Synchronous nasal rhinosporidiosis and inverted papilloma in a paediatric patient in Dodoma, Tanzania: Case report

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May 2, 2023

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ABSTRACT

Nasal rhinosporidiosis is a rare chronic granulomatous disease that is caused by Rhinosporidium seeberi. It affects the mucous membrane of various sites such as nasopharynx, conjunctiva and palate. Inverted papillomas are relatively rare, benign epithelial tumors of the nasal cavity that are locally aggressive, have recurrence tendency and undergo malignant transformation. Both entities are very rare in our setting and this is perhaps the first documented case in Tanzania.

KEYWORDS: Nasal mass, Rhinosporidiosis, Inverted papilloma, Granulomatous, Dodoma, Tanzania

KEY CLINICAL MESSAGE

Nasal rhinosporidiosis and inverted papilloma lesions may resemble the routinely encountered nasal polyps thus high index of clinical suspicion is necessary to establish their diagnoses.

Introduction

Nasal rhinosporidiosis refers to a chronic granulomatous disease of the nose that is caused by Rhinosporidium seeberi.¹-⁴ The disease affects both human beings and animals and is reported more commonly in hot tropical climates even though it is endemic in India and Sri Lanka.¹,⁵-⁸ On the other hand, sporadicity has been reported elsewhere such as Brazil, Africa and Argentina.⁶,⁷,⁹,¹⁰ Despite the disease being very rare in Tanzania, there are some countries that have reported an appreciable number of cases.⁸

Regarding race and sex predilection of rhinosporidiosis, there is no racial predominance reported and in terms of sex of predominance, males are more affected than females with the male to female ratio being 4:1.¹,⁹-¹¹ The disease also affects those individuals aged 15-40 years.¹,²,¹²

The mode of transmission of rhinosporidiosis may be by direct contact with spores and this can be through dust, infected clothing and swimming in stagnant water.¹,⁸,¹²-¹⁴

The diagnosis of nasal rhinosporidiosis is usually established by observing the characteristics of the implicated etiological agent in nasal tissue biopsies like sporangia. The sporangia when examined in nasal tissue biopsies may be visible at variable stages of maturation. On the other hand, rhinosporidiosis has a tendency of mimicking other nasal masses as it presents like a polypoidal mass.¹,⁷,¹⁵-¹⁷ Therefore a high index of suspicion by clinicians is of paramount importance in instituting the management of patients with nasal masses particularly in this era where the disease is on surge.
The variable clinical presentation of nasal rhinosporidiosis includes an indolent nasal growth, nasal obstruction, intermittent epistaxis, nasal itching and sneezing and yellowish foul smelling nasal discharge accompanied with blood-stained purulent nasal discharge.\(^1,9,10\)

The recommended treatment of choice for nasal rhinosporidiosis remains to be surgical excision of the nasal mass despite the reported high recurrence rate.\(^3,16,18\) Despite being amenable to surgery, there are reported deaths in patients who are not immunocompetent.\(^19\) Whenever accessible electro cautery of the base of the excised site should be done though cryosurgery can also be used.\(^20\) Systemic therapy with dapsone serves as an important adjuvant therapy.\(^1,20,21\)

To the best of our knowledge, this is perhaps the second reported case of nasal rhinosporidiosis in Central Tanzania and the first case of its unique nature due to synchronicity with inverted papilloma.

Being a rare benign tumor, inverted papilloma was described initially in 1854 by Ward and in 1855 by Billroth.\(^20,22\) This tumor accounts for 0.5-4% of all nasal tumors.\(^20,23\) The disease tends to peak in the 5\(^{\text{th}}\) to 6\(^{\text{th}}\) decade \(^23\) with male to female ratio being between 3:1 and 10:1.\(^20\) It is exceptional in the pediatric population by being very rare as only very few cases have been reported.\(^24\) Though inverted papilloma is known to be a benign tumor, yet it is characterized by its possibility of undergoing malignant transformation to carcinoma, local aggressiveness, high risk of synchronous or metachronous malignancy and has the propensity of local recurrence especially if incomplete surgical excision is entertained.\(^22-24\)

The commonest location for inverted papilloma is the lateral nasal wall and the paranasal sinuses. There are other rare anatomical sites being involved by inverted papillomas outside the sinonasal tract such as skull base,\(^25\) nasolacrimal duct,\(^26\) oropharynx,\(^27,28\) and nasopharynx.\(^29,30\)

The exact etiology of inverted papilloma is still debated to date thus unknown. There is a laid hypothesis that Human papillomavirus may be implicated in the development of inverted papillomas; particularly type 11.\(^31-35\) There are other proposed aetiological agents like chronic inflammation, allergy and occupational exposures.\(^23,33\) The treatment of choice remains to be surgical excision of the nasal mass which can be done endoscopically whenever equipment permits.\(^23,26\) Despite adequate treatment of an inverted papilloma, recurrence rate may be as high as 30 – 60 % of cases.\(^20\)

We are therefore reporting a paediatric patient who presented with a synchronous nasal rhinosporidiosis and inverted papilloma and was managed by endoscopic surgical excision of the nasal mass and kept on oral dapsone for 6 months postoperatively.

**Case presentation**

We are presenting a seven (7) year old male boy who presented at our outpatient otorhinolaryngology clinic at Benjamin Mkapa Hospital which is a zonal referral hospital in Central Tanzania with a 1-year history of left-sided nasal obstruction and intermittent epistaxis for 6 months. He had no history of cheek swelling, pain or numbness, loss or loosening of teeth or alveolar ridge fullness. There were no ophthalmological, otological or neurological complaints reported by the patient.

On physical examination, he had no external nose deformity but rather a friable left-sided obstructive nasal mass. He was not pale and had no any palpable peripheral lymph nodes. Laboratory results showed hemoglobin 11g/dl and elevated erythrocyte sedimentation rate (35mm/hour). A provisional diagnosis of pyogenic granuloma was made and consequently endoscopic surgical excision of the nasal mass under general anaesthesia was done. The surgically excised specimen was sent for histopathology.

Histopathological analysis revealed thick-walled sporangium containing numerous endospores (daughter spores) (Figure 1) and with further sections showing thick walled sporangium with endospores in different stages of development accompanied by mixed inflammatory cells mainly plasma cells (Figure 2). Another cross-section showed a papilla with delicate fibrovascular core admixed with thick walled sporangium, lined by stratified squamous epithelium with minimal surface keratinization (Figure 3). On the other hand, low power micrographs showed papillary arrangement with delicate fibrovascular core admixed with thick-walled
sporangium and the papillae are lined by stratified squamous epithelium with no surface keratinization (Figure 4)

**Figure 1:** Intermediate power view of thick-walled sporangium containing numerous endospores (daughter spores)

![Figure 1: Intermediate power view of thick-walled sporangium containing numerous endospores (daughter spores)](image)

**Figure 2:** A high-power view of large, thick walled sporangium with endospores in different stages of development accompanied by mixed inflammatory cells mainly plasma cells and lymphocytes.

![Figure 2: A high-power view of large, thick walled sporangium with endospores in different stages of development accompanied by mixed inflammatory cells mainly plasma cells and lymphocytes.](image)
**Figure 3:** A cross-section showing a papilla with delicate fibrovascular core admixed with thick-walled sporangium, lined by stratified squamous epithelium with minimal surface keratinization

**Figure 4:** Low power micrographs showing papillary arrangement with delicate fibrovascular core admixed with thick-walled sporangium and the papillae are lined by stratified squamous epithelium with no surface keratinization
The patient was then kept on oral dapsone at a dose of 50mg/day for 6-months and with no residual disease recurrence noted after 6-months of follow up.

Discussion
This case report from Central Tanzania at the largest zonal referral hospital has documented a case of synchronous nasal rhinosporidiosis and inverted papilloma in a paediatric patient and so far the first documented case of synchronous nasal rhinosporidiosis and inverted papilloma both in Central Tanzania and countrywide. Though sporadic, nasal rhinosporidiosis has been reported from about 70 countries with variable geographical features.\textsuperscript{12} Migration has attributed to the infrequently isolated cases in other parts of the world.\textsuperscript{37,38}

Nasal rhinosporidiosis is reported to be more common in younger age groups and also predominant in men with male to female ratio being 4:1.\textsuperscript{1,9-11} Such male predominance has been observed in our case report since the affected patient was a 7-year old boy.

The disease itself, nasal rhinosporidiosis and its causative organism, Rhinosporidium seeberii have been known for over ten decades and it’s a rare infective chronic granulomatous disease of the nose.\textsuperscript{1,3} On the other hand, attempts to isolate the causative organism in vitro to date has never been successful and its taxonomic rank remains unclear.\textsuperscript{39}

Being related to a group of fish parasites referred to as the DRIP clade, most pathologists and microbiologists initially considered it to be fungus on the basis of its characteristic to be stained by fungal stains such as Gomori methenamine silver (GMS) and periodic acid-Schiff (PAS).\textsuperscript{17}

Available literatures have shown some authors ending up proposing the class of Rhinosporidium seeberii to be Mesomyctozoa.\textsuperscript{14,40} Regarding the natural habitat for Rhinosporidium seeberii, water reservoirs and soil contaminate by wastes are the known habitats and this has been supported by fluorescent in-situ-hybridization techniques.\textsuperscript{40} On top of that, other aquatic microorganisms might be relevant to a possible synergistic action in the establishment of natural rhinosporidiosis.\textsuperscript{40}

The class Mesomyctozoa has two orders, which are the Dermocystida and the Ichthyophonida. In the order Dermocystida is the family Rhinosporideaceae that includes Rhinosporidium seeberii, Dermocystidium spp. and the rosette agent.\textsuperscript{1,40}

Pertaining the route of transmission for Rhinosporidium seeberii, it is still unclear to date on the route of transmission of the organism. Despite the unclear route of its transmission there is a presumed mode of infection from the natural aquatic habitat of Rhinosporidium seeberii through a traumatized epithelium commonly called trans epithelial infection and this is most common in the nasal cavity.\textsuperscript{1,10} On the other hand the various modes of spread of Rhinosporidium seeberii includes; auto-inoculation through spillage of endospores from polyps after trauma or surgery, haematogenous spread to distant sites, lymphatic spread and sexual transmission.\textsuperscript{10,40}

The notable prevalence of Rhinosporidiosis is marked in rural settings, particularly among people working or in contact with contaminated soil, stagnant water (ponds, or lakes) or sand.\textsuperscript{40} In our case report, the patient from a rural area reported a history of contact with contaminated pond water. Moreover, the patient reported a history of contact with feces of infected livestock and used to work in contaminated agricultural fields. Similar risk factors have been documented in the reviewed literatures.\textsuperscript{17,40}

Whereas several hundred people bathe in stagnant water, only few develop a progressive pattern of the disease thus implying existence of predisposing factors in the host where the possibility of nonspecific immune reactivity in the host, blood group and HLA types has been suggested as important in the pathogenesis of Rhinosporidium seeberii and also in the establishment of an initial focus of infection.\textsuperscript{1,17}

Rhinosporidiosis manifests as tumor-like masses, usually of the nasal mucosa or conjunctiva of humans and animals and patients with nasal involvement often have masses leading to nasal obstruction or bleeding due to polyp formation and it can spread to the nasopharynx, oropharynx, and the maxillary antrum.\textsuperscript{4,10} The
patient we are hereby reporting had an isolated friable mass localized in the nasal cavity with no involvement of other anatomical sites such as maxillary sinuses. The diagnosis of Rhinosporidiosis is established by observing the characteristic appearance of the organism in tissue biopsies and computerized tomography (CT) scans. The lesion is friable, vascular pedunculated or sessile polyp with a surface studded with tiny white dots due to spores beneath the epithelium, giving a ‘strawberry-like’ appearance.\textsuperscript{1} The lesion in our case report was similarly friable.

Systemic manifestation of rhinosporidiosis is rare and include multiple mucocutaneous, hepatic, renal, pulmonary, splenic or bone lesions associated with fever, wasting and even death.\textsuperscript{1,16,17}

Despite being a rare occasion, spontaneous regression of Rhinosporidial growths has been reported in animals and humans and therefore, medical and/or surgical intervention is necessary.\textsuperscript{1,16,17}

The treatment of choice for rhinosporidial growths remains to be wide local surgical excision and this reduced its recurrence rate.\textsuperscript{1,12} Surgical removal of the lesion with cauterization of the attachment base is almost curative in at least 90\% of the cases.\textsuperscript{1,12,41} Wide local surgical excision may be associated with remarkable morbidity due to hemorrhage and septal perforation and therefore limited surgical excision and adjuvant medical therapies, including antifungals such as griseofluvin and amphotericin B, trimethoprim-sulphadiazine, and sodium stibogluconate have been tried with varied success. All drugs are endospore-static rather than endosporicidal.\textsuperscript{1,17}

The only drug appearing to have clinical promise is Dapsone since it arrests the maturation of sporangia and promotes fibrosis in the stroma when used as an adjunct to surgery.\textsuperscript{1,40} It could therefore be expected that pre-surgical Dapsone would minimize both hemorrhage by promotion of fibrosis as well as preventing the colonization and infection of new sites after the release of endospores from the surgically traumatized polyps.\textsuperscript{12,41} Laser excision is becoming promising as a mainstream treatment of sinonasal rhinosporidiosis in the future.\textsuperscript{44} Our patient was kept on dapsone for 6-months after endoscopic nasal mass excision with no recurrence after 6-months of follow up.

Inverted papilloma describes the histological tendency of the epithelium inverting into the stroma. It has a characteristic and intact basement membrane that separates the epithelial component from the underlying connective tissue stroma.\textsuperscript{20} Similar to the recurrence tendency being exhibited by nasal rhinosporidiosis, inverted papilloma has recurrence tendency, local aggressiveness or destructive potential\textsuperscript{45} and association with sinonasal polyposis.\textsuperscript{25} Inverted papilloma has a tendency of malignant transformation where about 9\% of inverted papillomas transform to malignant tumors and hereby the most frequent malignant tumor derived from inverted papilloma is squamous cell carcinoma.\textsuperscript{6,47} The prognosis of squamous cell carcinoma (SCC) in inverted papillomas is poor with 5- and 10-year survival rate being 39.6\% and 31.8\% respectively. The poor prognostic indicators of SCC following inverted papillomas include elderly age, infiltration of the skull base or orbital involvement and moderate to poor differentiation histological pattern.\textsuperscript{47,48}

Human papillomavirus type 11 has been implicated in the pathogenesis of inverted papillomas. A preponderance of HPV type 6 and 11 has been detected in inverted papillomas compared to types 16 and 18. Low-risk or high-risk co-infections are rare.\textsuperscript{31,32} The clinical presentation of inverted papilloma includes nasal obstruction, epistaxis, nasal discharge and recurrent sinusitis and computerized tomography findings depict chronic osteitis and hyperostosis preoperatively.\textsuperscript{49} The clinical features of inverted papillomas resemble those of nasal rhinosporidiosis. The main stay of treatment of inverted papilloma is surgical excision of the nasal mass followed by postoperative follow up similar to nasal rhinosporidiosis due to risk of recurrence.\textsuperscript{36}

**Conclusion**

In Tanzania, rhinosporidiosis is non-endemic and in the Central zone, the disease is uncommon thus may pose diagnostic challenges. Sinonasal inverted papillomas are also rare in our settings. Presence of synchronous rhinosporidiosis and inverted papilloma supports the inflammatory theory for pathogenesis of inverted papilloma. It is therefore important for both clinicians and pathologists to have a high index of suspicion when managing patients with nasal masses even from non-endemic areas.
ACKNOWLEDGEMENT

The patients’ mother is highly acknowledged for providing a written informed consent to publish the case report.

CONFLICTS OF INTEREST

None declared

AUTHOR CONTRIBUTIONS

ZSA: Performed the surgery, collected information for the case and drafted the initial version of the manuscript. FZ performed histopathology and also provided critical feedback of the manuscript. AAK: Drafted the initial version of the manuscript. All authors read and approved the final version to be published in Clinical Case Reports

ETHICS STATEMENT

This report is in accordance with the Declaration of Helsinki.

CONSENT

The patients’ mother gave a written informed consent prior inclusion of the child in this report

FUNDING

None

DATA AVAILABILITY

The data that support the findings of this report are available from the corresponding author upon reasonable request.

References


