

Type II respiratory immunophlogosis: review of our case series in the light of the Clinical-Cytological-Grading (CGC)

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Abstract: In a recent scientific publication Gelardi and al. described the Clinical-Cytological-Grading as an additional score to be used in association with SNOT-22 et al NPS in the evaluation of patients with chronic sinusitis and nasal polyposis in order to identify those who are correctly eligible for biological therapy in clinical practice. In this paper, the authors review their series of patients with nasal polyposis treated with monoclonal antibodies in order to assess whether the prescription of the therapy was appropriate in the light of the GCC.

Keywords: Chronic Rhinosinosis, nasal polyps, monoclonal antibodies, mepolizumab, dupilumab, Clinical-Cytological-Grading.

1. INTRODUCTION

In a recent scientific publication Gelardi et al described the Clinical-Cytological-Grading as an additional score to be used in association with SNOT-22 et al NPS in the evaluation of patients with chronic sinusitis and nasal polyposis in order to identify those who are correctly eligible for biological therapy in clinical practice. According to Gelardi “ *CCG is a score based on both nasal cytology findings and comorbidities, including asthma, allergy and ASA hypersensitivity. For each variable, a score value was assigned: neutrophilic infiltrate was scored as 1, mast cell infiltrate was scored 1, eosinophilic infiltrate was scored 2 and eosinophilic + mast cell was scored 4; similarly, ASA hypersensitivity scored 1, asthma 2, allergy 2 and ASA sensitivity + asthma 3. The CCG was composed as the sum of these individual scores. CCG global score is classified as low-grade (score 1-3), medium-grade (4-6) and high-grade (≥ 7).* “ (1)(2)(3)(4)(5)(6)(7)(8)(9)(10)(11).

In this paper, the authors review their series of patients with nasal polyposis treated with monoclonal antibodies in order to assess whether the prescription of the therapy was appropriate in the light of the GCC.

2. PATIENTS AND METHODS

As reported in our previous work, From June 2020 to February 2022, 20 patients suffering from nasal polyposis underwent surgery at our Operating Unit and were enrolled in a study to evaluate the efficacy of biological therapy. The minimum follow-up time required for inclusion in the study was 12 months. Within one month of surgery, patients began biological therapy. Twelve patients, all of whom also had bronchial asthma, undertook therapy with mepolizumab. Eight patients, of whom only three also affected by bronchial asthma, undertook therapy with dupilumab.(12)(13)(14)(15)(16)(17)(18)(19)(20)(21)

All patients were screened for endoscopic objectivity classified according to Nasal Polip Score and patient-reported symptoms classified according to SNOT 22 (Sino Nasal Outcome Test) immediately before surgery, immediately after

surgery and before the start of biological therapy, 6 months and 12 months from the beginning of biological therapy.(22)(23)(24)(25)(26)(27)(28)(29)(30)(31)(32)(33)(34)(35)(36)

In the present work the patients were re-evaluated in the light of the GCC found preoperatively in order to establish the correctness of the prescription of biological therapy.

3. OBSERVATION AND RESULTS

In the group of patients undergoing Dupilumab therapy, 5 out of 8 had a CCG score that could be classified as medium-grade (4-6) while 3 out of 8 were in high-grade (> 7). In the group of patients receiving mepolizumab therapy 8 out of 12 were in the high-grade and 4 out of 12 in the medium grade. This significant difference in initial severity based on the GCC is due to the fact that currently Italian legislation allows the prescription of Mepolizumab only for patients suffering from bronchial asthma while direct prescription for nasal polyposis is not yet allowed for which patients treated with Mepolizumab were necessarily severe asthmatic patients with CRSwNP co-morbidities in whom the prescription of the biological drug was carried out by the allergist or pulmonologist specialist and who were followed in our operating unit regarding the post-operative course in the first year after surgery for nasal polyposis.

The results obtained at 6 and 12 months of treatment were excellent both in patients treated with Dupilumab and in those treated with Mepolizumab; there were no substantial differences in the results obtained between high-grade and medium-grade CCG patients.

4. CONCLUSIONS

We believe the GCC is extremely important in identifying patients eligible for biological therapy.

In our case series, the review carried out did not find anomalies or excessive prescriptions, probably because our selection is generally very careful and we limit the prescription of biological drugs only to patients with serious risk of relapse or relapse that has already occurred several times. We routinely carry out nasal cytology in preoperative patients with nasal polyposis, as well as carry out allergological and pneumological examinations and investigate the presence of hypersensitivity to acetylsalicylic acid, so the introduction of CCG does not involve any addition to our normal preoperative habits.

In the very near future, other biological drugs will be authorized for the treatment of nasal polyposis and this type of therapy will become commonly used. The cost of these therapies already poses today and will pose even more in the future a series of pharmacoeconomic problems, for which the fact of having an additional evaluation score that allows to correctly filter the insertion of patients in biological therapy avoiding cases of over-treatment, undoubtedly represents a very important advantage in our clinical practice.

REFERENCES

- [1] Gelardi M. et al – Chronic rhinosinusitis with nasal polyps: how to identify eligible patients for biologics in clinical practice – *Acta Otorhinolaryngologica Italica*, 2022;42;75-81
- [2] Ciprandi G, Gelardi M. Chronic rhinosinusitis with nasal polyposis: the role of personalized and integrated medicine. *Monaldi Arch Chest Dis*. 2021; 91DOI
- [3] Gelardi M, Iannuzzi L, De Giosa M. Non-surgical management of chronic rhinosinusitis with nasal polyps based on clinical cytological grading: a precision medicine-based approach. *Acta Otorhinolaryngol Ital*. 2017; 37:38-45. DOI
- [4] Gelardi M, Cassano M, Ciprandi G. The clinical relevance of the clinical cytological grading in patients with chronic rhinosinusitis with nasal polyps. *J Allergy Clin Immunol*. 2020; 146:462-463. DOI
- [5] Gelardi M, Piccininni K, Quaranta N. Olfactory dysfunction in patients with chronic rhinosinusitis with nasal polyps is associated with clinical-cytological grading severity. *Acta Otorhinolaryngol Ital*. 2019; 39:329-335. DOI
- [6] Gelardi M, Iannuzzi L, Quaranta N. Nasal cytology: practical aspects and clinical relevance. *Clin Exp Allergy*. 2016; 46:785-792. DOI
- [7] Fokkens WJ, Lund VJ, Hopkins C. European position paper on rhinosinusitis and nasal polyps 2020. *Rhinology*. 2020; 59:1-464. DOI

- [8] Orlandi RR, Kingdom TT, Hwang PH. International consensus statement on allergy and rhinology: rhinosinusitis. *Int Forum Allergy Rhinol.* 2016; 6:S22-209. DOI
- [9] Bachert C, Zhang L, Gevaert P. Current and future treatment options for adult chronic rhinosinusitis: focus on nasal polyposis. *J Allergy Clin Immunol.* 2015; 136:1431-1440. DOI
- [10] DeConde AS, Mace JC, Levy JM. Prevalence of polyp recurrence after endoscopic sinus surgery for chronic rhinosinusitis with nasal polyps. *Laryngoscope.* 2017; 127:550-555. DOI
- [11] Fokkens WJ, Lund V, Bachert C. EUFOREA consensus on biologics for CRSwNP with or without asthma. *Allergy.* 2019; 4:2312-2319. DOI
- [12] Hoy SM. Dupilumab: a review in chronic rhinosinusitis with nasal polyps. *Drugs.* 2020; 80:711-717.
- [13] Gevaert P, Calus L, Van Zele T. Omalizumab is effective in allergic and nonallergic patients with nasal polyps and asthma. *J Allergy Clin Immunol.* 2013; 131:110-116. DOI
- [14] Hopkins C, Gillett S, Slack R. Psychometric validity of the 22-item sinonasal outcome test. *Clin Otolaryngol.* 2009; 34:447-454. DOI
- [15] Asprea F. , Galletti B. , Emanuele A. , Fera G. . Immunità cellulare e poliposi nasale – *La Nuova Clinica Otorinolaringoiatria*,XLV,83,1993.
- [16] Detoraki A. et al. Mepolizumab improves sino-nasal symptoms and asthma control in severe eosinophilic asthma patients with chronic rhinosinusitis and nasal polyps: a 12 month real-life study – *Ther. Adv Respir. Dis.*, 2021, vol 15: 1-11 DOI: 10.1177/17534666211009398
- [17] Caparra A. , Asprea F. Poliposi etmoide-nasale: quale allergia? - *Rivista Italiana di Medicina e Chirurgia*,anno II, vol I, 1996.
- [18] Han JK, Bachert C, Fokkens W, Desrosiers M, Wagenmann M, Lee SE, Smith SG, Martin N, Mayer B, Yancey SW, Sousa AR, Chan R, Hopkins C; SYNAPSE study investigators. Mepolizumab for chronic rhinosinusitis with nasal polyps (SYNAPSE): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Respir Med.* 2021 Oct;9(10):1141-1153. doi: 10.1016/S2213-2600(21)00097-7. Epub 2021 Apr 16. PMID: 33872587.
- [19] Bachert C, Sousa AR, Lund VJ, Scadding GK, Gevaert P, Nasser S, Durham SR, Cornet ME, Kariyawasam HH, Gilbert J, Austin D, Maxwell AC, Marshall RP, Fokkens WJ. Reduced need for surgery in severe nasal polyposis with mepolizumab: Randomized trial. *J Allergy Clin Immunol.* 2017 Oct;140(4):1024-1031.e14. doi: 10.1016/j.jaci.2017.05.044. Epub 2017 Jul 4. PMID: 28687232.
- [20] Brusselle GG, Gevaert P. Mepolizumab for chronic rhinosinusitis with nasal polyps. *Lancet Respir Med.* 2021 Oct;9(10):1081-1082. doi: 10.1016/S2213-2600(21)00133-8. Epub 2021 Apr 16. PMID: 33872589.
- [21] Wu Q, Zhang Y, Kong W, Wang X, Yuan L, Zheng R, Qiu H, Huang X, Yang Q. Which Is the Best Biologic for Nasal Polyps: Dupilumab, Omalizumab, or Mepolizumab? A Network Meta-Analysis. *Int Arch Allergy Immunol.* 2021 Oct 4:1-10. doi: 10.1159/000519228. Epub ahead of print. PMID: 34607329.
- [22] Gevaert P, Van Bruaene N, Cattaert T, Van Steen K, Van Zele T, Acke F, De Ruyck N, Blomme K, Sousa AR, Marshall RP, Bachert C. Mepolizumab, a humanized anti-IL-5 mAb, as a treatment option for severe nasal polyposis. *J Allergy Clin Immunol.* 2011 Nov;128(5):989-95.e1-8. doi: 10.1016/j.jaci.2011.07.056. Epub 2011 Sep 28. PMID: 21958585.
- [23] Bachert C, Zhang N, Cavaliere C, Weiping W, Gevaert E, Krysko O. Biologics for chronic rhinosinusitis with nasal polyps. *J Allergy Clin Immunol.* 2020 Mar;145(3):725-739. doi: 10.1016/j.jaci.2020.01.020. PMID: 32145872.
- [24] Harvey ES, Langton D, Katelaris C, Stevens S, Farah CS, Gillman A, Harrington J, Hew M, Kritikos V, Radhakrishna N, Bardin P, Peters M, Reynolds PN, Upham JW, Baraket M, Bowler S, Bowden J, Chien J, Chung LP, Grainge C, Jenkins C, Katsoulotos GP, Lee J, McDonald VM, Reddel HK, Rimmer J, Wark PAB, Gibson PG. Mepolizumab effectiveness and identification of super-responders in severe asthma. *Eur Respir J.* 2020 May 21;55(5):1902420. doi: 10.1183/13993003.02420-2019. PMID: 32139455.

- [25] Patel GB, Peters AT. The Role of Biologics in Chronic Rhinosinusitis With Nasal Polyps. *Ear Nose Throat J*. 2021 Jan;100(1):44-47. doi: 10.1177/0145561320964653. Epub 2020 Oct 9. PMID: 33035132; PMCID: PMC7980424.
- [26] Bachert C, Han JK, Desrosiers M, Hellings PW, Amin N, Lee SE, Mullol J, Greos LS, Bosso JV, Laidlaw TM, Cervin AU, Maspero JF, Hopkins C, Olze H, Canonica GW, Paggiaro P, Cho SH, Fokkens WJ, Fujieda S, Zhang M, Lu X, Fan C, Draikiwicz S, Kamat SA, Khan A, Pirozzi G, Patel N, Graham NMH, Ruddy M, Staudinger H, Weinreich D, Stahl N, Yancopoulos GD, Mannent LP. Efficacy and safety of dupilumab in patients with severe chronic rhinosinusitis with nasal polyps (LIBERTY NP SINUS-24 and LIBERTY NP SINUS-52): results from two multicentre, randomised, double-blind, placebo-controlled, parallel-group phase 3 trials. *Lancet*. 2019 Nov 2;394(10209):1638-1650. doi: 10.1016/S0140-6736(19)31881-1. Epub 2019 Sep 19. Erratum in: *Lancet*. 2019 Nov 2;394(10209):1618. PMID: 31543428.
- [27] Hoy SM. Dupilumab: A Review in Chronic Rhinosinusitis with Nasal Polyps. *Drugs*. 2020 May;80(7):711-717. doi: 10.1007/s40265-020-01298-9. PMID: 32240527.
- [28] Boyle JV, Lam K, Han JK. Dupilumab in the treatment of chronic rhinosinusitis with nasal polyposis. *Immunotherapy*. 2020 Feb;12(2):111-121. doi: 10.2217/imt-2019-0191. Epub 2020 Feb 20. PMID: 32075470.
- [29] Harb H, Chatila TA. Mechanisms of Dupilumab. *Clin Exp Allergy*. 2020 Jan;50(1):5-14. doi: 10.1111/cea.13491. Epub 2019 Sep 30. PMID: 31505066; PMCID: PMC6930967.
- [30] Jonstam K, Swanson BN, Mannent LP, Cardell LO, Tian N, Wang Y, Zhang D, Fan C, Holtappels G, Hamilton JD, Grabher A, Graham NMH, Pirozzi G, Bachert C. Dupilumab reduces local type 2 pro-inflammatory biomarkers in chronic rhinosinusitis with nasal polyposis. *Allergy*. 2019 Apr;74(4):743-752. doi: 10.1111/all.13685. Epub 2019 Jan 21. PMID: 30488542; PMCID: PMC6590149.
- [31] Fujieda S, Matsune S, Takeno S, Asako M, Takeuchi M, Fujita H, Takahashi Y, Amin N, Deniz Y, Rowe P, Mannent L. The Effect of Dupilumab on Intractable Chronic Rhinosinusitis with Nasal Polyps in Japan. *Laryngoscope*. 2021 Jun;131(6):E1770-E1777. doi: 10.1002/lary.29230. Epub 2020 Nov 23. PMID: 33226139; PMCID: PMC8247406.
- [32] Bachert C, Mannent L, Naclerio RM, Mullol J, Ferguson BJ, Gevaert P, Hellings P, Jiao L, Wang L, Evans RR, Pirozzi G, Graham NM, Swanson B, Hamilton JD, Radin A, Gandhi NA, Stahl N, Yancopoulos GD, Sutherland ER. Effect of Subcutaneous Dupilumab on Nasal Polyp Burden in Patients With Chronic Sinusitis and Nasal Polyposis: A Randomized Clinical Trial. *JAMA*. 2016 Feb 2;315(5):469-79. doi: 10.1001/jama.2015.19330. PMID: 26836729.
- [33] Fujieda S, Matsune S, Takeno S, Ohta N, Asako M, Bachert C, Inoue T, Takahashi Y, Fujita H, Deniz Y, Rowe P, Ortiz B, Li Y, Mannent LP. Dupilumab efficacy in chronic rhinosinusitis with nasal polyps from SINUS-52 is unaffected by eosinophilic status. *Allergy*. 2022 Jan;77(1):186-196. doi: 10.1111/all.14906. Epub 2021 Jun 4. PMID: 33993501.
- [34] Fujieda S, Matsune S, Takeno S, Ohta N, Asako M, Bachert C, Inoue T, Takahashi Y, Fujita H, Deniz Y, Rowe P, Ortiz B, Li Y, Mannent LP. Dupilumab efficacy in chronic rhinosinusitis with nasal polyps from SINUS-52 is unaffected by eosinophilic status. *Allergy*. 2022 Jan;77(1):186-196. doi: 10.1111/all.14906. Epub 2021 Jun 4. PMID: 33993501.
- [35] Lipworth B, Chan R, Kuo CR. Dupilumab for nasal polyposis. *Lancet*. 2020 Jul 25;396(10246):233. doi: 10.1016/S0140-6736(20)30562-6. PMID: 32711789.
- [36] Gayatri B Patel. Anju T. Peters – Tehe Role of Biologics in Chronic Rhinosinusitis with nasal polyps – *Ear Nose Throat J* 2021 January;100(1)44-47