Primary atrophic rhinitis is a progressive chronic nasal disease characterized by sclerotic transformation of the mucous membrane and increased patency of the nasal passages due to atrophic changes in the underlying bones and mucosa [1, 2]. Histopathologically, the ciliary columnar epithelium which lines the nasal cavity is maximally lost and there is squamous metaplasia along with chronic inflammatory changes involving infiltration of monocytes, macrophages, and fibroblasts. Two different types of vascular involvement occur in PAR [3]. Type 1, which is more common, involves endarteritis obliterans, whereas type 2 is associated with capillary vasodilatation.

Primary atrophic rhinitis is a common condition in tropical countries like India, Pakistan, and Bangladesh. The condition usually affects young- and middle-aged adults, especially females (F:M = 5.6:1) [4].

1.1 Etiology of Primary Atrophic Rhinitis

Etiology of primary atrophic rhinitis is still a debatable topic, and it has kept various stakeholders like otorhinolaryngologists, microbiologists, epidemiologists, etc., interested for more than 100 years. Factors involved in its genesis include
autoimmunity, chronic sinus infection, hormonal imbalance, poor nutritional status, heredity, and iron deficiency anemia [5]. Chronic bacterial infection is considered one of the major causes of primary atrophic rhinitis, especially in highly densely populated regions of the world like countries of Southeast Asia, because sinonasal bacterial infections are contagious.

1.1.1  Bacteriology

*Klebsiella Ozaenae* is considered the most common causative agent [5]. Other infectious agents which have been implicated include *Coccobacillus foetidus-ozaenae, Bacillus mucosus, Diphtheroids bacillus, Bacillus pertussis, Haemophilus influenzae, Pseudomonas aeruginosa, Proteus mirabilis, and Staphylococcus aureus* [4]. According to the experience of physicians who treat upper respiratory tract infection, one cannot be sure whether these bacteria cause the disease or are merely secondary invaders. Few researchers have also isolated *Escherichia coli* from cases with primary atrophic rhinitis [6, 7]. Nutritional deficiency especially iron, fat-soluble vitamins like A, D, E, and K, and proteins leads to an increased susceptibility to recurrent upper airway infections [5].

1.1.2  Virology

With our experience during COVID-19 pandemic, various reports of development of loss of smell or anosmia in patients suffering from coronavirus infection have come to notice. It has to be investigated in detail that viruses causing flu-like symptoms like *rhinovirus, parainfluenza virus, respiratory syncytial virus, adenovirus, influenza virus*, and *coronavirus* could be the initiating agent which eventually leads to superimposed bacterial infection. There are many mechanisms that could be attributed for this. Viruses can damage ciliated cells, resulting in ciliostasis and therefore deterioration of mucociliary clearance [8]. Viruses also increase the risk of bacterial adherence to sinonasal mucosa, for example, rhinoviruses upregulate the expression of PAFR (platelet-activating factor receptor). One more example is TLR4 and TLR5 (toll-like receptors) pathways are altered after influenza virus infection resulting in decreased neutrophil attraction, thereby leading to increased bacterial attachment to the airway epithelial cells [9]. Literature is limited in establishing direct link between role of viral infections in atrophic rhinitis hence needs more multicenter studies to be confirmed.

1.1.3  Mycology

Concomitant fungal infection like *aspergillus* species have been isolated from patients diagnosed with atrophic rhinitis. Though no multicenter studies confirm the role of fungal infections in atrophic rhinitis, our clinical experience suggests that it is mainly due to contamination or nosocomially acquired. The only patients where
we saw *aspergillus* species as primary agents were cases of invasive fungal sinusitis causing atrophy.

All patients with a suspect of atrophic rhinitis should be subjected to detailed history, clinical examination including diagnostic nasal endoscopy, radiological examination, and laboratorial testing. In our practice, we do nasal swabbing at three consecutive intervals, 3–5 days apart and confirming the causative agent. The fourth and fifth nasal swabbing are done 1 month after confirmation and initiation of treatment and 6 months after completion of treatment, respectively.

1.2 Clinical Presentation

1.2.1 Signs

There are no reliable objective physical exam findings for the diagnosis of PAR. On endoscopic exam, patients universally have thick, adherent crusts that are yellow-green to gray-black. On removal of the crusts, marked atrophy of the turbinates, especially the inferior ones, can be seen. The turbinate atrophy creates an excessively patent nasal passage through which the posterior nasopharynx and upper portions of the soft palate can be seen. The nasal mucosa is markedly thin, pale, shiny, and bleeds easily. Less frequently encountered clinical signs of atrophic rhinitis include septal perforation, columellar necrosis, and a depressed nasal bridge [10].

1.2.2 Symptoms

Patients typically complain of excessive nasal crusting and “paradoxical” nasal obstruction despite the fact that the nasal cavities are actually enlarged, and foul smell emanating from the nasal cavity that is a source of embarrassment and occasional social rejection [11]. The sense of obstruction may be the result of crusting or disrupted airflow [12]. Other associated symptoms include facial pain, headache, mucosal dryness, dyspnea, epistaxis, sleep disturbance, and occasional mucopurulent rhinorrhea and anosmia. This last symptom most likely occurs as a result of atrophy of the olfactory epithelium in the nasal roof [13]. The feeling of “not getting air” is not alleviated with mouth breathing and often has a negative impact on psychological wellbeing, which manifests as anxiety, depression, anger, frustration, irritability, and fatigue. A unique symptom is *aprosexia nasalis*, where the patient becomes extremely preoccupied with the attempt to maintain a sensation of breathing such that they experience chronically decreased concentration [14].

1.3 Histopathology

Histopathologic studies demonstrate atrophic rhinitis to be a chronic progressive inflammatory process associated with atrophy and fibrosis. It is limited to the nasal mucosa, as the respiratory epithelium undergoes metaplastic change from ciliated
pseudostratified columnar to squamous epithelium with four distinct layers. The flattened squamous epithelium loses its ability for mucociliary clearance leading to secondary crusting. In addition, glandular atrophy occurs, affecting both serous and mucous elements. The remaining seromucinous glands fail to function properly, leading to decreased moisture availability and further crusting. Scanning electron microscopy shows that cilia are scarce or absent and that the mucus droplets that are produced appear to repel each other, making the mucus blanket ineffective. Universal findings include loss of cilia, goblet cells, and compound alveolar glands. Vascular structures are also affected in the disease process. Characteristic changes include endarteritis obliterans with associated thickening of the media and dilatation of the subepithelial capillaries [3]. Combined, these processes lead to poor circulation and decreased moisture and additional crusting. The damage to the cilia and mucosa found in atrophic rhinitis may contribute to the concurrent high incidence of sinusitis.

### 1.4 Diagnosis

Primary atrophic rhinitis is largely a diagnosis of exclusion focused on evaluation for the causes of secondary atrophic rhinitis. Long bereft of uniformly accepted diagnostic criteria, Ly et al. have offered seven signs and symptoms associated with 95% sensitivity and 77% specificity in their study of 22 patients. Each of the criteria must have been present for at least 6 months and include patient report of chronic nasal obstruction, recurrent epistaxis, and episodic anosmia or documentation by a physician of nasal purulence, nasal crusting, and two or more sinus surgeries. A final element, which more clearly identifies secondary atrophic rhinitis, is the identification of a chronic inflammatory disease associated with granuloma formation [15].

The diagnosis of atrophic rhinitis is made clinically and confirmed by carefully obtained endoscopically guided middle meatal cultures. Nasal biopsy specimens can show loss of the normal pseudostratified columnar epithelium and atrophy of the mucus glands. A nasal culture identifying *K. ozaenae* strongly suggests the diagnosis and the isolation of other associated organisms is also helpful. Multiple microorganisms are frequently cultured, including *Proteus*, *Escherichia coli*, *Staphylococcus aureus*, *pneumococci*, *Perez–Hofer bacillus*, and an atoxic form of *Corynebacterium diphtheriae*. *K. ozaenae* is an encapsulated gram-negative rod that is most often associated with and isolated in this disease. *K. ozaenae* displays a ciliostatic effect by creating intraciliary adherence that leads to poor mucociliary clearance.

The use of the endoscope is critical to obtain culture material and to avoid contaminated cultures. Characteristic nasal features include enlarged nasal cavities, resorption of the turbinates, mucosal atrophy, thick crusts, and ozena. The foul odor of atrophic rhinitis appears to be the most distressing symptom.

Because of the high incidence of concurrent sinusitis, CT is frequently included in the diagnostic evaluation of atrophic rhinitis. Pace-Balzan et al. list characteristic
changes identified by CT as the following: (1) Mucosal thickening of the paranasal sinuses. (2) Loss of definition of the osteomeatal complex secondary to resorption of the ethmoid bulla and uncinate process. (3) Hypoplasia of the maxillary sinuses. (4) Enlargement of the nasal cavities with erosion and bowing of the lateral nasal wall. (5) Bony resorption and mucosal atrophy of the inferior and middle turbinates. The expansion of the nasal cavities at the expense of the maxillary sinuses is the most prominent CT feature. An additional finding is the decreased extent of anteroposterior pneumatization of the maxillary sinuses [16, 17].

1.5 Management

1.5.1 Medical Therapy

The goal of therapy is to clear secondary bacterial infections, reduce the amount of crusting, and relieve the associated foul odor. Routine mechanical crust removal under rigid endoscopic guidance is an important part of therapy. At home, the patient must practice vigorous intranasal cleansing with a salt water or sodium bicarbonate solution. As methanol appears to directly activate cool thermoreceptors within the nasal mucosa, it may be added to nasal lubricants. Use of a cool mist humidifier at home may be beneficial. For those with severely debilitating symptoms and psychological manifestations, referral to psychosocial services is appropriate.

Since the vascular supply is already compromised, vasoconstrictive nose drops should be avoided. Long-term antibiotic use, guided by sinus cultures and sensitivities, is the mainstay of medical therapy. Although tetracycline has traditionally been used to treat this disease, more recent studies suggest the use of ciprofloxacin. Borgstein et al. report success with a regimen of ciprofloxacin 250 to 500 mg twice a day for 4 weeks [18]. Dudley suggests direct instillation of a topical aminoglycoside into the nose to avoid systemic absorption and to increase the availability to the nasal mucosa [19]. However, purulent secretions, which appear to be the best indicator of active disease, may interfere with aminoglycoside efficacy because their activity decreases as the pH level decreases. Superimposed acute bacterial sinusitis is a clear indication for the appropriate systemic antibiotics.

As Mitomycin-C has antiproliferative effects through its ability to inhibit fibroblast activity, the drug has been used as an antiscarring treatment after various ophthalmologic procedures since 1980. Using Mitomycin-C after endoscopic sinus surgery can reduce postoperative adhesions. The new use of Mitomycin-C in PAR has significantly reduced the degree of scabbing and the severity of epistaxis, and it has enhanced the normalization of secretion. Therefore, the topical use of Mitomycin-C associated with continued medical treatment is recommended in patients with a PAR [20].

Occasionally, medical management does not yield satisfactory results, and surgical intervention is required.
1.5.2 Surgical Therapy

A variety of surgical procedures to treat primary atrophic rhinitis exists. Each operation attempts to close or narrow the nasal cavity and to make the air passage more physiologic. The primary goal of surgical therapy is the reduction of symptoms to improve quality of life. Young’s operation describes bilateral closure of the nostrils one side at a time at a 3-month interval. This procedure can be performed at any age and, by report, is surprisingly well tolerated. Modification of Young’s procedure is described by Gadre et al. Partial nostril closure reduces the nares to a diameter of 3 mm or less. The advantage yielded by partial closure is that it allows for serial endoscopic examination [21]. Rigid nasal endoscopy demonstrates a significant decrease in the amount of crusting present by 1 month after surgery, with almost complete disappearance of crusts by 6 months. In addition, by scanning electron microscopy, cilia tend to increase in length and appearance but not in number after closure. The length of closure varies from 3 to 5 years depending on whether one or both nostrils are involved. The surgical slit provided in a modified Young’s operation allows endoscopy to show the most appropriate time to reverse the closure. Implantation of various materials to decrease the nasal lumen patency has also been used to manage atrophic rhinitis. However, artificial implants of acrylic resin and Dacron are extruded in up to 80% of cases. Earlier, Girgis described the use of a dermofat graft placed in the nasal floor through a sublabial incision [5]. Autogenous bone graft material harvested from the iliac crest and implanted in the nasal septum, floor, and lateral nasal wall is referred to as endonasal microplasty. As with the dermofat graft, the major problem encountered with bone graft is the tendency for reabsorption. Finally, Rasmy describes an osteoperiosteal flap with bone from the anterior wall of the maxillary sinus to form the obturating membrane for nasal closure [22].

Treatments may ameliorate but will not cure atrophic rhinitis. Allergists should seek to become familiar with atrophic rhinitis because of the overlap of symptoms with other forms of chronic rhinosinusitis as well as the common presence of concomitant allergic rhinitis in these patients. The progressive nature, poorly understood etiologic mechanisms, and several contributing or concurrent disease processes related to primary atrophic rhinitis render a multidisciplinary approach to management essential.

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