Hyponatremia in COPD: A Little Known Complication

La hipo natr emia en la EPOC, una complicación poco conocida

To the Editor,

Chronic obstructive pulmonary disease (COPD) is a chronic inflammatory disease, and in some patients, extrapulmonary manifestations can worsen prognosis.¹ COPD patients often have other concomitant diseases, particularly cardiovascular conditions, and it has been postulated that COPD plays a significant role in the pathogenesis of these processes.²

Hyponatremia developing during hospitalization for a COPD exacerbation is relatively common, and is associated with a poorer clinical course.³ Low sodium in blood may be a sign of water retention due to other comorbidities, such as heart or kidney failure, drug treatments, adrenal insufficiency after withdrawal of corticosteroids, or syndrome of inappropriate ADH secretion (SIADH). Diseases that may present with SIADH include lung infections (pneumonia, pulmonary abscess, tuberculosis, aspergillosis), asthma, COPD, lung tumors, cystic fibrosis, and acute respiratory failure.⁴ Hypoxia is associated with ADH secretion,⁵ but hypercapnia is more commonly associated with this phenomenon.

Both in stable COPD and during exacerbations, hyponatremia, due to its prevalence, its impact on prognosis, and varying etiologies (which can coexist), is a challenge for the clinician and requires appropriate follow-up and treatment. Although the relationship between COPD and SIADH is often mentioned in the literature, we did not find any references to hyponatremia caused by SIADH in COPD (Medline and Pubmed searches, keywords: SIADH and COPD).

For this reason, we believe that our report of a patient with SIADH due to COPD is of interest and provides a good illustration of certain aspects of the differential diagnosis and treatment.

Our patient was an 84-year-old man, active smoker, with a history of benign prostate hypertrophy and exacerbator phenotype COPD with emphysema, and very severe obstruction (FEV1 27%), receiving treatment with silodosin, omeprazole, and glycopyrronium/indacaterol. He presented with intense dyspnea and cough with greenish expectoration. The only finding of note on physical examination was the presence of disperse rhonchi in both hemithoraxes and the absence of edema or signs of fluid overload. O₂ saturation was 89% with home oxygen therapy at 21 per minute (lpm). Clinical laboratory tests showed microcytic anemia (hemoglobin 10 g/dl), plasma sodium 111 mEq/l (normal value [NV]: 135–155 mEq/l), plasma osmolality 229 mOsm/l (NV: 280–300), PCR 64 mg/l (NV: 0–5), normal creatinine levels, urinary sodium 76 mEq/l (NV: 54–150), and urine osmolality 273 mOsm/l

References
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The heterogeneous causes, in normal ranges of 138–142 mmol/L, may include SIADH, adrenal, or non-salt loss due to chronic kidney disease. The patient’s present sodium level of 124 mmol/L is consistent with hyponatremia, typically with a plasma osmolality that is lower than blood osmolality. Hyponatremia may present as a sign of various conditions, including SIADH, SIADH-like states, or other causes that may lead to decreased serum sodium levels.

The patient’s history of COPD exacerbation and smoking habits are relevant considerations. Hyponatremia in patients with COPD may be multifactorial, with underlying causes such as fluid retention, diuretic use, or chronic kidney disease. The patient’s recent exacerbation of COPD may have contributed to the hyponatremia, as COPD exacerbation can lead to increased fluid retention and diuresis.

In summary, the patient’s symptoms and laboratory results are consistent with hyponatremia, likely due to SIADH or a SIADH-like state. Further evaluation and treatment, including diuretic adjustment, hydration status, and underlying causes, are necessary to address the patient’s hyponatremia and manage their COPD exacerbation.


References


Response to Omalizumab in a Patient With Chronic Eosinophilic Pneumonia and Poor Response to Corticosteroids

Respuesta a omalizumab en paciente con neumonía eosinofila crónica y mala respuesta al tratamiento con corticoides

To the Editor,

We report the case of a 55-year-old woman, former smoker since September 2012 (18 pack-years), with a history of allergic rhinoconjunctivitis and bronchial asthma. No infiltrates were observed in a chest X-ray performed in 2012. Skin prick tests showed sensitization to cat dander and grass and olive pollen.

She was admitted in 2014 for an acute episode of dyspnea, breath sounds, and non-productive cough without fever. Chest X-ray revealed an alveolointerstitial pattern predominantly in the lung bases. Chest computed tomography showed bilateral patchy ground glass infiltrates. Bronchoscopy was performed with transbronchial biopsy and bronchoalveolar lavage; neutrophils: 11%; eosinophils: 85.9%; lymphocytes: 0.6%. Biopsy showed a histological pattern of pulmonary eosinophilia suggestive of chronic eosinophilic pneumonia (CEP), with a focal pattern typical of organizing pneumonia. Lung function tests highlighted a restrictive pattern with carbon monoxide diffusion changes: FVC 1830 – 59%; FEV$_1$ 1410 – 54% and FEV$_1$/FVC 77%; DLCO 32%; KCO 63%; TLC 61%; and RV 86%. All immunological tests were negative; IgE 493 UI/ml. In the 6-min walk test, initial saturation was 97%, distance walked 440 m, and final saturation 85%.

CEP was diagnosed, with no known occupational or environmental risks, although a relationship with the administration of anti-inflammatories (celecoxib) could not be ruled out. This drug was discontinued, and treatment began with corticosteroids, resulting in both clinical and radiological worsening.

Given the poor response to treatment with corticosteroids, a surgical biopsy was performed, and the pathology study reported squamous-like interstitial pneumonia with eosinophils, consistent with CEP. The patient was placed on the lung transplantation waiting list. Lung function tests prior to the introduction of omalizumab were: FVC 1430 – 47%; FEV$_1$ 1120 – 43%; FEV$_1$/FVC 78%; DLCO 24%; KCO 55%; TLC 44%; RV 81%.

In a review of the literature, 2 cases$^{1,2}$ of CEP with a favorable response to omalizumab were identified, so treatment began with this drug, producing clinical improvement and functional stabilization, so we decided to gradually withdraw the corticosteroids. Twenty-four months after starting omalizumab, the patient has shown a remarkable improvement in her symptoms without corticosteroids, confirming the reversal of her previous functional decline noted from the introduction of this drug (Fig. 1). The patient was taken off the lung transplantation waiting list when the adverse effects of steroid treatment had resolved. When mepolizumab came on the market, this therapeutic option was proposed to the patient, but she refused it in view of her good progress.

CEP is an idiopathic disease characterized by an abnormal accumulation of eosinophils in the interstitial and alveolar spaces. Standard treatment is systemic corticosteroids. Response is usually so rapid and favorable, that if no response is observed, alternative diagnoses must be considered.

Our patient presented a poor response to high-dose corticosteroids, so a surgical biopsy was performed, which confirmed the initial diagnosis. We identified 2 cases of CEP with response to omalizumab in the literature$^{1,2}$ involving patients with elevated IgE and poor response to corticosteroids (or a requirement for high doses). In both cases, treatment with omalizumab reversed deterioration, and produced improvements in lung function tests.

Omalizumab is a humanized anti-IgE antibody, usually indicated for the treatment of persistent allergic asthma. Numerous effects that go far beyond IgE immunomodulation have also been described.$^{3-11}$ Omalizumab reduces basophil Fc epsilon RI alpha receptor expression.$^{2,6}$ It also induces a decrease in triptase, Th2 cytokines (IL-4 and IL-13), and chemokines (IL-8 and RANTES), irrespective of IgE levels. Similarly, it reduces cytokine expression (IL-5, IL-10, and IL-13) in dendritic cells,$^{6,12}$ and interferes with their ability to activate CD4. It also reduces eosinophil numbers$^{8,9}$ in both sputum and lung tissue, monocytes,$^{8}$ fraction of expired nitric oxide (FENO),$^{9,10}$ and endothelin-1 concentrations in exhaled breath condensate.$^{10}$ Moreover, stimulation of IgE increases the deposit of collagen I, III, and IV, and fibronectin in the Erk1/2 MAPK

![Fig. 1. Functional progress of our patient. The arrow indicates the time of starting omalizumab.](attachment:image)

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