Chronic Rhinosinusitis's With Nasal Polyps

Abstract

Chronic Rhinosinusitis is a chronic disease which negatively affects quality of life. When associated with nasal polyps, there is worsening of the condition and it becomes harder to treat due to the high rates of recurrence and the increased morbidity rates. The condition, though having a set method of treatment, still has unknown etiology and pathophysiology which makes it extremely hard to diagnose and evaluate. Due to these unknown factors, treatment is still not as precise and effective, we still rely on systemic drugs like corticosteroids which most often do not resolve the disease and we then present surgical options, though effective still do not pose as an effective cure, which may be a factor in the high rate of recurrences. However, there have been giant leaps in the specialized research of this particular topic, leading to classification through biomarkers allowing us to study and consolidate data on the disease pathology and all of the different options causing recurrences, which further enhances our understanding of how this disease affects a diverse population. The majority of the treatment given in this disease is not evidence based but rather based on clinical observation and experience. Therefore, with CRSwNP we are confronted with more questions than answers, which is problematic as the disease can often be associated with comorbidities leading to further decrease in quality of life. Hence, this review article aims to aggregate and compile this valuable research and highlight the strides which have already been made while promoting additional research so that the disease can become more manageable without any recurrence.

Keywords: Chronic, Rhinosinusitis, Nasal Polyp, Recurrence, Nasopharynx.

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Introduction

Nasal cavity is an integral part of cephalic region, divided into two smaller cavities by nasal septum and structurally maintained by a frame work of bone and cartilage. Anteriorly, it opens to the external environment through apertures known as nares while it opens posteriorly into nasopharynx via choanae. Each cavity has three parts namely the respiratory area, the vestibule and the olfactory area. The nasal cavity is surrounded by paranasal sinuses which are mucosal lined, air containing cavities. All paranasal sinuses except the sphenoid sinus open into nasal cavity via ducts draining through ostia while the sphenoid sinus opens into the posterior roof.(1) Inflammation of adenoidal cavity and para-nasal sinuses is called chronic rhinosinusitis, with four major symptoms: facial tenderness or pressure, decreased or loss of smell, nasal discharge and nasal obstruction of which two must be present for a period of twelve weeks or more. The diagnosis must be supported along with objective evidence is provided on physical examination via anterior rhinoscopy or endoscopy and radiography.(2) Nasal polyps are defined as benign inflammatory lesions which develop from mucosa of nasal sinuses and cavities, mostly present at outflow tracts, which have high rate of recurrence but still have unknown etiology.(3) There are two types of organization of chronic rhinosinusitis, phenotypic and endotypic. The phenotypic classification of chronic rhinosinusitis is separated into CRSwNP (chronic rhinosinusitis with nasal polyps) and CRSsNP (chronic rhinosinusitis without nasal polyps). The endotypic classification is more complicated based on various genetic factors as well as examination of expression of various proteins, and has been discussed at length later in the article.(4) Nasal polyps are linked with other diseases as well, like

cystic fibrosis, persistent asthma and aspirin exacerbated respiratory disease (AERD), however, due to the high prevalence it is most commonly linked with chronic rhinosinusitis.(5) CRSwNP affects twenty five to thirty percent of the population which is minimal, however, it is associated with high morbidity and leads to increasing poor quality of life. This makes the disease essential to diagnose, evaluate and treat in clinical settings while all efforts must be made to increase the knowledge around its etiology and pathogenesis.(6)

Epidemiology

Adenoidal polyps are seen in thirty six percent of aspirin intolerance patients, seven percent of asthma patients, 0.1 percent of children, and roughly twenty percent of cystic fibrosis patients. Churg-Strauss Syndrome, hypersensitive fungal sinusitis, cilia dyskinetic syndrome (Kartagener's), and Young Syndrome are all disorders linked to nasal polyps. Nonallergic asthma has a higher prevalence of nasal polyps than hypersensitive asthma (thirteen percent vs. five percent, P 0.01). Recurrences occur in about forty percent of surgical polypectomies subjects. Chronic rhinosinusitis has a substantial influence on value of life, with symptoms similar to those of conventional debilitating illnesses such congestive heart failure, back pain of chronic type, and chronic obstructive pulmonary disease. Notwithstanding these findings, only two percent of people with CRS have been formally identified by a physician. CRSwNP levels rise by age, through a forty two year average onset across all ethnic groups. There appears to be a genetic component to the progress of nasal polyps. To standardise medical care, consideration of different types of diagnosis, and gather significant relative investigative data, a categorization arrangement for staging adenoidal polyps is planned.

Amidst the general population, CRSwNP is fairly common. Despite the efficacy of existing medicines, there are still various unmet requirements. The high prevalence of unrestrained signs, the common reappearance of nasal polyps following surgercal treatment, and the long-standing side effects of oral corticosteroids all point to the need for innovative medicines to meet these unmet requirements. The effectiveness of biologics in the actual world has yet to be recognized, despite encouraging findings from randomised controlled studies.(1)

Six investigations looked at the occurrence of CRS with NP in the all-purpose population. The frequency in South Korea was 2.5–2.6 percent of the overall population, which came out to be higher than that in the United States (1.1 percent of the overall population). Males (3.2–3.7 percent) had a higher prevalence of CRSwNP than females (2.0–3.3 percent), and the 60–69-year-olds had the highest occurrence. In the United States, NP came out in 6.1–31 percent of the population with chronic rhinosinusitis, and in Denmark, it was found in twenty four percent of the population with chronic rhinosinusitis.(2)

Uncontrolled CRS with NP is when 3 or greater of the succeeding symptoms: nasal obstruction on almost all days of a week, rhinorrhea/postnasal leak on most days of a week, face associated tenderness/heaviness on most days of a week, hyposmia, sleep trouble/exhaustion, adenoidal endoscopy with unwell mucosa; symptoms (as above) continue regardless saving treatment in the previous six calendar months. In literature, there is no mention of the occurrence of unrestrained CRS with NP in the overall CRS with NP population. Only two Belgian investigations found forty one point eight percent and forty percent uncontrolled CRSwNP among CRSwNP patients who had previously had NP surgery.(3)

Symptoms

The most prevalent symptoms described by individuals with CRSwNP were facial aching, nasal overcrowding, anosmia, sneeze, and head pain. In North America, 60–92.2 percent of patients experienced facial pain, while in Europe, 31–45 percent reported facial pain and in Asia, 19–100 percent reported facial pain.(4) Nasal congestion was reported by 95–100 percent of CRSwNP

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patients in North America, 73–88 percent of CRSwNP patients in Europe, and 76–81% of CRSwNP patients in Asia. Patients with CRSwNP in North America reported losing their sense of smell 56–84 percent of the time, 35–90 percent of the time in Europe, and 30–100 percent of the time in Asia. 88 percent of patients in North America26, 12–73 percent of patients in Europe8, and 27–51 percent of patients in Asia experienced sneezing. Patients in North America experienced headache 33–95.8 percent of the time, 20–41 percent of the time in Europe, and 2–76 percent of the time in Asia.(4)

Risk Factors

The most common risk reasons for development of CRSwNP were asthma, genetic polymorphisms, and ageing. Males, cigarette smoking, hypersensitivity, growths, CRS-related indications, tobacco usage, bronchitis of chronic type, occupation, aspirin intolerance, increased serum levels of Interleukin-5 or Interleukin-13 cytokines, decreased schooling levels, overweightness, decreased S100A8/9 (calprotectin) protein levels, first- or second-degree relatives with CRS with NP, higher Lund-Mackay score (LMS), increased blood eosinophil and tissue sums.(5)

Etiopathogenesis

The exact etiopathogenesis of CRSwNP is still unknown. However, major strides have been made in determination of factors affecting and causing the chronic disease. In normal circumstances, the airway epithelial layer offers the primary line of resistance against entry of external bodies by formation of physical barrier through construction of tight junctions between cells, also helps to create homeostasis. There is also the mechanism of clearance and mucus production which help in prevention or stopping of exposure to the pathogens. Finally, there is also presence of inducible innate immune system which helps in guarding of the respiratory epithelium. Any single factor or a combination of the aforementioned factors may be deranged and this can lead to onset of a chronic airway disease like Chronic rhinosinusitis with nasal polyps, asthma,etc.(7)

There are several hypotheses for the onset and progression of CRSwNP:

1) Microbial colonization

Staphylococcus aureus and Pseudomonas aeruginosa are the most common bacterial pathogens of the nasal cavities. Colonization of nasal cavities by such organisms can lead to defect in airway epithelium giving way to development of chronic inflammation. Similarly, fungi have also been thought to cause this process.

2) Innate Immune System Dysregulation

Several innocuous factors such as elevation of oncostatin M, member of IL-6 can lead to extensive tissue defect. Another observation is the prescence of elevated beta defensins, lysozymes and PLUNC proteins as opposed to normal controls. Faults in mucus production can also be seen which can lead to impaired mucocilary clearance leading to chronic disease.

3) Dysregulated Adaptive Immune System

It was observed that there were elevated levels of naive B cells, activated plasma cells and sevral types of immunoglobulins in patients with CRSwNP.

All of the aforementioned variables can cause CRSwNP to develop, either directly or indirectly. As a result, it's thought that CRSwNP has an essentially deficient sino-nasal mucosa, which might promote colonisation via pathogens or antigens, resulting in persistent inflammation helped by a malfunctioning immune system.(6)

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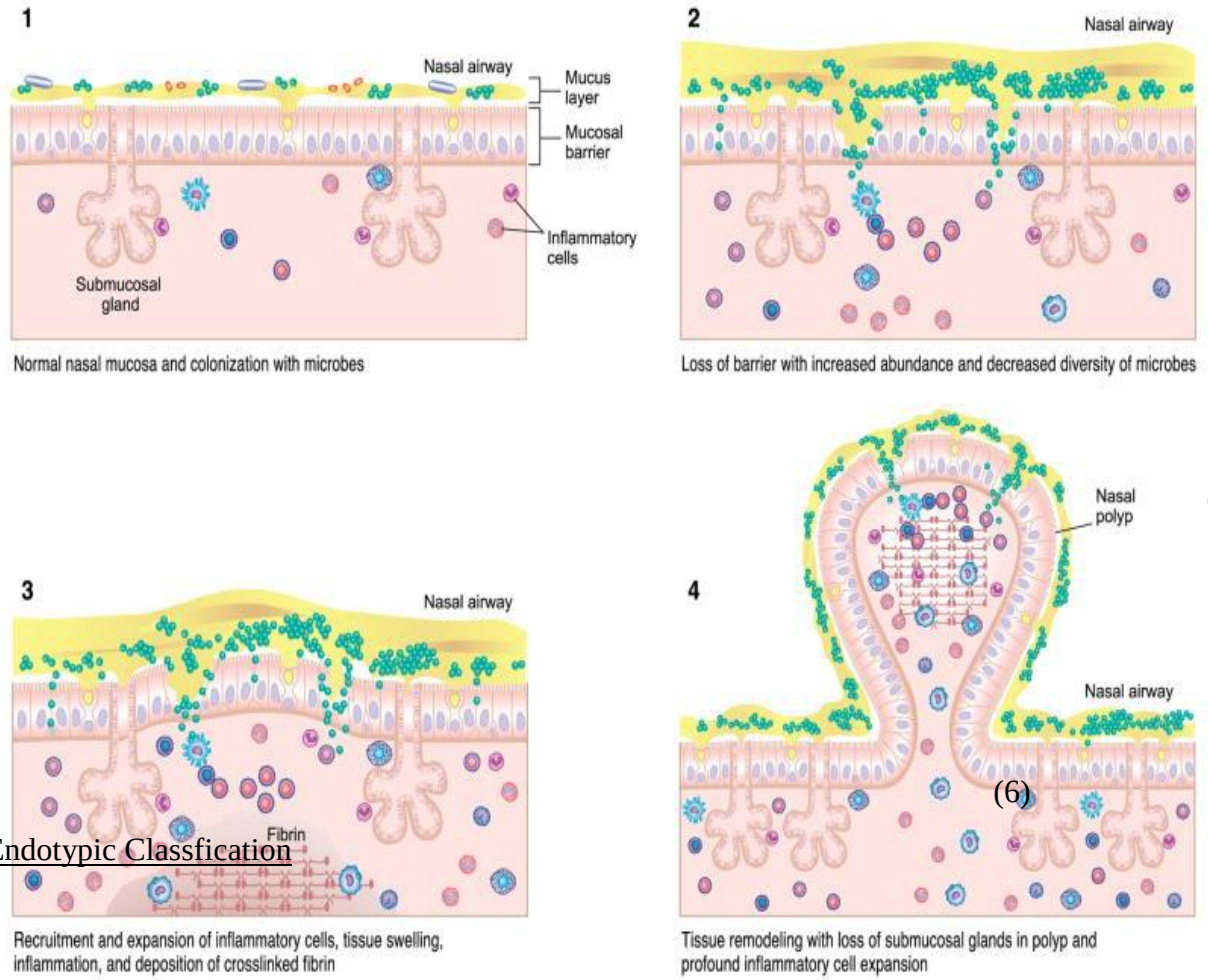

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Endotypic Classfication

CRSwNP can be categorized into two classifications, the phenotypic classification and the endotypic classification. The phenotypic classification is not extremely useful nowadays as morphology of two diseases can be alike but not have the same cause. The endotypic classification is slowly emerging to be highly useful as it is based on the underlying pathological mechanism. The endotypic classification is carried out by measurement of biomarkers which are naturally occurring molecules or genes which can help in identification of particular process or disease. Ideally, a biomarker should be easily identified, easily obtained, specific to particular disease and have high sensitivity. The biomarkers for CRS are often taken from peripheral blood, nasal secretions, nasally exhaled breath and tissue from nasal biopsies. There are variety of biomarkers which are used in classification and evaluation namely IgE, eosinophilia, various cytokines, periostin, p-glycoprotein, etc.(4) Through evaluation of these biomarkers, we can separate into biological subtypes or endotypes which can also have a large impact on treatment.(8)

However, factors such as genetics can affect the biomarkers and the entirety of the classification as seen through recent studies. Initially, CRSwNP was first characterized as having a type 2 inflammatory response, which included an increase in tissue eosinophilia as well as an increase in basophils, mast cells, IgE, and type 2 cytokines. However, all of the research was conducted on a European population; however, when identical tests were undertaken on an Asian population, the results were drastically different. In comparison to the European population, they had no tissue eosinophilia and lower levels of IL-5, but higher amounts of type-1 IFN. Thus, though this process of classification is still evolving we can say identifying the inflammatory endotype to enact patient classification rather than clinical phenotypes can provide a more accurate description of the condition. Thus, we may conclude that CRSwNP is a disease with a wide range of clinical manifestations.(9)

Histopathology

Sinonasal growths are mucosal swellings of benign type that can appear in one of 4 histologic types:

(i)An edematous, eosinophilic nasal polyp is most prevalent (85-90%) branded by oedema, hyperplasia of the epithelium of goblet cell, deepening of basement membrane, the existence of many leukocytes, chiefly eosinophils.

(ii) A fibrous inflammatory polyp is characterized by inflammation of chronic type and metaplastic alterations in the underlying epithelium.

(iii) One with uncommon form has substantial hyperplasia of the seromucinous glands but other than that resembles the edematous type of polyp.

(iv) Another growth with uncharacteristic stroma is the fourth form, which happens to be extremely rare.

To avoid misinterpretation of a tumour, this latter polyp necessitates awareness and rigorous histological testing. This latter polyp demands vigilance and thorough histological testing to avoid misinterpretation of a tumour.(10)

Differential Diagnosis

1. Eosinophilic Chronic Rhinosinusitis
2. Hypersensitive Fungal Rhinosinusitis
3. Aspirin-Exacerbated Respiratory Disease
4. Cystic Fibrosis(6)

Comorbidities

CRSwNP are frequently connected to further major medical conditions that might worsen the illness's harshness. In a comprehensive reflective research encompassing over four hundred thousand primary care patients, CRS with NP patients had a suggestively higher pre-morbid occurrence of rhinosinusitis of acute type, hypersensitive rhinitis, rhinitis of chronic type, asthma, gastro-esophageal reflux syndrome, and sleep apnea.(6)

In the same study, the connection between asthma and CRSwNP became clearer. A great majority of asthmatics (88 percent) have at least some radiographic evidences of sino-nasal inflammation 1. CRSwNP is believed to afflict 7% of asthmatics, with asthma being described in 26–48% of CRSwNP patients. Patients with CRS with NP were 7.5 times more likely to have asthma than those with CRSsNP. Furthermore, greater sino-nasal inflammation has been linked to a worsening of asthma symptoms.(6)

Thus, with aging as well as preponderance to comorbidities the value of life does decrese rapidly in patients with diseases of chronic type such as CRSwNP.

Role of Inflammatory Cells

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There has been a link discovered amongst high blood eosinophil count and CRSwNP relapse times. A straight link between recurring CRSwNP and blood basophil levels was also discovered in some major studies. The blood basophil and eosinophil sums of CRSwNP patients were highly interrelated. Patients who suffered a disease relapse had significantly greater preoperative neutrophil-to-lymphocyte, eosinophil-to-lymphocyte, and basophil-to-lymphocyte proportions than those who did not. Mean blood eosinophil counts decreased suggestively from before to after endoscopic sinus surgery in patients with histologically established eosinophilic-type CRSwNP.(7)

The evidence suggests that blood eosinophil and basophil counts must be involved for normal preoperative work-up of CRS with NP patients in order to provide correct prognostic evidence, implement sensible postoperative follow up rules, and deliver focused post operative medicinal therapies.(8)

Precision Medicine and Treatment

Precision medicine is a medical concept that aims to personalise healthcare by tailoring medical decisions, procedures, and products to each patient. Precision medicine, which is based on a thorough understanding of disease causes, typically combines diagnosis and treatment to determine the best course of action. Precision medicine's cornerstones are patient involvement in treatment decision-making, prediction of treatment success, methods to avoid disease progression, and tailored endotype-driven treatment. Appropriate and standardised endotyping, as well as knowledge of biomarkers that predict therapy efficacy, are required for endotype-driven treatment.(9)

Precision medicine application approaches to the therapy of illnesses of upper airway such as CRS with NP will be a major endeavour for the coming decade. Precision medicine includes endotype-driven treatment, which is especially useful for patients with unrestrained severe disease. Once we are able to identify the patient(s) with the phenotypic and endotype that will profit the maximum from the treatments, monoclonal antibodies could be a possible new therapeutic.(10)

A crucial difficulty in achieving cost-effectiveness will be the capacity to forecast which patients will reply favourably to a specific antibody of monoclonal type. In an ideal world, we would be able to identify these people earlier in the illness and treating it to avoid many surgeries in the coming years ahead, as well as the progression of lower airway disease.(11)

The most common treatment for CRSwNP is pharmacological, which includes topical and/systemic glucocorticosteroids, irrigations of saline, and antibiotics occasionally when required. If conservative methods are unsuccessful, surgical methods is performed, followed by continuous medical care. New therapy strategies based on particular management of the Th2 inflammatory endotype commonest in CRS with NP that have previously proven success in randomised measured trials and possible alternatives in the sooner future.(12)

Newer treatments option in CRSwNP include using

1. Anti-Immunoglobulin E
2. Anti-Interleukin-5
3. Anti-Interleukin-4/Interleukin-13(13)

As more clinical trials of biologic treatments for CRS are completed, cost-effectiveness analysis will be required. In future studies, these therapies should be compared against surgery as part of the medical therapeutic alternatives.(14)

The treatments that are currently accessible are mostly based on clinical experience and are not backed up by evidence-based medicine. We will only treat CRSwNP symptomatically until we have a complete understanding of the disease's underlying aetiology.(15)

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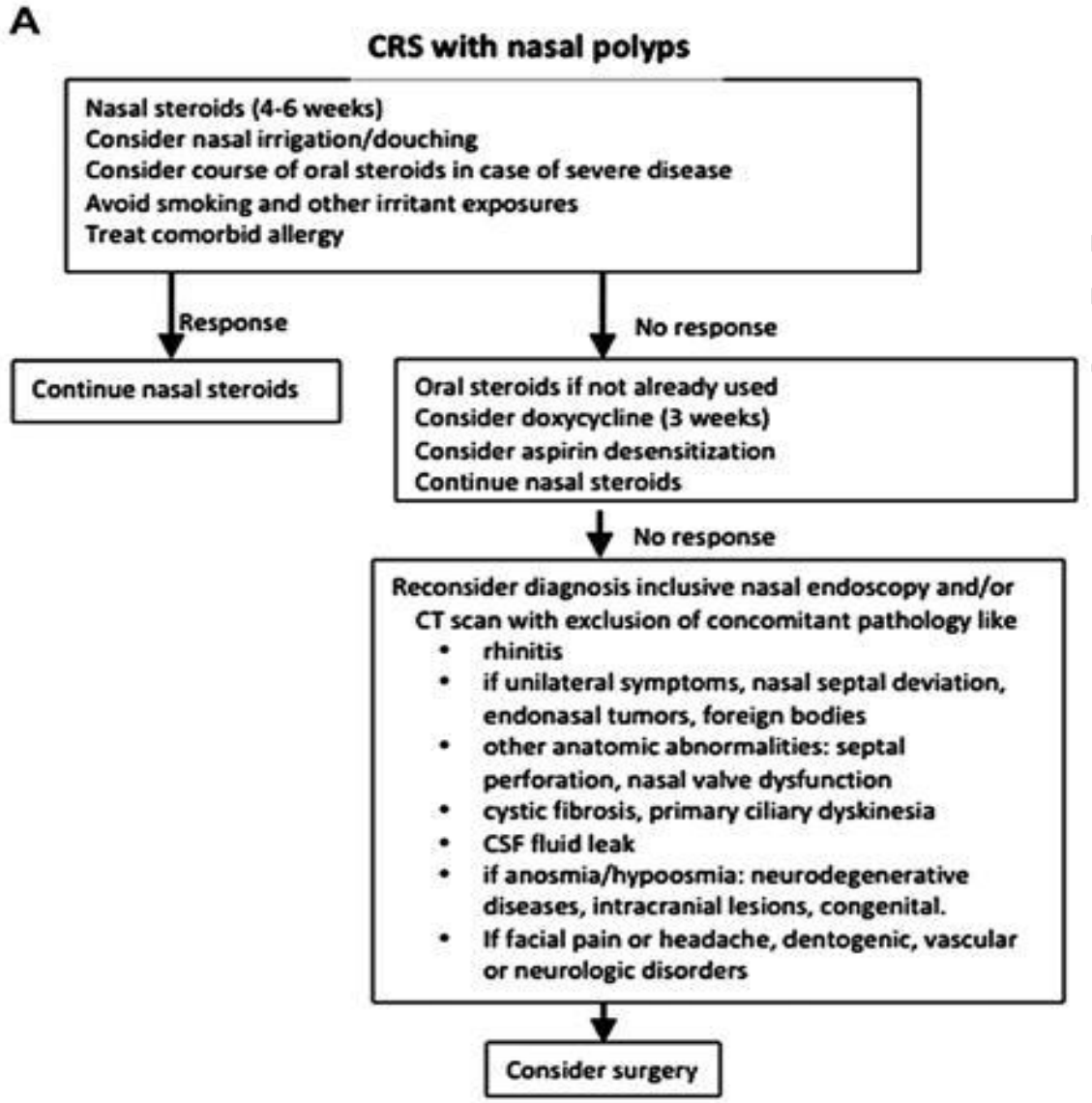
Fig. 1 CRS with nasal polyps



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Conclusion

Chronic Rhinosinusitis with Nasal Polyps is a fairly common though overlooked disease which affects a large number of individuals arising from different populations. This disease though considered minor significantly decreases the quality of life of the patient which requires that we perform extended research on this topic, particularly the treatment. Though, we have made a breakthrough in understanding the pathology of the disease, by classifying the various endotypes with the help of biomarkers, the studies remain viable in a smaller population and have not been conducted successfully on a large scale. The treatment options are also a little dated which poses a concern for the masses affected. Thus, the increasing research and solutions being given are highly valuable and help to innovate methods of treatment, and ultimately understanding the disease in a better way.

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