overexpression of transforming growth factor β (TGF-β), which has a recognized capacity to promote tissue fibrosis.

IgG4-RD includes different entities that affect one or more organs synchronously or metachronously,[3] traditionally defined with their own nomenclature[4] as fibrosing thyroiditis (Riedel's thyroiditis), retroperitoneal fibrosis (Ormond's disease), autoimmune pancreatitis, and Mikulicz's disease, etc. Clinical suspicion is essential for diagnosis, as the initial clinical picture can be nonspecific and heterogeneous, and the patient may be referred to many different consultants, delaying the diagnosis that will finally be reached by combining clinical criteria and laboratory and histological findings.[5] The difficulty increases if we take into account that 16% of patients show spuriously normal IgG4 levels,[6] and that raised IgE[7] and peripheral eosinophilia may also be encountered in up to 25%.[8] Airway, interstitial, pleural effusion, or mediastinal lung involvement[9,10] occurs in 14% of cases but involvement of the pancreas, lacrimal and salivary glands, and kidney are more common. It is important to consider that IgG4-RD may also be associated with other autoimmune diseases and malignancies,[11] and some cases have resolved spontaneously.[12] In the differential diagnosis of lung involvement, we must consider cancer, infections, and interstitial diseases. Our patient's chest CT scan suggested lepidic adenocarcinoma, due to findings of peribronchovascular consolidations and multiple bilateral pulmonary nodules with right paratracheal and left supraclavicular lymphadenopathies. Finally, the IgG4 titer and pathology study were inconclusive.

Although IgG4-RD has not yet been described in association with thromboembolic disease, it has been associated with vascular inflammatory phenomena of the aorta and peripheral arteries.[13] We believe, therefore, that there is an interesting possibility that this disease predisposes to vascular damage or induces a hypercoagulable state that would warrant special attention in the follow-up of patients and justify an update of the recommendations for thromboembolic prophylaxis.

References

1. Hamano H, Kawa S, Horiuchi A, Unno H, Furuya N, Akamatsu T, et al. High serum IgG4 concentrations in patients with sclerosing pancreatitis. N Engl J Med. 2001;344:732–8.
2. Yount WJ, Dorner MM, Kunkel HG, Kabat EA. Studies on human antibodies VI. Selective variations in subgroup composition and genetic markers. J Exp Med. 1968;127:633–46.
3. Pieringer H, Parzer I, Wöhrer A, Reis P, Oppl B, Zwerina J. IgG4-related disease: an orphan disease with many faces. Orphanet J Rare Dis. 2014;9:110.
4. Stone JH, Khosroshahi A, Deshpande V, Chan JK, Heathcote JG, Aalberse R, et al. Recommendations for the nomenclature of IgG4-related disease and its individual organ system manifestations. Arthritis Rheum. 2012;64:3061–7.
5. Umehara H, Okazaki K, Masaki Y, Kawano M, Yamamoto M, Saeki T, et al. Comprehensive diagnostic criteria for IgG4-related disease (IgG4-RD), 2011. Mod Rheumatol. 2012;22:21–30.
6. Khosroshahi A, Cheryk LA, Carruthers MN, Edwards JA, Bloch DB, Stone JH. Brief report: spuriously low serum IgG4 concentrations caused by the prozone phenomenon in patients with IgG4-related disease. Arthritis Rheumatol. 2014;66:213–7.
7. Della Torre E, Mattoo H, Mahajan VS, Carruthers M, Pillai S, Stone JH. Prevalence of atopy, eosinophilia, and IgE elevation in IgG4-related disease. Allergy. 2014;69:269–72.
8. Khosroshahi A, Deshpande V, Stone JH. The clinical and pathological features of IgG(4)-related disease. Curr Rheumatol Rep. 2011;13:473–81.
9. Inoue D, Zen Y, Abo H, Gabata T, Demachi H, Kobayashi T, et al. Immunoglobulin G4-related lung disease: CT findings with pathologic correlations. Radiology. 2009;251:260–70.
10. Ryu JH, Sekiguchi H, Yi ES. Pulmonary manifestations of immunoglobulin G4-related sclerosing disease. Eur Respir J. 2012;39:180–6.
11. Ebbo M, Grados A, Bernit E, Vély F, Boucraut J, Harlé JR, et al. Pathologies associated with serum IgG4 elevation. Int J Rheumatol. 2012;2012:602809.
12. Baltaxe E, Shulimzona T, Lieberman S, Rozenman J, Perelman M, Segel MJ. Enfermedad pulmonar relacionada con IgG4 – Tres casos no tratados con resultado benigno. Arch Bronconeumol. 2016;52:e1–52.
13. Kasashima S, Kawashima A, Endo M, Matsumoto Y, Kasashima F, Zen Y, et al. A clinicopathologic study of immunoglobulin G4-related disease of the femoral and popliteal arteries in the spectrum of immunoglobulin G4-related periarteritis. J Vasc Surg. 2013;57:816–22.

Dionis Fernandez-García,[a] Montserrat León-Fábregas,[b,*] Nuria Mancheño-Franch,[b] Véronique Benavent-Corai[b]

[a] *Servicio de Neumología, Hospital Universitari i Politècnic, Valencia, Spain*
[b] *Servicio de Anatomía Patológica, Hospital Universitari i Politècnic, Valencia, Spain*

* Corresponding author.
E-mail address: mont1151@separ.es (M. León-Fábregas).

1579-2129/

Combination Therapy in Patients with Acute Respiratory Failure: High-Flow Nasal Cannula and Non-Invasive Mechanical Ventilation☆

Terapia combinada en pacientes con insuficiencia respiratoria aguda: alto flujo por cánula nasal y ventilación mecánica no invasiva

To the Editor,

Non-invasive mechanical ventilation (NIMV) is a first-line the treatment in the management of patients with acute and chronic exacerbated respiratory failure.[1] Protocols and clinical guidelines recommend initial continual use until the patient's respiratory failure has stabilized, after which rest periods can be introduced to give the patient the opportunity to chat, get washed, eat, and give the skin a break from the pressure of the mask.[2] During these periods, the patient receives oxygen therapy, usually by nasal prongs or a Venturi mask, regulating the flow of oxygen/FiO_2 to maintain saturations of 88%–92%.[3] In more severe or unstable patients, these rest periods are accompanied by significant dyspnea or desaturation that need to be corrected with high FiO_2 levels of over 50%. These patients are usually reconnected to the respirator, depriving them of their periods of rest from NIMV. We report the case of a patient with acute respiratory failure who used high-flow nasal cannula (HFNC) as an alternative therapy during the periods of disconnection from NIMV.

This was an 83-year-old woman, with a diagnosis of hypoventilation-obesity syndrome, receiving night-time NIMV. She had a giant umbilical hernia that caused significant ventilatory compromise. She attended the emergency room due to dyspnea and a low level of consciousness, blood pressure: 158/86 mmHg, heart rate: 86 bpm; breathing rate: 32 breaths/min; $SatO_2$ 86%, with O_2 at 6 bpm and a Glasgow score of 10. Physical examination was significant for peripheral cyanosis, tachypnea, and abdominal breathing. Pulmonary auscultation revealed bilateral crackles and rhonchi. Clinical laboratory tests were significant for BNP 241 mg/dl and

☆ Please cite this article as: Segovia B, Velasco D, Jaureguizar Oriol A, Díaz Lobato S. Terapia combinada en pacientes con insuficiencia respiratoria aguda: alto flujo por cánula nasal y ventilación mecánica no invasiva. Arch Bronconeumol. 2019;55:166–167.

leukocytes: 10 400 (neutrophils: 70.6%). PCR for influenza type A-H1 subtype was positive. Arterial blood gases showed a pH of 7.07; pO_2: 38 mmHg; pCO_2: 107 mmHg; HCO_3: 31 mg/dl. Chest X-ray revealed right basal opacity with blunting of the left costophrenic angle. The principal diagnosis was acute respiratory failure with severe respiratory acidosis due to viral pneumonia caused by type A-H1 influenza. NIMV began with a V60 respirator in ST mode, regulated with IPAP 21 cm H_2O, EPAP 10 cm H_2O, and a back-up breath rate of 16 breaths/min. Clinical assessment carried out at 1 h showed an improved level of consciousness (Glasgow 14), respiration (25 breaths/min) and arterial blood gases (pH: 7.18 mmHg; pCO_2: 82 mmHg; pO_2: 65 mmHg; HCO_3: 30 mg/dl; FiO_2: 35%; alveolar arterial O_2 gradient: 64.5). Arterial blood gas at 6 h showed pH: 7.33 (2) 78 mmHg; pCO_2: 50 mmHg; HCO_3: 26.4; FiO_2: 35%; alveolar arterial O_2 gradient: 91.5. The patient was admitted to the respiratory observation area, and prescribed NIMV in shifts. During the first attempt at disconnection from NIMV using a Venturi mask at 35%, the patient developed significant work of breathing, respiratory rate 40 breaths/min, and arterial O_2 saturation (SpO_2) 70%, so we decided to use HFNC at 60 l/min with FiO_2 of 50%. The patient improved and recovered the level of comfort she had experienced with NIMV; her respiration rate normalized and SpO_2 stabilized at 93%. The patient continued to alternate between NIMV and HFNC during hospital admission until discharge 8 days later. Arterial blood gases at discharge were pH 7.45, pCO_2 42 mmHg, pO_2 57 mmHg, and HCO_3 29.2 mg/dl. Chest X-ray showed that the radiological infiltrate had disappeared. The patient continued to receive domiciliary NIMV at night and during the day after eating, as she had done before admission.

This was a patient with acute respiratory failure and severe respiratory acidosis due to viral pneumonia caused by influenza A-H1, in which the use of HFNC allowed the patient to take NIMV rest periods without undue stress. HFNC has proven to be useful in the treatment of patients with hypoxemic respiratory failure, and evidence is emerging to suggest its usefulness in hypercapnic respiratory failure.[4] It has multiple mechanisms of action, of which the most important are its ability to increase alveolar recruitment, improve the ventilatory pattern, generate a positive expiratory pressure, and flush CO_2 from the dead space.[5] By supplying the gas at a temperature of 37 °C and 100% humidity, HFNC is better tolerated and more comfortable for the patient.[6] Numerous studies have demonstrated a significant reduction in respiratory rate, heart rate, dyspnea score, supraclavicular and thoracoabdominal retraction, and asynchrony, and a significant improvement in SpO_2 in patients with acute hypoxemic respiratory failure treated with HFNC.[7] In COPD patients with hypercapnia, HFNC improves the effectiveness of breathing, reduces pCO_2, work of breathing, and rapid, shallow breathing index, as an indicator of respiratory work load.[8]

There are few publications on the outcomes of combined therapy with NFNC and NIMV. Frat et al.[9] published a prospective observational study in which they alternated the use of NFNC and NIMV in subjects with acute hypoxemic respiratory failure, the majority of which met criteria for ARDS. Compared with conventional oxygen therapy, the use of HFNC improved oxygenation levels and symptoms of respiratory distress. Despite a lower impact on oxygenation compared with NIMV, HFNC was better tolerated. The study concluded that this technique can be used as a bridge between NIMV sessions. Spoletini et al.[10] subsequently published a review of the mechanisms of action and the clinical implications of HFNC. Among the potential clinical applications, they highlighted its use during NIMV rest periods, thanks to the physiological and subjective benefits, and its advantages over conventional oxygen therapy.

HFNC and NIMV may be complementary techniques in the management of patients with acute respiratory failure. The combined use of NIMV and HFNC offers advantages over conventional NIMV oxygen therapy in more severe and unstable cases, as was the case in our patient. Studies are needed to address the role of NIMV-HFNC combination therapy in patients with acute respiratory failure.

References

1. Esquinas AM, Benhamou MO, Glossop AJ, Mina B. Noninvasive mechanical ventilation in acute ventilatory failure: rationale and current applications. Sleep Med Clin. 2017;12:597–606.
2. Rochwerg B, Brochard L, Elliott MW, Hess D, Hill NS, Nava S, et al. Official ERS/ATS clinical practice guidelines: noninvasive ventilation for acute respiratory failure. Eur Respir J. 2017;50:1602426.
3. Davidson AC, Banham S, Elliott M, Kennedy D, Gelder C, Glossop A, et al. BTS/ICS guideline for the ventilatory management of acute hypercapnic respiratory failure in adults. Thorax. 2016;71 Suppl.:ii1–35.
4. Díaz Lobato S, Mayoralas Alises S. New approaches to the treatment of respiratory failure: high flow therapy. Med Clin (Barc). 2016;147:397–8.
5. Mauri T, Turrini C, Eronia N, Grasselli G, Volta CA, Bellani G, et al. Physiologic effects of high-flow nasal cannula in acute hypoxemic respiratory failure. Am J Respir Crit Care Med. 2017;195:1207–15.
6. Roca O, Hernández G, Díaz Lobato S, Carratalá JM, Gutierrez RM, Masclans JR, Spanish Multidisciplinary Group of High Flow Supportive Therapy in Adults (HiSpaFlow). Current evidence for the effectiveness of heated and humidified high flow nasal cannula supportive therapy in adult patients with respiratory failure. Crit Care. 2016;20:109.
7. Sztrymf B, Messika J, Bertrand F, Hurel D, Leon R, Dreyfuss D, et al. Beneficial effects of humidified high flow nasal oxygen in critical care patients: a prospective pilot study. Intensive Care Med. 2011;37:1780–6.
8. Bräunlich J, Köhler M, Wirtz H. Nasal highflow improves ventilation in patients with COPD. Int J Chron Obstruct Pulmon Dis. 2016;11:1077–85.
9. Frat JP, Brugiere B, Ragot S, Chatellier D, Veinstein A, Goudet V, et al. Sequential application of oxygen therapy via high-flow nasal cannula and noninvasive ventilation in acute respiratory failure: an observational pilot study. Respir Care. 2015;60:170–8.
10. Spoletini G, Alotaibi M, Blasi F, Hill NS. Heated humidified high-flow nasal oxygen in adults. Chest. 2015;148:253–61.

Bárbara Segovia,[a] Diurbis Velasco,[b] Ana Jaureguizar Oriol,[b] Salvador Díaz Lobato[b,*]

[a] *Sanatorio Colegiales, Universidad de Buenos Aires, Buenos Aires, Argentina*
[b] *Servicio de Neumología, Hospital Universitario Ramón y Cajal, Madrid, Spain*

* Corresponding author.
E-mail address: sdiazlobato@gmail.com (S. Díaz Lobato).

1579-2129/