The role of IL-17 in chronic rhinosinusitis with nasal polyp

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Objectives: Recently, IL-17 is known to play an important role in inflammatory disease including CRS. It is known to be increased in CRS with nasal polyp (NP). In this study, we evaluated the expression of IL-17 in CRS tissues and identified the cellular source of IL-17 in CRS with NP.

Methods: The expression of IL-17 in human CRS tissues were evaluated using PCR and immunohistochemistry (n=20 each group). And the cellular sources of IL-17 were evaluated with double staining immunohistochemistry using confocal microscopy. IL-17A, CD68, CD163, ELA2 CD56, CD4 and CD11c antibodies were used to evaluate the cellular sources of IL-17. Eosinophilic and noneosinophilic polyps were evaluated (n=5 each sample).

Results: PCR and IHC showed that IL-17 expressions were increased in both eosinophilic and non- eosinophilic polyps, with significantly higher expression in noneosinophilic nasal polyp. Confocal staining revealed that about 60% of CD68+ M1 macrophage, 30% of ELA2+neutrophil and 10% of CD4 T cell coexpressed IL-17 irrespective of eosinophilic and noneosinophilic polyp, showing that M1 macrophage and neutrophil were major sources of IL17 in nasal polyp. NK cell, M2 macrophage and dendritic cells did not produce IL-17 in both eosinophlic and noneosinophilic nasal polyp.

Conclusions: These data showed that iL-17 were highly expressed in nasal polyp and the major cellular sources are macrophage and neutrophil, suggesting that IL-17 might be used as target therapy in CRS with NP. In addition, M1 macrophage or neutrophil can also be used as a cellular target in CRSwNP.

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Effect of prostaglandin D2 on VEGF release by nasal polyp fibroblasts

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Introduction:
Vascular endothelial growth factor (VEGF) is known to be associated with the pathogenesis of chronic rhinosinusitis with nasal polyps (CRSwNP). VEGF is produced by a variety of cells including fibroblasts. It was recently reported that prostaglandin (PG) E2 induces VEGF release by nasal polyp fibroblasts. However, little is known regarding possible regulation of VEGF by other PGs. We have reported that molecules that regulate PGD2 metabolism play roles in the pathogenesis of CRS including in local eosinophilia and type 2 cytokine production. In the present study, we sought to determine whether PGD2 regulates VEGF release by nasal polyp fibroblasts.

Method:
Nasal polyp fibroblasts were established from nasal polyps. These fibroblasts were stimulated with serial dilutions of PGD2 or PGD2 receptor (DP/CRTH2)-selective agonists in the presence or absence of receptor-selective antagonists. The concentration of VEGF in the culture supernatants was determined using ELISA.

Results:
5 mM of PGD2 significantly induced VEGF release by nasal polyp fibroblasts. VEGF release was also obtained by stimulation with a DP receptor-selective, but not with a CRTH2 receptor-selective agonist. In addition, PGD2-induced VEGF release was significantly inhibited by pre-treatment with DP receptor-selective antagonists. In contrast, pre-treatment with a CRTH2 receptor-selective antagonist significantly enhanced PGD2-induced VEGF release.

Conclusion:
PGD2 stimulates VEGF production via DP but not CRTH2 receptors in nasal polyp fibroblasts.

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Allergic rhinitis and asthma are inflammatory allergic airway diseases characterized by Th2-skewed eosinophilic inflammation, mucus hypersecretion, and airway hyperresponsiveness. The excessive activation of Th2 cells due to insufficient suppression of regulatory T cells (Tregs) is thought to play a major role in the initiation and development of allergic airway diseases. Several studies have shown that stem cells provide a significant reduction in allergic airway inflammation and improve lung function in animal models. The immunomodulatory effects of stem cells in allergic airway diseases may be mediated by the upregulation of Tregs and increases in several soluble factors such as prostaglandin E2, transforming growth factor-β, interleukin-10, and indoleamine 2, 3-dioxygenase.

Recently, it has been reported that culture supernatant of mesenchymal stem cells (MSCs) and MSC-derived extracellular vesicles (EVs) also ameliorate allergic airway inflammation. We found strong immunosuppressive ability of culture supernatant derived from adipose stem cells (ASCs), which contains the ASC secretome, in asthmatic mice. Furthermore, EVs derived from ASCs ameliorated allergic airway inflammation and improved lung function through the induction of regulatory T cells expansion. These culture supernatant and EVs derived from ASCs may be a promising candidate for a novel cell-free therapy for allergic airway diseases that have many advantages over stem cells themselves, including safety, ease of handling, ability to be stored for long periods, and usage in patients. Although we need more information about culture supernatant and EVs derived from MSCs before use in therapy, this strategy could be used to treat many immunological diseases in the near future.

References

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International Session 1

Dental sinusitis (from an otolaryngologist perspective)

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It is crucial to give careful consideration to dental causes in diagnosing and treating maxillary sinusitis. Due to anatomical proximity to the maxillary sinus inferior wall, approximately 10% of maxillary sinusitis cases is considered as dental origin. Especially, sinusitis induced by iatrogenic causes is rapidly increasing in relation to the development of invasive dental surgeries. Diagnosing sinus disease of dental origin requires a thorough evaluation of the patient’s subjective symptoms and past medical history and their correlation with physical findings including periodontal disease. Etiology of dental sinusitis could be classified as, endodontic infection, sinus penetration during endodontic procedure, dislocation of tooth fragments into the maxillary sinus, opening of an oroantral communication, penetration of dental implants, and tears of the sinus mucosa during augmentation procedure. The typical odontogenic infection is now considered to be a mixed aerobic-anaerobic infection, with the latter outnumbering the aerobic species involved. Treatment of dental sinusitis usually requires a combination of medical and surgical management. Anatomical knowledge of the sinus-teeth relationship as well as pathophysiological understanding of sinusitis is required in treating dental sinusitis. Effective control of the infection source, including tooth or implant, is mandatory to prevent recurrence. If initial medical treatment is failed, surgical procedure should be considered. Classically, a modified Caldwell-Luc approach is indicated for removing the sources of infection. More recently, less invasive endoscopic shaver-assisted techniques have been advocated for treatment of dental sinusitis. In our previous study, despite appropriate medical treatment, the majority of patients with paranasal sinusitis related to the dental implant required surgical treatment after all. Findings of paranasal sinus CT may be important in determining treatment option.

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The use of an endonasal Doppler to locate the vascular pedicle of a nasoseptal flap prior to harvesting in patients who had previous irradiation to the nasopharynx

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Aim:
To assess the survival rates of nasoseptal flaps (NSF) harvested with and without the use of an endonasal Doppler (Minidop Detector, Koven®, USA) to locate the vascular pedicle in patients who had previous irradiation to the nasopharynx (NP).

Method:
Retrospective chart review

Results:
Between May 2012 and Jan 2018, a NSF was used to cover the nasopharyngeal surgical wound in 16 patients who had previous irradiation to the NP in a tertiary referral centre. 10 cases had endoscopic nasopharyngectomies for recurrent T1 nasopharyngeal carcinoma (NPC), 3 cases underwent combined maxillary swing and endoscopic nasopharyngectomies for recurrent T1 NPC, 1 cases had revision flap surgery for NSF failure, 1 case had endoscopic debridement for nasopharyngeal soft tissue necrosis, 1 had transclival resection of a recurrent clival chordoma. Endonasal Doppler was not used to locate the vascular pedicle of NSF before harvesting in 9 cases, and 4 out of 9 flaps survived (44%). Endonasal Doppler was used to locate the vascular pedicle with the aim to protect it during harvesting in 7 cases. A positive identification was achieved in 5 cases, and all 5 flaps survived (100%). The pedicle could not be located in 2 out of 7 cases. As a result, a NSF with wide pedicle based from the sphenoid ostium to the roof of the posterior choana was harvested, but eventually the distal end of the flaps developed ischaemia. The Pearson Chi-Square Test of Independence showed statistically significant better NSF survival rates in patients who had a positive identification of the vascular pedicle using the endonasal Doppler (p=0.017).

Conclusion:
Radiotherapy can cause stenosis or occlusion of the posterior septal branch of sphenopalatine artery. Using an endonasal Doppler to locate the vascular pedicle of a NSF harvested to cover a nasopharyngeal wound in patients who had previous irradiation to the NP increases the survival rate. Positive localization of the pedicle helps surgeon to protect the pedicle during harvesting and a negative Doppler should alert surgeon to consider other reconstructive options.

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International Session 1

Vasculaized flap to cover nasopharyngeal defects

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With the improvement of endoscopic instruments and development of binostrils 4-hands technique, endoscopic nasopharyngectomy can feasibility excise early recurrent nasopharyngeal cancer (rT1, rT2a) and selected advanced (rTb and rT3) diseases. The next challenge is to cover the defect to prevent osteoradionecrosis.

Nasoseptal flap is a reliable vascular flap based on the posterior septal artery (PSA) of the sphenopalatine artery. PSA divides into superior and inferior branches ether lateral (2/3) or medial (1/3) to the sphenoid ostium. The main stem or the superior branch can be 1mm as close as to the sphenoid ostium. So injury of the pedicle is possible in sphenoidotomy. Post radiation cases would increase the chance of flap failure. Lastly, tumor involvement of the sphenoid floor and rostrum would jeopardize the choice of using nasoseptal flap.

Inferior turbinate flap is an alternative vascular flap to cover the nasopharyngectomy defect. It is based on the posterior lateral nasal artery of the sphenopalatine artery. However, the size of the flap is not as large as nasoseptal flap. Inferior meatal mucosal wall and even part of the nasal floor mucosa can be used to enlarge the size of the flap.

Temporoparietal fascia flap based on the superficial temporal artery is another alternative vascular flap. Lateral scalp incision is necessary to harvest the flap. The flap passed medial to the zygomatic arch and pass through a pathway in the pterygoid region created by endoscopic medial maxillectomy and removal of posterior and lateral wall of maxilla. The flap can reach to the contralateral Fossa of Rosseumnullar of the nasopharynx. We would share a case of using temporoparietal fascial flap after failure of nasoseptal and inferior turbinate flap.

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Dr. Lee developed his special interests on rhinology, endoscopic skull base surgery in particular endoscopic nasopharyngectomy and surgery for sleep apnea. Dr. Lee had been to the New York Presbyterian Hospital in New York and the Hospital Professor Edmundo Vasconcelos Hospital in Brazil to learn rhinology and endoscopic skull base surgery. And he had been a visitor to the Medical College of Wisconsin in USA and Chung Gang Memorial Hospital in Taiwan to learn sleep apnea surgery. Dr. Lee collaborate with neurosurgeons in the Prince of Wales Hospital and developed the first centre which provides endoscopic anterior skull base surgery service in Hong Kong since 2007.
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