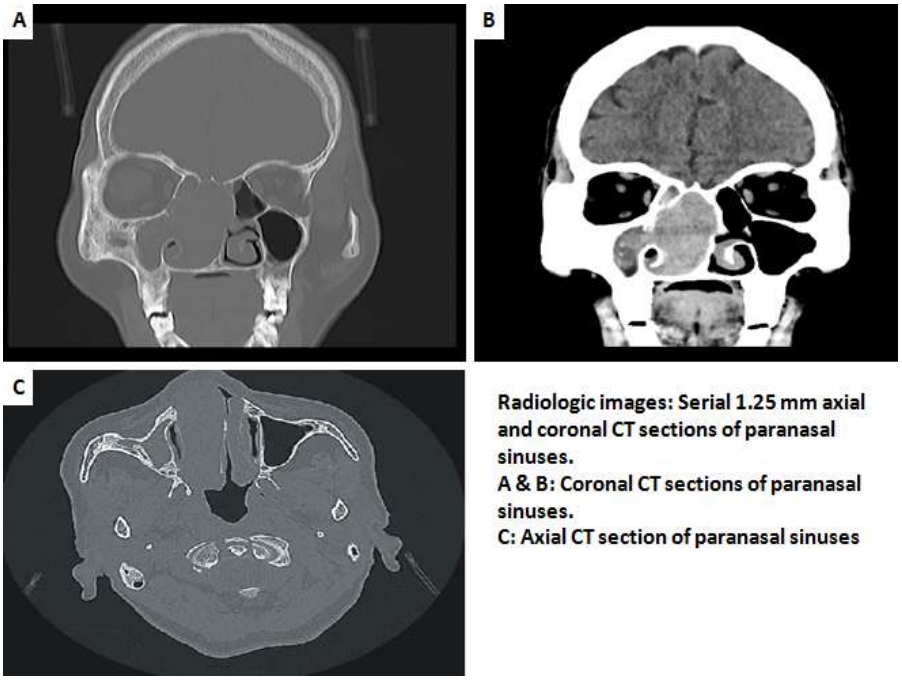

Figure 1: Serial 1.25mm axial and coronal CT sections of the paranasal sinuses showing extensive tumour growth into the right maxillary, ethmoid, frontal, sphenoid sinuses, and the right nasal cavity

The patient received analgesics and antibiotics. She was counselled on the nature of her medical condition. Following informed consent, a diagnostic nasal endoscopy with surgical debulking of the right sinonasal mass was performed on the second day of admission. The endoscopic/surgical findings include a large friable haemorrhagic tumour in the right nasal cavity extending from the lateral wall of the nose into the roof of the nasal cavity with a skull base defect in the medial part of the cribriform plate of the ethmoid bone. There was evidence of posterior septal bone destruction. The surgery was well tolerated, and the harvested sinonasal mass was sent for histological evaluation.

Pathologic findings

The specimen comprised multiple greyish-white, soft-to-firm solid, partly friable tissues aggregating to measure 4cm × 3cm × 1cm. Their cut surfaces were greyish-white and solid, with some gritty calcified and frond-like areas (Figure 2).

Histologic sections of the tissue showed an exophytic neoplastic growth that appeared to be arising from the surface epithelium. It comprised delicate arborising papillary fronds and crowded glands lined by cuboidal to pseudostratified epithelium with cytologic atypia and infrequent mitosis. There were areas of mixed inflammation and necrosis (Figure 3). A preliminary diagnosis

of malignant sinonasal carcinoma with the differentials of (1) papillary variant of intestinal-type sinonasal adenocarcinoma; (2) nasopharyngeal papillary adenocarcinoma; (3) low-grade papillary adenocarcinoma of salivary gland origin; (4) metastatic papillary thyroid carcinoma; and (5) Metastatic lung adenocarcinoma was made.

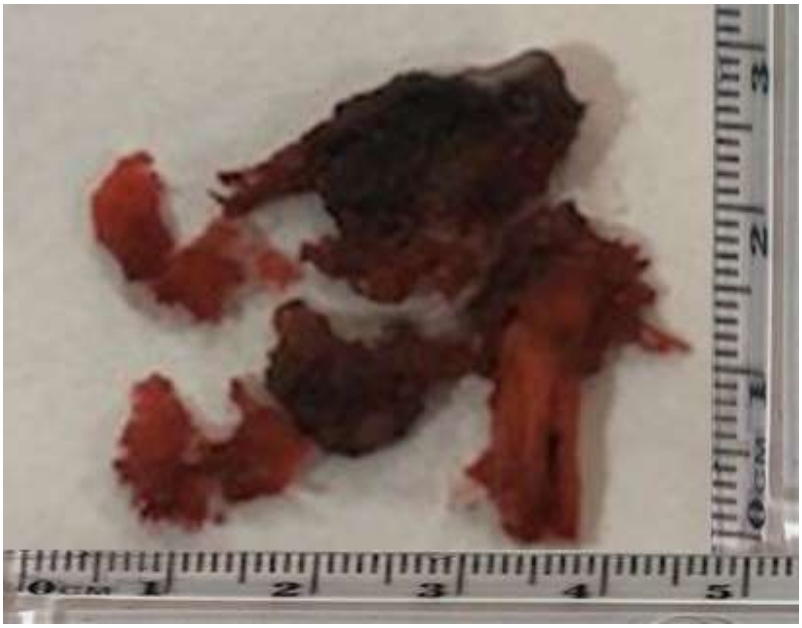

Figure 2: Gross picture of the harvested sinonasal mass during the debulking surgery

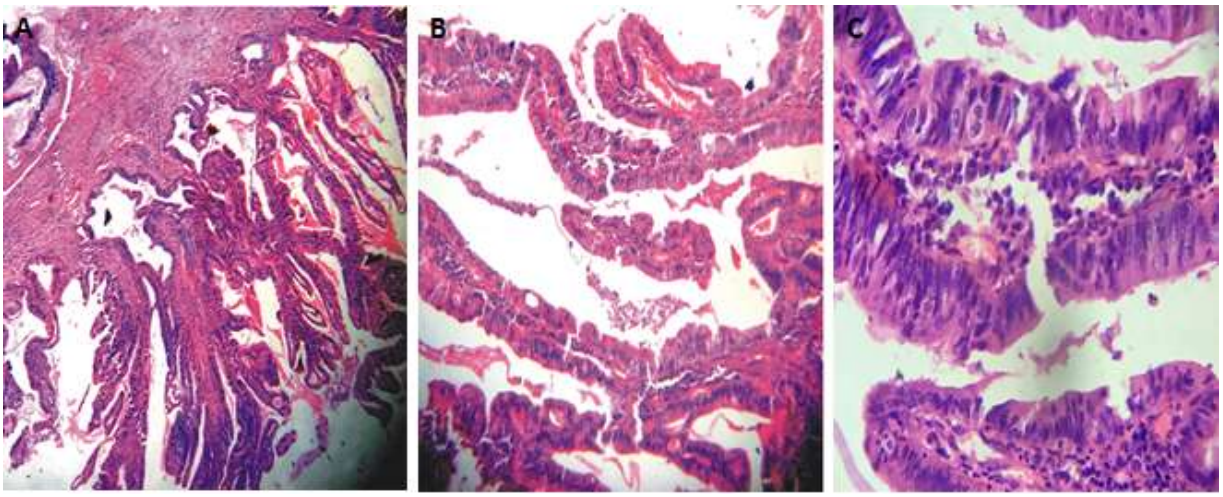

Figure 3: Photomicrographs (Haematoxylin & Eosin) of the sinonasal mass
A: H&E at x40 magnification. B: H&E at x 100 magnification. C: H&E at x 400 magnification

Immunohistochemistry showed that the tumour cells lining the glandular structures were strongly and diffusely positive for CK20, epithelial membrane antigen (EMA) and CDX-2.

CK-7 was strongly positive but patchy in these tumour cells (Table 1 and Figure 4). The tumour cells were also weakly positive for Napsin-A (diffuse and weak) and thyroglobulin (patchy and weak) (Table 1 and Figure 4). They were entirely negative for S100 and TTF-1 (Table 1). Following immunohistochemistry, a final histologic diagnosis of a papillary variant of intestinal-type sinonasal adenocarcinoma was made.

Table I: Immunohistochemistry staining pattern of the sinonasal mass

IHC Marker	*Reactivity*
CK-7	Patchy, but strongly positive; (++).
CK-20	Diffusely and strongly positive; (+++).
EMA	Diffusely and strongly positive; (+++)
CDX-2	Diffusely and strongly positive; (+++)
TTF-1	Negative; (-).
Thyroglobulin	Patchy and weakly positive; (+).
Napsin-A	Diffusely and weakly positive: (+).
S-100	Negative; (-).

- Negative, + Weakly positive, ++ Moderately or strongly positive and patchy, +++ Strongly positive

Post-surgical biopsy clinical management

The patient had mild left nasal epistaxis a day after the debulking surgery, for which a nasal pack was administered, and the bleeding stopped on the second postoperative day. Following the histopathologic report of the debulked sinonasal tissue, the patient was counselled on the need for neoadjuvant radiotherapy and an extensive radical surgical resection, including maxillectomy. She was discharged home four days after admission, on antibiotics, analgesics, nasal decongestant, and nasal irrigation twice daily. She had two postoperative two-weekly follow-up visits with stable conditions. However, she refused a follow-up postoperative paranasal sinus CT, neoadjuvant radiotherapy, and radical tumour resection with maxillectomy. She was followed up bi-monthly for two years, and she occasionally complained of recurrent nasal obstruction, rhinorrhoea and epistaxis. However, she still refused further management.

Discussion

ITAC is a rare tumour with emerging epidemiology. Its incidence and sex distribution vary in different parts of the world. The reported age-standardised incidence rates per 100,000 person-years of sinonasal adenocarcinoma were 0.65 in men and 0.26 in women in Europe (Italy), 0.058 in men and 0.034 in women in the United States (US). [11,12] The reported gender ratio (men/women) is 1.69 in Italy and 2.66 in the US. [11,12] The median age at diagnosis is 64-68 years. [11-13] The male-to-female ratio of sinonasal adenocarcinoma is as high as 6:1 in reported cases.[14] A study by Ajiya *et al*. in Kano State, Nigeria, showed that 32.1% of the 137 patients diagnosed with malignant sinonasal neoplasm were farmers. [15] Sinonasal adenocarcinoma accounted for only 5.1% of the total 137 malignant sinonasal tumours analysed in a report. [15] Of the 22 sinonasal malignant tumours reported in another study by Alabi *et al.* at Ilorin, Nigeria, none were ITAC. [8]

The papillary variant of ITAC is a rare tumour that commonly affects males with occupational exposure to hardwood and leather dust. [1] About 88% of ITAC have been attributed to occupational exposure, especially to wood dust

(relative risk: 29.4) and products in the textile industry (relative risk: 3.5).[11,16] Other associated but uncommon occupational risk factors of ITAC include agriculture, food manufacturing, shoemaking, vehicle driving, and textile work.[1,17] The risk factor for ITAC recognised in the index case, a retired farmer, is possible long-term exposure to agricultural produce or products, including pesticides and chemical fertilisers.

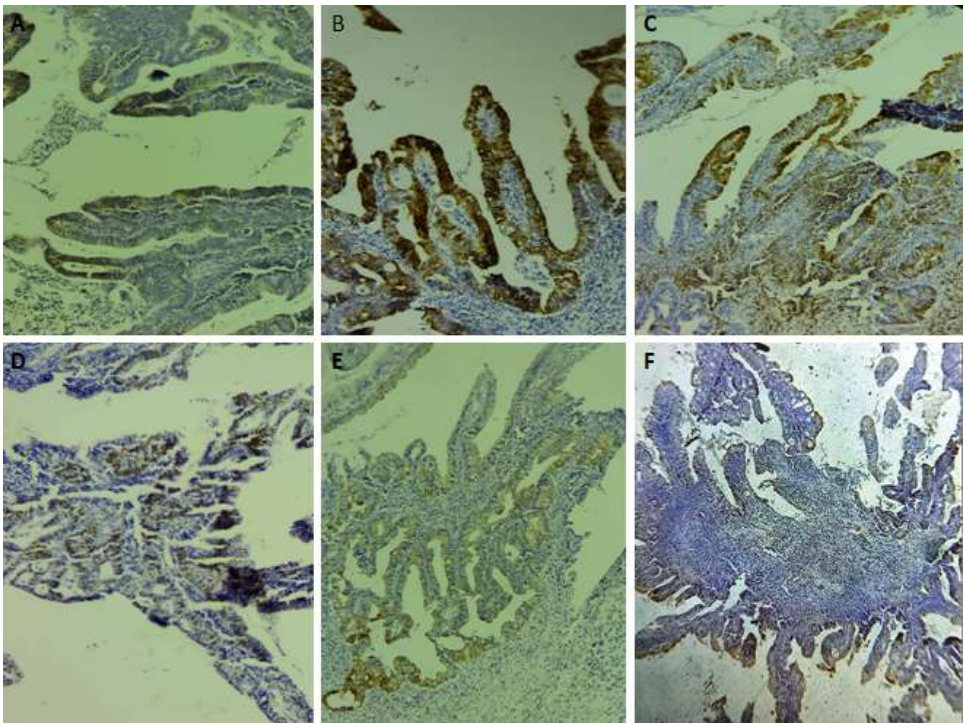

Figure 4: Immunohistochemical photomicrographs of the sinonasal mass
A: CK-7 Immunostain (x40 magnification). B: CK-20 Immunostain (x40 magnification) C: EMA Immunostain (x40 magnification). D: CDX-2 Immunostain (x40 magnification). E: Napsin-A Immunostain (x40 magnification). F: Thyroglobulin Immunostain (x40 magnification)

Histogenesis of ITAC is not yet well understood. The tumour cells have been postulated to be derived from the stem cells of the overlying respiratory epithelium of the sinonasal. [1] The frequent presence of squamous metaplasia and dysplasia of the sinonasal epithelium in the vicinity of the tumour led to the postulation of the pathogenesis of the tumour to possibly be due to the development of these precursor lesions, which will cause impaired mucociliary clearance and prolonged contact of carcinogenic substance in the mucosa. [1] The recognised genetic abnormalities in this tumour include K-RAS or H-RAS mutation - detected in about 15% of the cases, and TP53 mutations - seen in 18-44%. [1] The H-RAS mutation, chromogranin, and c-erb B-2 expressions are associated with more aggressive tumour behaviour. [1]

Immunohistochemistry studies have shown ITACs to be consistently diffusely positive for CK20, epithelial membrane antigen, CDX-2, villin, MUC2, and STAB2 but variably positive for CK7 and CEA. [12] Diffuse-positive immunohistochemical expressions of ITAC for B72.3, Ber EPL, BRST-1, Lue-M1, and human milk fat globule (HMFG-2) have also been reported. [1] Chromogranin-A and synaptophysin-positive

cells may be present, scattered or in clusters, in the neuroendocrine cells within the tumour. [18,19] The possibility of a metastatic intestinal or lung adenocarcinoma to the sinonasal region is very rare. This possibility was ruled out in the index case by a thorough clinical examination and radiologic investigations, including chest and abdominal examination, colonoscopy, plain chest x-ray, and abdominopelvic ultrasound, all of which had normal findings. In addition, the histologic morphology and immunohistochemistry features of the tumour cells of the index case ruled out differentials of metastatic lung adenocarcinoma (TTF1-), metastatic intestinal adenocarcinoma (CK 7++, napsin A +, thyroglobulin +), non-intestinal type sinonasal adenocarcinoma (CK20+++, EMA+++, CDX2+++), nasopharyngeal papillary adenocarcinoma (TTF1-, CK20+++, thyroglobulin +, napsin A+), and low-grade papillary adenocarcinoma of salivary gland origin (S100-, CK20+++).

Transnasal endoscopic surgery is the treatment modality for non-extensive, resectable ITAC. [16] However, adjuvant radiotherapy with or without chemotherapy with aggressive surgical resection is recommended for advanced stages and high-grade lesions. [3,16] The index patient had an extensive sinonasal tumour that occupied the right maxillary sinus and extended into the right ethmoid, frontal, and sphenoid sinuses and the right nasal cavity. The planned definitive treatment for the patient involved a combination therapy of neoadjuvant radiotherapy with aggressive surgical tumour resection and maxillectomy. However, the patient opted out of any further management.

Conclusion

The papillary variant of intestinal-type sinonasal adenocarcinoma is a rare tumour that commonly affects males with occupational exposure to sawdust and leather dust. There are few reported cases worldwide and no known reported cases in Nigeria. Even fewer reported cases are associated with exposure to agricultural produce or products. It can be easily misdiagnosed as either a salivary sinonasal tumour or a metastatic adenocarcinoma if not appropriately investigated. A high index of suspicion, including identification of its associated occupational risk factors and early diagnosis using CT or MRI, histology, and immunohistochemistry, are essential for effective management.

Informed Consent: Informed consent was obtained from the patient to use the patient's data and clinical information in a journal article.
Ethical considerations: The Health Research and Ethics Committee of Afe Babalola University Ado-Ekiti Multi-System Hospital, Ekiti State, Nigeria, approved this study with reference number AMSH/REC/KEU/183. The article also maintained confidentiality.

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Authors' Contributions: UKE, OOAO, AA, IOA, and MCJ participated in data acquisition through clinical management, pathological and radiological analysis, and data analysis and interpretation. UKE drafted the manuscript while OOAO, AA, IAO and MCJ revised the manuscript for sound intellectual content. All the authors approved the final version of the manuscript.
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