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Greetings from Micro Labs. We are happy to bring you “Allergy Connections” which contains latest and interesting news in the field of Allergy.

This issue contains:

- 1. Relationship between Allergic Rhinitis and Autoimmune Thyroid Diseases**
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- 3. Analysis of Biomarkers in predicting the postoperative recurrence of chronic rhinosinusitis with nasal polyps**
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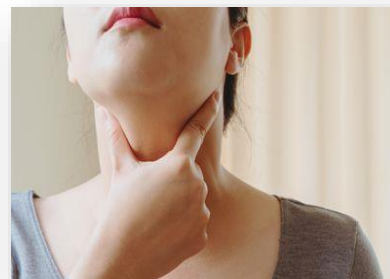
Best Regards,

Medical Team, Micro Labs Ltd

Relationship between Allergic Rhinitis and Autoimmune Thyroid Diseases

Introduction

Autoimmune thyroid diseases (AITD) including Hashimoto's thyroiditis (HT) and Graves' disease (GD) impacts around 5% of the population.¹ AITD involves the histological infiltration of self-directed T and B cells into the thyroid gland in addition to producing thyroid autoantibodies and disrupting the production of thyroid hormones.² Several autoimmune diseases, including sinusitis, asthma, chronic middle ear effusions, lymphoid hypertrophy with obstructive sleep apnoea, disrupted sleep, and other problems are frequently linked to allergic rhinitis (AR), a prevalent autoimmune condition.³ Only a few studies have assessed the relationship between AR and AITD and revealed a significant frequency of AR in GD and a high incidence of HT in individuals with AR. So, this study intended to determine if AR was a risk factor for AITD development.⁴



Methods

This retrospective cohort study utilized records of patients with AITD, specifically GD and HT, and included AR patients aged 18 to 75 years. AR was diagnosed by a medical history and physical examination. Symptoms included obvious rhinorrhea, pallor of the nasal mucosa, and red, watery eyes. Additional symptoms included nasal congestion, itching, and sneezing. Patients who were pregnant or lactating, taking thyroid-affecting drugs (e.g., amiodarone, interferon, iodinated contrasts, lithium), or having a history of thyroid treatment with radioiodine or chest and neck radiotherapy were excluded. Based on the data obtained during the initial visit, the patients were divided into four groups: Group 1: Patients diagnosed with AR who present with HT; Group 2: Patients without an AR diagnosis who come with HT; Group 3: Patients with AR who present with GD; Group 4: Patients without AR who present with GD. Then, the parameters such as thyroid stimulating hormone (TSH), free triiodothyronine (FT3), free thyroxine (FT4), thyroid peroxidase antibodies (TPOAb), thyrotropin receptor antibody (TRAb), eosinophil count, and IgE were evaluated. SPSS software version 25 was used for analyzing the statistical data.

Results

Overall, 4,515 individuals were included and 41.7% were diagnosed with both AR and AITD. The average age of the patients with both illnesses was 45.71 ± 24.14 years, the mean duration of AITDs was 7.32 ± 2.11 years, and 81% of them were female. When compared to the non-AR cohort, the cumulative incidence of total AITDs, HT, and GD was considerably greater in the AR cohort (log-rank test, $P=0.001$). After one year of follow-up, the AR cohort showed a 50%

greater risk of developing AITDs and HT, and after two years, there was a 50% increased risk of developing GD. The incidence rate ratios for HT, GD, and total AITDs were 2.64, 1.73, and 1.51, respectively (Figure 1). Female sex was associated with higher risk group AITDs. A history of both bronchial asthma and skin allergy, female sex, greater WBCs, more eosinophils, and diagnosis are all associated with an increased risk of HT. People with a history of skin allergies, greater levels of IgE and vitamin D, and older ages for occurrence of AR were all considered lower risk. Women with greater WBCs and female sex were at increased risk for GD, but people with higher IgE and eosinophil counts were at reduced risk.

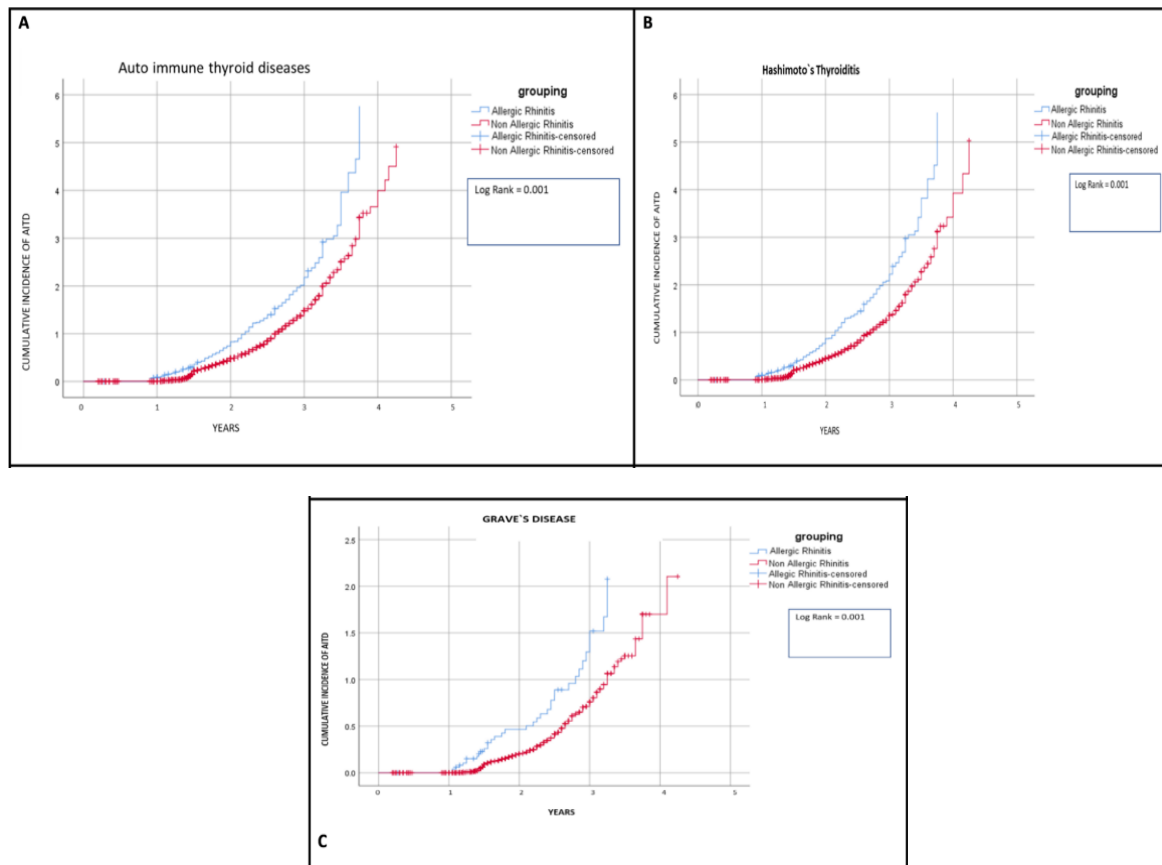


Figure 1. Cumulative incidence of AITDs, HT, and GD in patients with AR

Discussion

The increased prevalence of AITD in AR patients raises the possibility that thyroid autoimmunity is a result of persistent immunological activation in AR. The importance of environmental triggers was further supported by seasonal fluctuations, with HT diagnoses rising in the winter and GD diagnoses peaking in the summer. In individuals with GD, elevated IgE levels raise the possibility of immunological overlap between autoimmune and allergy processes.⁴ The prevalence of AR in GD and HT patients investigated by Amino et al. was inconsistent with the current study findings of increased GD risk in AR patients (42.9%, $p=0.05$).⁵

Conclusion

Patients with AR have an increased risk of developing HT and GD. The time between AR diagnosis and the development of HT or GD was rather consistent, indicating a relationship between AR and the subsequent onset of these ATIDs. Seasonal changes in HT and GD diagnosis indicated environmental factors and ATID development. HT diagnoses were more common in the winter months, particularly February and December, whereas GD diagnoses increased during the summer, with May and August being the most common months.

Screening for Autoimmune thyroid disorders (AITD) should be conducted at the time of diagnosis of allergic rhinitis as it could be a risk factor for AITD.

References

1. Antonelli A et al. Autoimmune thyroid disorders. *Autoimmun Rev.* 2015 Feb;14(2):174-80.
2. Tomer Y. Mechanisms of autoimmune thyroid diseases: from genetics to epigenetics. *Annu Rev Pathol.* 2014; 9:147-56.
3. Fröhlich E, Wahl R. Thyroid Autoimmunity: Role of Anti-thyroid Antibodies in Thyroid and Extra-Thyroidal Diseases. *Front Immunol.* 2017 May 9; 8:521.
4. Allam MM et al. Association between allergic rhinitis and development of autoimmune thyroid diseases in Egyptian patients. *BMC Endocr Disord.* 2024 Dec 31;24(1):202.
5. Amino N et al. Association of seasonal allergic rhinitis is high in Graves' disease and low in painless thyroiditis. *Thyroid.* 2003 Aug;13(8):811-4.

Use of Nasal allergen provocation test in individuals allergic to hen's egg white allergens

Introduction

Food allergy (FA) is a major clinical issue because of its rising frequency and pathomechanism, which involves a complex interplay of genetic, epigenetic, and environmental variables.¹ On average, 13% of adults and 12% of children report having FA symptoms. Sensitisation to peanut allergens is reported by 0.6% of patients, 3% for milk, 1% by hen's egg, 0.6% for fish, and sensitisation to shellfish by 1.2% of patients.² The problem of hen's egg white allergy primarily affects children in infancy and early childhood, where the incidence of sensitization to this allergen is estimated at 16.5%, with diagnosis confirmed by an oral food challenge including the allergen in 8.9%. Nearly 3% of the general population has been diagnosed with hen's egg white allergy, which is associated with symptoms of FA as determined by skin prick tests or sIgE expression assays.³ Nasal allergen provocation test, an essential component for the diagnosis of allergies which got triggered by environmental factors. The possibility of using this technique to diagnose food allergies has received more attention lately. This study aimed to determine the beneficial role of NAC for the patients who were allergic to hen's egg white allergens.⁴

Methods

A total of 57 participants were included in the study, comprising 32 patients who were allergic to hen's egg white allergens and 25 healthy controls, who were free of allergies and had not

become sensitized to any allergens. Patients with positive skin prick tests for hen's egg allergies were included. Those with a history of anaphylactic shock, external nasal deformities and nasal cavity structural abnormalities, atrophic rhinitis, recent vaccinations, surgeries performed within the last eight weeks, acute upper respiratory tract infections that were active or had occurred within the 4 weeks prior to the study, uncontrolled asthma, severe systemic conditions, and systemic immunotherapy were excluded. Hen's egg white allergen is used in the nasal allergen provocation test, which is evaluated by measuring the levels of tryptase and sIgE in nasal lavage fluid, as well as by utilizing the visual analog scale (VAS) and optical rhinometry (OR).

Results

The severity of nasal symptoms and flow rates measured by OR significantly increased with increasing doses of the hen's egg white allergen used in the Nasal Food Challenge (NFC). Nasal obstruction was the most common symptom measured by the VAS, and it was most noticeable in the individuals who were allergic to hen's egg protein (mean 5 cm, range: 2–7 cm on the VAS) when 100 µg vs. control group. Prior to the subjective complaints as assessed by the VAS scale being reported (i.e., beginning 30 minutes into the study), there were significant differences in nasal patency as determined by OR compared to the control group. Variability in blood flow inside the blood vessels was found to differ between the study group and the control group, with values of 0.03, 0.04, 0.06, 0.20, 0.31, and 0.34 OD and −0.01, 0.01, 0.01, 0.01, 0.05, and 0.04 OD, respectively (Figure 1). In the analysis of symptoms as measured using the VAS scale, the study groups differed in terms of nasal itching at 30 min (AUC=0.4752), 45 min (AUC=0.7616), 60 min (AUC=0.9808), and 75 min (AUC=0.9984); for nasal discharge, the AUC values were 0.224 at 30 min, 0.712 at 45 min, 0.976 at 60 min, and 0.9952 at 75 minutes into the study. The highest difference between the study groups in terms of nasal blockage was noted 75 minutes into the investigation (AUC = 1).

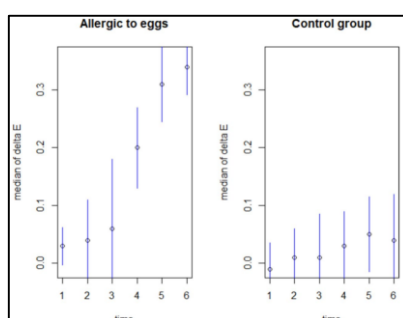


Figure 1. Objective assessment of changes in nasal patency as measured by optical rhinometry.

Discussion

The study highlighted that the nasal food challenge test is an effective diagnostic tool for detecting the allergy, thereby providing an alternative tool for oral food challenge methods. The result also showed a moderate nasal response ($\Delta E=0.34$ OD) in optical rhinometry, proving

that reactivity can be measured in allergic individuals while maintaining a strong safety profile with no severe reactions.⁴ In another study, a nasal allergen provocation test was carried out against shellfish allergy and found similar specificity and sensitivity to NFC, thereby promoting it as a diagnostic method for detecting food allergies.⁵

Conclusion

For patients with food allergies, a nasal food challenge using the hen's egg white allergen is a useful diagnostic alternative. More attempts at standardizing the procedure are necessary because there haven't been enough studies conducted thus far.

Nasal food challenge provides a valuable diagnostic insight with minimal risk, thereby improving the testing methods for allergens.

References

1. Sicherer SH and Sampson HA. Food allergy: A review and update on epidemiology, pathogenesis, diagnosis, prevention, and management. *J Allergy Clin Immunol.* 2018 Jan;141(1):41-58.
2. Perkin MR et al. Randomized Trial of Introduction of Allergenic Foods in Breast-Fed Infants. *N Engl J Med.* 2016 May 5;374(18):1733-43.
3. Osborne NJ et al. Prevalence of challenge-proven IgE-mediated food allergy using population-based sampling and predetermined challenge criteria in infants. *J Allergy Clin Immunol.* 2011 Mar;127(3):668-76. e1-2.
4. Krzych-Fałta E et al. Nasal food challenge with hen's egg white allergen. *Allergy Asthma Clin Immunol.* 2025 Jan 12;21(1):3.
5. Gelis S et al. Usefulness of the Nasal Allergen Provocation Test in the Diagnosis of Shellfish Allergy. *J Investig Allergol Clin Immunol.* 2022 Dec 15;32(6):460-470.

Analysis of Biomarkers in predicting the postoperative recurrence of chronic rhinosinusitis with nasal polyps

Introduction

Chronic rhinosinusitis (CRS) is an inflammatory condition of the upper airway that primarily affects the nasal cavity and sinus mucosa. It is classified as CRS with nasal polyps (CRSwNP) and CRS without nasal polyps (CRSsNP) depending on the presence of nasal polyps.¹ It was estimated that between 0.5 and 4.0% of people suffer from CRSwNP worldwide.² Currently, the primary treatment option for CRSwNP is surgery. But there's a chance of a postoperative recurrence, which makes the therapy more complicated. To mitigate the disease impact and economic burden on CRSwNP patients, healthcare practitioners must investigate postoperative recurrence risk factors and optimize CRSwNP therapy and management procedures. Eosinophilic cationic protein (ECP), a biomarker, and a heme enzyme called myeloperoxidase (MPO) are also used as indicators for the endotype diagnosis of CRS.³ Also, Immunoglobulin E (IgE) plays a crucial role in the pathophysiology of nasal polyposis.⁴ Eosinophil activation and its accumulation at inflammatory areas are mediated by C-C motif chemokine ligand 4 (CCL4).⁵ Despite their potential significance, few studies have looked into whether ECP/MPO,

IgE, and CCL4 can predict postoperative relapse of CRSwNP and act as risk factors for recurrence. This study attempts to address this gap by examining biomarkers that can help avoid postoperative CRSwNP recurrence.³

Methods

This retrospective study was carried out among 270 CRSwNP patients who received surgical treatment where 230 patients were allocated to the non-relapse group and 40 instances to the relapse group. Individuals who met the CRSwNP and Davos scoring criteria and were at least 18 years old underwent endoscopic sinus surgery, had intact clinical data and case records, and had not taken any drugs for four weeks previous to the procedure were included. Patients with fungal sinusitis, polyps in the nose of the posterior maxillary sinus, a history of endoscopic sinus surgery, compromised heart, lung, or kidney function, infectious illnesses, or immune system disorders were excluded. Serum samples were taken from both groups prior to surgery to assess ECP/MPO, IgE, and CCL4. Receiver operating characteristic (ROC) curves were utilized to assess these markers' predictive potential for postoperative relapse in CRSwNP patients. The association between these variables and postoperative relapse was examined using Spearman's correlation coefficients. Univariate and multivariate analyses were used to determine factors affecting postoperative relapse of CRSwNP.

Results

ECP/MPO, IgE, and CCL4 were significantly greater in the relapse group than in the non-relapse group. The area under the curve (AUC) for predicting postoperative recurrence of CRSwNP by each indicator was about 0.800, while the combined detection's AUC was more than 0.900. There was a substantial positive connection between postoperative recurrence of CRSwNP and ECP/MPO, IgE, and CCL4. Upon univariate analysis, the Davos score of nasal polyps, smoking history, postoperative infection, ECP/MPO, IgE, and CCL4 were all substantially associated with the postoperative relapse of CRSwNP. By multivariate analysis, ECP/MPO, IgE, and CCL4 were found to be independent risk factors for postoperative recurrence of CRSwNP. Furthermore, a nomogram for predicting the postoperative relapse risk of CRSwNP was formulated based on the binary Logistic regression analysis. The total score ranged from 0 to 550 points, allowing prediction of the postoperative recurrence risk of CRSwNP within a range of 10%-90% (Figure 1).

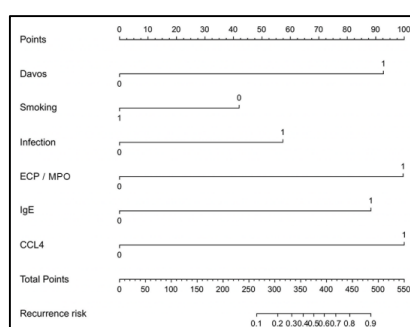


Figure 1. Nomogram for postoperative relapse risk of CRSwNP.

Discussion

The serum levels of IgE, CCL4, and ECP/MPO in relapse group were abnormally higher than those of the non-relapse group. This suggests that these markers may be involved in the pathological course of CRSwNP and contribute to its postoperative recurrence. The greatest predictive performance was shown by IgE, which was followed by CCL4 and ECP/MPO.³ Similar to the results of this study, Zheng M et al. revealed that the relapse group had significantly higher levels of ECP/MPO, IgE, and CCL4 than the non-relapse group; additionally, IgE showed the highest sensitivity (82.4%) in predicting CRSwNP recurrence, and ECP/MPO presented the highest specificity (83.7%).⁶

Conclusion

ECP/MPO, IgE, and CCL4 are all reliable indicators of postoperative relapse in CRSwNP patients and combining them can improve prediction accuracy even further. These indicators have a strong and positive correlation with postoperative relapse and serve as risk factors for recurrence.

Early detection of ECP/MPO, IgE and CCL4 could predict and prevent the recurrence of CRS with nasal polyps after surgery.

References

1. Fokkens WJ et al., European Position Paper on Rhinosinusitis and Nasal Polyps 2020. *Rhinology*. 2020 Feb 20;58(Suppl S29):1-464.
2. Sanchez-Collado I et al. Prevalence of Chronic Rhino-sinusitis with Nasal Polyps in Catalonia (Spain): a retrospective, large-scale population-based study. *Rhinology*. 2022 Oct 1;60(5):384-396.
3. Wang W et al. Risk factors for postoperative relapse of chronic rhino-sinusitis with nasal polyps and improvement in clinical treatment. *Am J Transl Res*. 2024 Dec 15;16(12):7609-7617.
4. Bachert C et al. Total and specific IgE in nasal polyps is related to local eosinophilic inflammation. *J Allergy Clin Immunol*. 2001 Apr;107(4):607-14.
5. Chu HH et al. CCL4 Regulates Eosinophil Activation in Eosinophilic Airway Inflammation. *Int J Mol Sci*. 2022 Dec 18;23(24):16149.
6. Zheng M et al. Expression of immunological and inflammatory biomarkers in chronic rhino-sinusitis with nasal polyps and its predictive value for recurrence. *Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi*. 2019 Mar 7;54(3):174-180.

Case Report on Invasive Fungal Rhinosinusitis with Intracranial and Orbital Involvement

Introduction

Fungal sinusitis can be either invasive or non-invasive. The progression of invasive fungal rhinosinusitis from the orbit to the skull can be lethal. The overall survival rate is almost 50%, even though the reported survival rates fluctuate.¹ In addition to systemic antifungal medications, treatment entails significant surgical excision, involving ocular exenteration and craniotomy. However, when intracranial expansion is included, total removal could be difficult.² Recent findings suggest that when antifungal medication is used in conjunction with

substantial resection, disease control can still be accomplished. This case report highlighted the successful treatment of invasive fungal rhinosinusitis with endoscopic surgery and voriconazole emphasizing conservative surgery and long-term monitoring.³

Case Presentation

A 59-year-old man with untreated diabetes mellitus had gradual vision loss in his right eye over a month. Magnetic resonance imaging (MRI) of the sinus revealed a tumor-like lesion in the right orbit. The right orbital apex was reached by a soft tissue mass with associated bone damage noted upon contrast-enhanced computed tomography (CT) of the sinus (Figure 1). Both cavernous sinus invasion and inflammation had progressed to the dura mater. There was no infiltration of the brain parenchyma detected by sinus MRI. The cerebral vasculature was found to be free of aneurysms and stenosis or blockage on magnetic resonance angiography (MRA). The patient had elevated levels of β -D-glucan (28.5 pg/mL) and hemoglobin A1c (11.4%) during lab investigation. Due to high β -D-glucan levels, invasive fungal rhinosinusitis was taken into consideration. A biopsy was carried out and confirmed *Aspergillus* infection, and treatment was initiated with 400 mg of intravenous voriconazole (VRCZ). The lesion spread to the cavernous sinus, so endoscopic sinus surgery (ESS) was carried out on the twelfth day following the biopsy, and Draf type III and transseptal approach was performed to remove it. The nasal septum was removed, and the left sphenoid sinus was visualized, followed by the right sphenoid sinus, where the internal carotid artery prominence was identified as the posterior limit. A right internal carotid artery stenosis was noted by MRA on the fourteenth day following surgery; however, the development of collateral blood vessels meant that the risk of cerebral infarction was low. As a result, the treatment plan consisted of regular imaging follow-up. A month following the procedure, MRA revealed a total occlusion of the right internal carotid artery. However, the patient did not experience a cerebral infarction due to the formation of collateral blood vessels. The treatment approach was determined to be regular imaging follow-up. One month following the procedure, the patient's MRA revealed that the artery was completely blocked, but no cerebral infarction had occurred. The patient's VRCZ dosage was progressively lowered to 200 mg per day while trough levels were tracked, and 35 days after surgery, the patient was released. At one week after surgery, the β -D-glucan level was 15.1, dropped to 14.9% at two months, and then dropped to less than 6.0 at six months, where it has stayed steady ever since. Eight months following surgery, the lesion at the right orbital apex had decreased, according to a contrast-enhanced CT scan of the sinus (Figure 2, axial section). Cerebrovascular disease showed no symptoms of progression or recurrence. Even after two years, the patient is still receiving oral VRCZ medication, and there has been no improvement in eyesight.



Figure 1. Contrast-enhanced CT of the sinus (axial section)

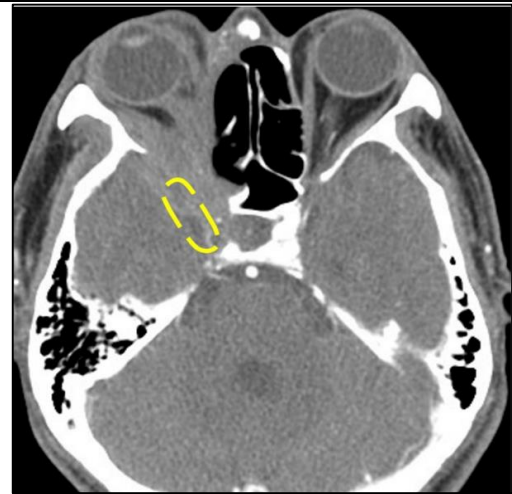


Figure 2. Contrast-enhanced CT of the sinus eight months after surgery (axial section)

Discussion

Endoscopic surgery (ESS) has expanded its range of indications and techniques, with VRCZ being the first-line treatment for central nervous system aspergillosis and invasive fungal rhinosinusitis. ESS in combination with VRCZ is used to treat the illness, and it gradually reduces residual lesions, making it a potential treatment option for intracranial lesions. However, after surgery, internal carotid artery stenosis was found, emphasizing the importance of MRA/MRI surveillance.³ Similar investigations on invasive fungal rhinosinusitis have demonstrated improved survival rates when azole antifungal medication is used in conjunction with surgery.⁴

Conclusion

There have been cases of invasive fungal rhinosinusitis involving the orbitals and brain. By combining VRCZ treatment with ESS to eliminate as much of the lesion as feasible, the illness can be managed even in situations when total removal is challenging. Furthermore, MRA is essential for assessing the cerebrovascular system since this condition might result in cerebrovascular consequences.

Invasive fungal rhino sinusitis can be managed with endoscopic surgery along with voriconazole and regular MRI monitoring could detect further complications.

References

1. Kasapoglu F et al. Acute invasive fungal rhinosinusitis: evaluation of 26 patients treated with endonasal or open surgical procedures. *Otolaryngol Head Neck Surg.* 2010 Nov;143(5):614-20.

2. Kondo E et al. Two Cases of Invasive Aspergillus Sinusitis and Mastoiditis Successfully Treated with Voriconazole. *Practica otorhinolaryngologica*. 2007;100(6):473.
3. Nishimura H, Maruyama R, Yatomi M, Tsukahara K. Invasive Fungal Rhinosinusitis with Intracranial and Orbital Involvement: A Case Report. *Cureus*. 2024 Nov 17;16(11): e73868.
4. Tessler I et al. Impact of azole antifungal treatment on outcome in acute invasive fungal rhinosinusitis with orbitocranial involvement: a surgical perspective. *Rhinology*. 2023 Dec 1;61(6):561-567.



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