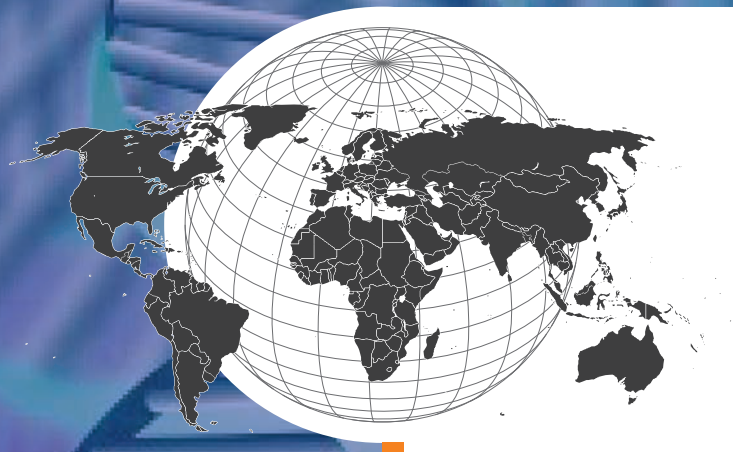

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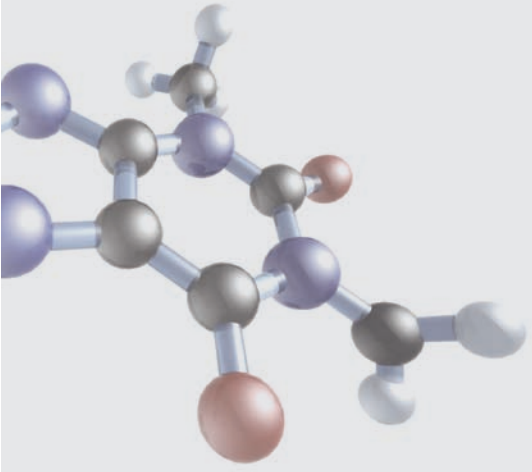

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Original Article

Respiratory papillomatosis in northern Nigeria: A 7-year review

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ABSTRACT

Background: Recurrent respiratory papillomatosis (RRP) is a benign disease of the upper respiratory tract caused by human papilloma virus (HPV), which can occur at any part of the upper aerodigestive tract. The aim of this study was to determine the prevalence and clinical outcome of RRP in northern Nigeria. **Materials and Methods:** This study was a retrospective review of patients with the diagnosis of RRP who presented to the National Ear Care Center over a 7-year period (2005-2011). All the case notes of these patients were retrieved, and information gathered from the clinical records were entered into SPSS statistical software and analyzed descriptively. The results were presented in tables and figures. **Results:** A retrospective review of 24 patients in the age range of 3-51 years with a mean age of 13.4 years was done. There were 14 males and 10 females. The firstborn male children were more affected than the females. The duration of symptoms before presentation varied within the range of 1-276 months, with an average of 48.3 months. Laryngoscopic examination revealed 15 supraglottic, 3 transglottic, and 6 glottic masses. A clinical diagnosis of juvenile-onset recurrent respiratory papillomatosis (JORRP) was made in 20 patients, while adult-onset (AORRP) diagnosis was made in 4 patients. The majority of the patients had direct laryngoscopy and clearance biopsy with tracheostomy (in over 50%). The treatment outcome showed that 18 patients had improved satisfactory postoperative voice, 5 had not improved to their satisfaction, and 1 patient was equivocal. **Conclusion:** RRP is still a challenge because it has delayed presentation. Juvenile onset is the most commonest. It occurs more among males, first born and treatment still remains DL + biopsy clearance + tracheostomy in our setting.

Keywords: Adult onset, direct laryngoscopy, juvenile onset, papillomatosis, respiratory

Introduction

Recurrent respiratory papillomatosis (RRP) is a benign disease of the upper respiratory tract caused by human papilloma virus (HPV), which can occur at any portion of the upper aerodigestive tract. This viral disease has been most extensively described in the larynx and trachea, and, although benign, can cause significant airway obstruction in some instances.[1] RRP was first described as a distinct lesion of the larynx in children[2] by Sir Morrell Mackenzie in 1871. It is a rare disease characterized by recurrent proliferation of benign squamous cell papilloma in the larynx as well as in the other parts of the aerodigestive tract.[2]

RRP is a benign disease with significant morbidity and rare mortality as a result of upper airway obstruction. There are reports of a minimal risk of malignant transformation in the

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literature,[3] and on this basis, some researchers have described it as a malignant disease[3] The course of RRP is variable depending on the disease recurrence and presentation of the patients, and this has been classified into aggressive and nonaggressive types. The patient with aggressive type suffers from rapid recurrence of the disease. There are multiple surgical procedures for its management. Over 90 subtypes of HPV are known,[4] with only a few subtypes causing RRP. These subtypes are RRP 6 and 11, which have also been incriminated in condyloma acuminata (genital warts). Several studies have shown that HPV subtype 11 is associated with more aggressive disease. Lindeberg *et al*.[5] in their previous report have classified the disease into juvenile-onset recurrent respiratory papillomatosis (JORRP) and adult-onset recurrent respiratory papillomatosis (AORRP) based on whether the diagnosis was made before or after 12 years of age, respectively.[5] The two types of papillomatosis are distinguished according to a number of clinical, histological, and virological peculiarities: Juvenile (type I) and red recurrent papillomatosis in adults (type II).[6] The disease has been observed in patients during the immediate postnatal period and in patients as old as 84 years.[7] Type I is most commonly diagnosed within the pediatric age group, commonly 2-4 years of age, with dysphonia being the most common presenting complaint.[8,9]

About 75% of JORRP cases have been diagnosed by 5 years of age. Children who are diagnosed at a younger age have a higher risk for disease progression, with a high rate of recurrence of the disease compared with children diagnosed later in life.[10] Among AORRP cases, the peak incidence is between 20 and 40 years of age, with a slight male predilection.[9] Previous studies have documented high prevalence among firstborn individuals, children of young primagravid mothers, and individuals from families of low socioeconomic status.[7,11,12]

The aim of this study was to determine the prevalence and clinical outcome of RRP in Northern Nigeria.

Materials and Methods

This was a retrospective review of all patients with the diagnosis of RRP who presented over a 7-year period (2005-2011) to the National Ear Care Center, the only national center for the care of ear, nose, and throat diseases. Ethical approval was obtained from the Ethical Review Committee of the hospital for this research to be carried out. All the consecutive case notes of patients with clinical diagnosis of respiratory papillomatosis were retrieved, and information gathered from the clinical records included the biodata, clinical presentation, examination findings, treatment offered, and outcome.

All the information retrieved was entered into the statistical software SPSS version 16.0 (released in 2007 by SPSS Inc., Chicago) and analyzed descriptively, with the results presented in tables and figures.

Results

A retrospective review of 24 patients was done. They were in the age range of 3-51 years, with a mean age of 13.4 years (SD = ±2.5) and a median age of 10.0 years. There were 14 males and 10 females with the M:F ratio of 1.4:1.0. The modal age encompassed the under-fifteen patients, with specifically those aged 6-10 years having the highest occurrence [Table 1]. Data on position among siblings indicated that the clinical condition was commonest among the firstborn male children [Table 2]. All the patients (100%) presented with a history of voice changes (hoarseness), out of which 3 patients (12.5%; 2 males and 1 female) presented with a positive history of difficulty in breathing. Histories of allergy and smoking were found only in 2 males (8.3%; one each). The duration of symptoms before presentation varies 1-276 months [Table 3], with a mean duration of 48.3 months (SD = ±13.6) and median of about 18.0 months [Table 3]. Laryngoscopic examination revealed 15 supraglottic masses (9 males and 6 females), 3 transglottic masses (1 male and 2 female), and 6 masses limited to the glottic region alone (4 males and 2 females). A clinical diagnosis of JORRP was made in 20 patients (12 males and 8 females), while AORRP was made in 4 patients (2 males and 2 females). A majority of the patients had

Table 1: Age-sex frequency table

Age group (years)	Frequency (%)		Total
	Male	Female	
1-5 Years	3 (12.5)	3 (12.5)	6 (25.0)
6-10 Years	4 (16.6)	4 (16.6)	8 (33.2)
11-15 Years	5 (20.8)	1 (4.2)	6 (25.0)
21-25 Years	—	1 (4.2)	1 (4.2)
31-35 Years	—	1 (4.2)	1 (4.2)
36-40 Years	1 (4.2)	—	1 (4.2)
51-55 Years	1 (4.2)	—	1 (4.2)
Total	14 (58.3)	10 (41.7)	24 (100)

Table 2: Sibling position — sex frequency

Sibling position	Male (%)	Female (%)	Total (%)
First	7 (29.2)	3 (12.5)	10 (41.7)
Second	2 (8.3)	3 (12.5)	5 (20.8)
Third	1 (4.2)	0 (0)	1 (4.2)
Fourth	0	1(4.2)	1 (4.2)
Last	1 (4.2)	0	1 (4.2)
Not volunteered	3 (12.5)	3 (12.5)	6 (25.0)
Total	14 (58.3)	10 (41.7)	24 (100)

Table 3: Duration — sex frequency

Duration (months)	Frequency		Total
	Male (%)	Female (%)	
1	1 (4.2)	2 (8.3)	3 (12.5)
2	1 (4.2)	1 (4.2)	2 (8.3)
6	0 (0)	1 (4.2)	1 (4.2)
9	0 (0)	1 (4.2)	1 (4.2)
10	0 (0)	1 (4.2)	1 (4.2)
12	4 (16.7)	0 (0)	4 (16.7)
24	2 (8.3)	1 (4.2)	3 (12.5)
30	1 (4.2)	0 (0)	1 (4.2)
36	1 (4.2)	0 (0)	1 (4.2)
84	0 (0)	1 (4.2)	1 (4.2)
96	1 (4.2)	1 (4.2)	2 (8.3)
120	1 (4.2)	0 (0)	1 (4.2)
125	0 (0)	1 (4.2)	1 (4.2)
144	1 (4.2)	0 (0)	1 (4.2)
276	1 (4.2)	0 (0)	1 (4.2)
Total	14 (58.3)	10 (41.7)	24 (100)

Table 4: Treatment options received — sex frequency

Treatment options	Frequency		Total
	Male (%)	Female (%)	
DL+Biopsy clearance with tracheostomy	9	4	13
DL+Biopsy clearance without tracheostomy	3	3	6
Microlaryngoscopy+Tracheostomy	0	1	1
Microlaryngoscopy without tracheostomy	2	0	2
DAMA	0	2	2
Total	14 (58.3)	10 (41.7)	24 (100)

DL = Direct laryngoscopy, DAMA = Discharged against medical advice

direct laryngoscopy and clearance biopsy with temporary tracheostomy (in over 50%) in our cohort study as the route for anesthesia [Table 4]. The outcome of treatment based on patients and caregivers' assessment showed that 18 had better postoperative voice than in the preoperative period after decannulation and before discharge, while 5 did not improve to their satisfaction (reasons not known, which is one of the deficiencies of the study), and 1 patient was equivocal on the outcome of the treatment. All the patients were relieved of their respiratory symptoms after treatment. Thirteen (54.2%) were lost to follow-up after discharge, while only 11 (45.8%) went for follow-up visits for 2-24 months with a mean period of 8.55 months. The voice assessment on follow-up indicated that 7 (63.6%) patients were satisfied with their voice quality.

Discussion

RRP is a benign disease of the upper respiratory tract caused by HPV, which is a viral infection that can occur at any portion of the upper aerodigestive tract.[13] RRP is a benign disease, although it can have significant morbidity and rare mortality secondary to airway obstruction. In a previous report by Linderberg *et al*.,[5]RRP was categorized as JORRP and AORRP on the basis of the age of first presentation;[1,14] however, at our center, the age limit for the pediatric group was 15 years, and this constituted about 83.3% of the patients seen in our study. This is in contrast to findings within the Danish population, where the prevalence was higher among the adults (3.94/100,000) than in the juvenile group (3.62/100,000) and it was similar to a study finding from the USA where juvenile onset was commoner than the adult onset.[4,13]

A researcher earlier found the presence of the disease in patients during the immediate postnatal period and in patients as old as 84 years;[7] however, the minimum age limit for our study was 3 years of postnatal age compared to the report above, and the maximum age recorded in our study was 51 years. JORRP is most commonly diagnosed at 2-4 years of age; however, the modal age group was 6-10 years in our study, with dysphonia or hoarseness being the most common presenting complaint;[8,9] this is similar to what was found in our study, with very few patients presenting with both the dysphonia and respiratory difficulty. The majority of JORRP patients (75%) have been diagnosed by 5 years of age; this was at variance with our study, where diagnosis was found to have been made in the range of 6-10 years of age. It was found to be commoner among males than females in our study, which is similar to what was found in the literature worldwide but at variance with studies done in Asia that found higher prevalence in females. In our study, most pediatric patients were firstborn and had young primagravid mothers, similar to the anecdotal observations from previous investigations that found RRP among firstborn individuals of low socioeconomic status; however, the socioeconomic status could not be ascertained in our study.[7,11,12] This was one of the drawbacks observed in the context of our retrospective study.

The commonest presentation from the literature in children with RRP is hoarseness,[14] which is similar to what we found in our study; this was followed by airway obstruction.[14] The average duration of symptoms, from the previous report, before diagnosis was about 13 months,[14] which was at variance with our finding of a mean duration of 48.3 months, and this was a late presentation; this may be due to an anecdotal observation of delayed referral from the general practitioners whom these patients were likely to have seen first; self-medication[15] (either orthodox or traditional); and also the fact that most patients in our setting (according to a previous study in Nigeria) believed that waiting to consult a specialist is a time-consuming, expensive venture.[11] The minimum cost in Nigeria to access a specialist was about N2000.00-N2500.00 (13-17 USD), whereas over 60% of the people had less than 1 USD per day to spend.[15,16] Other contributory factors, from

studying a previous report, may be the low literacy level, low socioeconomic factor, traditional beliefs, and sparse distribution of specialists.[15] Commonly, children with these problems were misdiagnosed as having asthma, croup, or chronic bronchitis by primary care physicians.[4] The classic triad of RRP symptoms is progressive hoarseness, stridor, and respiratory distress. Any infant or child with these symptoms may require laryngoscopy, either indirect or fiberoptic, to rule out neoplasia, with JORRP being the most common.[4]

Previous reports have shown that there is no definite treatment for RRP; the most widely used treatment is surgical excision with microlaryngoscopy or direct laryngoscopy with clearance biopsy, which was the modality of treatment adopted in this study, and a majority of our patients had the treatment once except for 2 patients who had recurrence and were reoperated on. Other contributory factors to some of this drawback are poor follow-up and the study being a retrospective study by design. The goals of any treatment modality must be to secure an adequate airway,[13] which was done in all our patients, as some had tracheostomy to secure the airway due to imminent airway obstruction; to improve and maintain an acceptable voice; and to facilitate disease remission while limiting morbidity and complications.[17] In order to achieve the above, there is need for a secured airway through careful examination of the airway, and precise removal of papillomas. Removal of papillomas with cold steel instruments, as was done in our study, is the oldest method but still reliable and affordable. Many surgeons still prefer it because it does not burn healthy tissue, as that might result in scarring and loss of vocal function, neither of which was not documented in our study. On the other hand, previous reports in the literature have documented that there is more blood loss in surgical excision and also a possibility that blood and fragments of infected tissue can contaminate the lower airway.[7] In the developed setup, the CO_2 laser has been a favored method of endoscopic laryngeal surgery in children since the 1970s.[18]. When used at a low power setting with an operating microscope, the laser offers precise excision, excellent hemostasis, and minimal thermal injury to underlying tissues. However, this option is not available at our facility, and to our knowledge not available anywhere else in Nigeria. Despite the method used in the treatment of the lesion, 75% outcome satisfaction was still achieved. Given the large number of procedures needed and the high cost of treatment per patient, the ideal goal would be prevention of the disease in the first place. Recent studies have reported the most interesting and promising development in the prevention of RRP: The use of quadrivalent HPV vaccine (GARDASILTM; Merck and Co., Inc., Whitehouse Station, NJ, USA). This vaccine is currently licensed by the Food and Drug Administration (FDA) for the prevention of cervical cancer, adenocarcinoma *in situ*, intraepithelial neoplasia grades 1-3, vulvar and vaginal intraepithelial neoplasia grades 2-3, and genital warts associated with HPV 6, 11, 16, and 18.[19] It is not available in Nigeria.

Follow-up was a challenge in our setting, as less than 50% of the patients treated returned for it. This may be related to poor understanding of the course of the disease they received treatment for or to socioeconomic factors, all of which were not covered in this present study. Future study will be beneficial to find out the correlation between socioeconomic factors and papillomatosis in our environment.

Conclusion

In conclusion, RRP is a challenge: Delayed presentation, misdiagnosis, and mismanagement are the likely reasons for delayed presentation, as some were initially managed for asthma before referral. Juvenile onset is still the type most commonly seen among the under-10 age group, in males more than in females, and more among the firstborn children of primigravid women; the common presentation is hoarseness, and the treatment modality is direct laryngoscopy and biopsy clearance with tracheostomy with good outcome. Follow-up remains a challenge.

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Conflicts of interest

There are no conflicts of interest.

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