

SINONASAL POLYPOSIS AND FUNGUS: A GROWING RELATIONSHIP

Atif Hafeez Siddiqui¹, Arsalan Ahmed Sheikh², Tariq Zahid Khan¹, M. Saleem Marfani³ & Arif Ali¹

1. Dow University of Health Sciences

2. Liaquat University of Medical & Health Sciences, Jamshoro

3. College of Medicine - Qassim University

Corresponding Author Email: dr.atifhafeez@gmail.com

ABSTRACT

OBJECTIVES: To determine the frequency of underlying fungus in nose and paranasal sinuses in patients present with nasal polyposis. **METHODOLOGY:** A total of 324 patients presented with nasal polyps were included in this study. Data collected from all the patients admitted in ENT department with diagnosis of nasal polyposis. All the relevant information about their presenting symptoms was recorded in a proforma. Post operatively the removed material was sent for histopathology and fungal culture. Later the findings of biopsy and culture reports were also recorded and analysed. **RESULTS:** Out of 324 patients 159 were males and 165 were females. Underlying fungus was present in 226(69.75%) and out of them, 102(45.13%) were males and 124(54.86%) were females with a P value of 0.039. The mean age was 25.95 ± 9.32 (15-45) years for the patient with fungus. Aspergillus was the commonest organism found. **CONCLUSION:** Underlying fungus was found in a significantly high number of patients presented with nasal polyps and Aspergillus was the commonest organism found.

KEYWORDS

Sinonasal polyps, Fungus, Aspergillus

INTRODUCTION

Nasal Polyps are a common clinical entity. They are basically the prolapsed lining of sinus mucosa. The incidence is 1% to 4% of the total population (Bateman, 2003). The nasal polyps can be the result of chronic rhinosinusitis (Bikhazi, 2004; Hadley, 1997), but more commonly they are the result of a hypersensitivity response to an offending antigen. The complex immunological reaction results in increased edema and inflammation of narrow areas of mucosal contact such as osteomeatal complex (OMC) causing obstruction of sinuses (Stammberger, 1997; Mian, 2002; Zacharek, 2004). This results in stasis of mucin and thus also leads to chronic rhinosinusitis. Further the inhalation and entrapment of fungal spores find an ideal environment their growth (Mian, 2002). The presence of fungus in paranasal sinuses was first reported by Miller, et al. as allergic aspergillosis of paranasal sinuses in 1981 (Mian, 2002; Schubert, 2008; Millar, 1982). Since then there has been a worldwide increase in reported cases of fungal infections of nose and paranasal sinuses. Such fungal infections occur most commonly in young and otherwise healthy, immuno-competent individuals (Schubert, 2008; Gupta, 2003). These individuals most commonly present with nasal polyps mainly causing nasal obstruction and discharge (Mian, 2002). Therefore a high index of suspicion regarding fungal infection exists in atopic individuals presenting with the diagnosis of nasal polyposis. Polyps when remain untreated may acquire locally aggressive behaviour which may get further attenuated by the presence of fungus. The polyps may extend intracranially by eroding skull base, while erosion of lamina papyracea leads to orbital extension resulting in proptosis, visual impairment and other ophthalmic symptoms (Marfani, 2010). Nasal septal deviation, external nasal deformity and facial asymmetry may also be the consequence. Presence of underlying fungus in cases of nasal polyposis increases the chances of recurrence (Mian, 2002). Present study highlights this very serious but often hidden aspect of nasal polyps and also the importance of investigating for underlying fungus in such patients, a finding that has changed the line of treatment both in terms of surgical options and medical therapy to minimize the complications as well as the

recurrence. The aims of this study were to determine the frequency of underlying fungus in nose and paranasal sinuses in patients present with nasal polyposis.

METHODOLOGY

This non-interventional, descriptive study was conducted in the Department of ENT- Head and Neck Surgery, Dow Medical College and Civil Hospital, Karachi from January 2008 to February 2014. A total of 324 patients were included by non-probability, purposive technique. All cases of nasal polyposis of all ages and gender reported for the first time or with recurrence after treatment, who were immuno-competent and otherwise healthy were included in this study. Patients with malignant conditions of nose and paranasal sinuses, immuno-compromised status and diabetes were excluded from this study. Data was collected from all the patients admitted in this department with diagnosis of nasal polyposis through OPD on basis of clinical examination. Routine hematological and biochemical investigations were carried out. CT scan of nose and paranasal sinuses were obtained preoperatively in every case. Endoscopic sinus surgery was performed in all selected cases. The specimen of material removed from nose and paranasal sinuses was sent for histopathology and fungal culture. All the relevant information was recorded in a purposely designed pro forma. Data analysis was done on SPSS version 16.00. Relevant descriptive statistics like frequency and percentage of fungus in cases of nasal polyps were calculated for quantitative variables, sex and presenting symptoms. Mean \pm SD (Range) was calculated for quantitative variable age. Fisher's exact was used to compare between variable fungus genders wise with level of significance at $P \leq 0.05$.

RESULTS

A total of 324 cases of nasal polyposis were included in this study, out of which 159 were males and 165 were female. Underlying fungus was found in 226(69.75%) subjects. Out of them

102(45.13%) were males and 124(54.86%) were females (TableNo.1).

| Table 1. Characteristics of nasal polyposis Patients (n = 324) | |
|--|------------------|
| Characteristics | n (%) |
| Age | |
| Mean \pm SD Years | 25.74 \pm 9.64 |
| Gender | |
| Male | 159(49.07) |
| Female | 165(50.93) |
| Fungus | |
| Positive | 226(69.75) |
| Negative | 98(30.24) |
| Nasal Polyp (Laterality) | |
| Unilateral | 142(43.8) |
| Bilateral | 182(56.2) |

The fungus could not be found in 98(30.24%) subjects, in which 57(58.2%) were males and 41(41.8%) were females with a significant P-value of 0.039 (Table No.2). 142(43.82%) subjects had unilateral and 182(56.17%) subjects had bilateral disease (Table No.1). Out of 226 patients with underlying fungus,

113(50.0%) had unilateral polyposis and a same number of patient's i.e 113(50.00%) patients had bilateral disease. Among 98 patients without fungus, 29(29.6%) had unilateral involvement while in 69(70.4%) patients the polyps were bilateral with a significant P-value of 0.001 (Table No.2).

| Table 2. Association of fungus with gender and unilateral and bilateral nasal polyps (n = 324) | | | | | |
|--|------------------------------------|------|----------|------|---------------------|
| Characteristics | Fungus in nasal polyposis patients | | | | Fisher's Exact Test |
| | Positive | | Negative | | P-values |
| | N | % | n | % | |
| Gender | | | | | 0.039 |
| Male | 102 | 45.1 | 57 | 58.2 | |
| Female | 124 | 54.9 | 41 | 41.8 | |
| Nasal Polyp | | | | | 0.001 |
| Unilateral | 113 | 50.0 | 29 | 29.6 | |
| Bilateral | 113 | 50.0 | 69 | 70.4 | |

Out of 324 patients, 263(81.17%) sought medical advice for the first time regarding the disease while only 61(18.82%) patients had recurrent polyposis. Out of 61 patients with recurrent disease 51 (83.60%) patients had fungus. The youngest patient included in the study was 9 years old boy and oldest patient was a 50 years old lady with mean of 25.74 \pm 9.64 (9-50) year. The youngest patient with underlying fungus was 15 years old and the oldest patient was 45 years old with the mean age of 25.95 year and standard deviation of \pm 9.32 (15-45) years. Aspergillus was the commonest specie cultured in 166 (73.45%) out of 226 patients who had histopathologically proven fungus.

DISCUSSION

Nasal polyposis has long been considered and treated as a simple and straight forward pathology but during the recent years it has been stressed in international literature that this disease deserves a lot of attention. Since the exact etiology of nasal polyposis is still debatable and many factors have been attributed for contributing in their formation and growth, therefore it is important to thoroughly investigate the condition because it may be an indicator of some sinister pathology like fungal sinusitis or malignancy. Our study revolves around the relationship of fungus with nasal polyps. Frequency of fungal involvement in nose and PNS with nasal

polyps is much commoner than that has been assumed previously. The freely floating fungal spores in the environment are readily inhaled by general population. These spores may settle down in the sinuses and initiates a hypersensitivity reaction that ultimately leads to the formation of polyps in certain individuals. On the contrary these spores when get access to the nose or PNS of an individual already having nasal polyps because of any of its wide spectrum of etiological factors, they find a favourable environments with local edema, thick inspissant mucin, low pH because of decreased ventilation, to flourish and sets a vicious circle of inflammatory process. Various studies suggest the major role of anterior ethmoid area in pathophysiology of the nasal polyposis. Several important anatomical landmarks like uncinate process, ethmoid infundibulum and hiatus semilunaris are associated with anterior ethmoid. They all collectively form a functional unit, termed as ostiomeatal complex (OMC). This OMC contains ostia of anterior ethmoid, maxillary and frontal sinuses and considered as the key area in development of polyps (Zacharek, 2004). Chronic irritation due to any reason in the narrow areas of ethmoidal air cells causes mucosal edema and subsequently obstruction of natural ostia resulting in impeded mucociliary clearance, bacterial over growth and release of chronic inflammatory mediators like cytokines which attract other inflammatory cells (Zacharek, 2004). The number of mast cells is high within the polyps. Eosinophils play a key role in inflammatory process in patients of nasal polyps with underlying fungus. Eosinophil seems to increase production of interleukins resulting in a vicious circle of inflammatory process (Bikhazi, 2004). In this series of 324 patients presented with the diagnosis of allergic nasal polyps in the Department of ENT and Head and Neck Surgery, Dow Medical College and Civil Hospital, Karachi, along with search of underlying fungus to find out their frequency in these cases, the different clinical presentations of the disease were also observed.

In our study we found 226(69.75%) individuals to have mycopathologically and / or histopathologically proven underlying fungus. Typically the microscopic description of the specimens mostly confirmed multiple polypoidal fragment lined by pseudostratified ciliated columnar epithelium. Myxoid underneath stroma, with necrotic nonspecific inflammatory exudate predominantly composed of Eosinophil. Fungal hyphae identified on special stains with the evidence of tissue invasion. This description exactly matches with the criteria for diagnosing allergic fungal sinusitis mentioned in the literature (Mian, 2002; Schubert, 2004; Rupa, 2001; Eloy, 1997). The finding of significantly high percentage (69.75%) of our patients having fungus along with nasal polyps is also strongly supported by the previous studies performed internationally (Mian, 2002; CorRadini, 2003; Schubert, 2001; Rupa, 2001). One of the earliest published study in Pakistani literature, describing specifically the relationship between nasal polyp and fungal sinusitis was conducted in early nineties by Iqbal K. et al. (Iqbal, 1993). Only 12 patients of nasal polyposis were included in that study out of which 10(83.33%) patient had histopathologically proven fungus along with polyps. Another large series of 200 cases of nasal polyps to find out the aetiological factors surprisingly showed underlying fungus in only 14% of their patients (Akthar, 2004). Our finding about presence of fungus in young and otherwise healthy individuals is similar to the reports appearing in international as well as local literature (Mian, 2002; Schubert, 2004; Gupta, 2003; Schubert, 2001; Uri, 2003). The

difference in gender distribution regarding presence of polyps in our study was negligible as there were 49.07% males as compared to 50.92% females but a significant “p value” of 0.039 in statistical analysis of frequency of fungus along with polyps in males and females indicates difference in occurrence of fungus among them. This finding is contrary to the literature which indicates that sex distribution does not have much value in the course of disease. The diagnosis of presence of fungus is based on histological criterion that has been discussed above. The fungus cultures has certain limitation and negative fungal culture does not necessarily means the absence of fungus as well (Mian, 2002; Schubert, 2004). Out of 226 histopathologically proven patient with fungus, we were able to obtain positive culture in 166 (73.45%) patients. Aspergillus as the commonest organism has been mentioned in most studies (Mian, 2002; Schubert, 2004; Gupta, 2003; Schubert, 2001; Rupa, 2002; Akthar, 2004; Jain, 2013). A lesser number of positive fungus culture in comparison to histopathological finding can be attributed to the improper handling, storage and transport of specimen send for fungal culture. Another possibility is that histologically unrecognizable fungal agents might be responsible for the infection. Recurrence rate is high in nasal polyps even after surgical eradication especially if they are accompanied with underlying fungus (Mian, 2002; Schubert, 2004; Schubert, 2000, Kuhn, 2000). Recurrence may be related to the severity of individual's atopy, extension of the disease, incomplete surgical eradication or improper postoperative medical therapy. The allergic fungal polyps often reported to cause bony erosion with intra cranial and intra orbital extension (Ghegan, 2006; Al Swiahb, 2011). Remaining fungal spores in such difficult approachable areas might start their reproduction and thus they can set the whole disease process again resulting in recurrence. Although our study does not comprises the rate of recurrence after treatment but at the time of presentation, it was noted that majority of our patient i.e. 263(81.17%) came up with primary presentation and only 61(18.82%) patients had recurrent disease. Out of 61 cases of recurrent disease, 51(83.60%) patient had underlying fungus. Allergic nasal polyp can be unilateral but mostly they involve multiple sinuses bilaterally. In our series 142(43.82%) subjects had unilateral involvements while 182(56.17%) had bilateral disease. The significant “p value” in this regard indicates the variable attitude of the disease process and also that fungus growth along with polyps was significantly higher in limited disease.

CONCLUSION

The conducted study indicates that the frequency of underlying fungus was significantly high in cases of nasal polyposis and Aspergillus was the commonest organism identified in these cases. The disease has statistically significant preponderance towards feminine gender. The fungus was found both in cases of unilateral and bilateral nasal polyposis without a significant statistical difference All the subjects were young immunocompetent and otherwise healthy as the mean age was falling in the middle of third decade of life.

ACKNOWLEDGEMENT

Authors are thankful to Raja Fahad Hussain in typing this manuscript. We are also grateful to all the senior & junior colleagues for their guidance, support & help in this research work,

and also our staff nurses for being extremely helpful in collecting and retrieving data from ward record.

REFERENCES

- Akthar, M. R., Ishaq, N., & Saadatullah, S. (2004). Aetiology of nasal polyp: a study of 200 cases. *Pak J Otolaryngol* , 20, 9-11.
- Al Swiahb, J. N., & Al Dousary, S. H. (2011). Bone erosion associated with allergic fungal sinusitis. *Saudi Med J* , 32(4), 417-419.
- Bateman, N., Fahy, C., & Woolford, T. (2003). Nasal Polyps: still more questions than answers. *J Laryngol* , 117,1-9.
- Bikhazi, N. B. (2004). Contemporary management of nasal polyps. *Otolaryngol Clin N Am* , 37, 327-337.
- CorRadini, C., DelN. M., Schiavino, D., Patriarca, G., & Paludetti, G. (2003). Allergic fungal sinusitis: a naso-sinusal specific hyper reactivity for an infectious disease? *Acta Otorhinolaryngol Ital* , 23(3), 168-174.
- Eloy, P., Bertrand, B., Rombeaux, P., Delos, M., & Trigaux, J. P. (1997). Mycotic sinusitis. *Acta Otorhinolaryngol Belg* , 51, 339-352.
- Ghegan, M. D., Lee, F. S., & Schollosser, R. J. (2006). Incidence of skull base and orbital erosion in allergic fungal rhinosinusitis. *Otolaryngol Head Neck Surg* , 134(4), 592-595.
- Gupta, A. K., Ghosh, S., & Gupta, A. K. (2003). Sinonasal aspergillosis in immunocompetent Indian children: an eight year experience. *Mycoses* , 46, 455-461.
- Hadley, J. A., & Schaefer, S.D. (1997). Clinical evaluation of rhinosinusitis: history and physical examination. *Otolaryngol Head Neck Surg* , 117(3), 8-11.
- Iqbal, K., Saqlain, G., & Jalisi, M. (1993). Nasal Polyposis and fungal sinusitis. *Pak J Otolaryngol* , 9, 173-176.
- Jain, S., Das, S., Gupta, N., & Malik, J. N. (2013). Frequency of fungal isolation and antifungal susceptibility pattern of the fungal isolates from nasal polyps of chronic rhinosinusitis patients at a tertiary care centre in North India. *Med Mycol* , 51(2), 164-169.
- Kuhn, F. A., & Javer, A. R. (2000). Allergic fungal sinusitis: a four years follow up. *Am J Rhinol* , 14, 149-156.
- Marfani, M. S., Jawaid, M. A., Shaikh, S. M., & Thaheem, K. (2010). Allergic fungal rhinosinusitis with skull base and orbital erosion. *J Laryngol Otol* , 124(2), 161-165.
- Mian, M. Y., Kamal, S. A., Senthikumar, G., Abdullah, A., & Pirani, M. (2002). Allergic fungal rhinosinusitis: current status. *Pak J Otolaryngol* , 18(3), 36-40.
- Millar, J. W., Jhonston, A., & Lamb, D. (1982). Allergic aspergillosis of paranasal sinuses. Abstract in the proceedings of 143rd meeting of the Pathological society of Great Britain and Ireland. *Journal of Pathology* , 137, 56.
- Rupa, V., Jacob, M., & Matthews, M. S. (2001). Increasing diagnostic yields in allergic fungal sinusitis. *J Laryngol Otol* , 115, 636-638.
- Rupa, V., Jacob, M., Matthews, M. S., Job, A., Kurien, M., & Chandi, S. M. (2002). Clinicopathological and mycological spectrum of allergic fungal sinusitis in South India. *Mycoses* , 45 (9-10), 364-367.
- Schubert, M. S. (2000). Medical treatment of allergic fungal sinusitis. *Ann Allergy asthma Immunol* , 85, 90-101.
- Schubert, M. S. (2001). Fungal rhinosinusitis: diagnosis and therapy. *Curr Allergy Ashtma Rep* , 1, 268-276.
- Schubert, M. S. (2004). Allergic fungal Sinusitis. *Otolaryngol Clin N AM* , 37 , 301-326.
- Stammberger, H. (1997). Examination and endoscopy of the nose and paranasal sinuses. In N. Mygind, & T. Lindholt (Eds), *Nasal polyposis: an inflammatory disease and its treatment* (120-136). Copenhagen (Denmark): Munksgaard.
- Uri, N., Cohen-Kerem, R., Elmalah, I., Doweck, I., & Greenberg, E. (2003). Classification of fungal sinusitis in immunocompetent patient. *Otolaryngol Head Neck Surg* , 129(4), 372-378.
- Zacharek, M. A., Peter, N., & Karen, J. F. (2004). The office management of recalcitrant rhinosinusitis. *Otolaryngol Clin N AM* , 37, 365-379.