Dialysis-induced hypereosinophilia in the ICU

Cyrielle Desnos¹,² · Augusta D’Huy¹,² · Jean Simon Rech²,³ · Cédric Rafat⁴ · Aude Gibelin¹,²

Received: 21 July 2022 / Accepted: 10 October 2022 / Published online: 18 November 2022
© The Author(s) under exclusive licence to Italian Society of Nephrology 2022

The case
Herein we share our experience with a 70-year-old woman who was hospitalized in our intensive care unit (ICU) for SARS-CoV-2-related acute respiratory distress syndrome complicated by ventilator-acquired pneumonia, with septic shock and anuric acute kidney injury requiring continuous veno-venous hemodialysis (CVVHD). Standard of care for Covid pneumonia includes dexamethasone 6 mg per day, which we associated with ivermectine 15 mg monodose on Day 1 (D1) as a prevention for parasitosis under corticosteroids. Her eosinophil count was < 500/mm³ at ICU admission, thus she developed hypereosinophilia (> 1.5 × 10³/mm³) at Day 68, which increased to 6.7 × 10³/mm³ at Day 78.

The patient was treated with albendazole for 10 days as a test treatment in the hypothesis of a parasitic cause and a diagnostic work-up of hypereosinophilia was carried out: no evidence was found for hemopathy or cancer, vasculitis (negative autoimmune screening), drug hypersensitivity, viral infection (HSV 1/2, CMV, EBV, VZV, HHV-6, HHV-8, parvovirus B19 viral negatives PCRs), nor for parasitic infection (serology for toxocariasis, filariasis, anguillosis, trichinellosis and hydatidosis were all negative).

The onset of hypereosinophilia was observed 3 days after the first intermittent hemodialysis (IHD) session which replaced CVVHD. After each IHD session, hypereosinophilia worsened (Fig. 1), reaching a peak level of 6.7 × 10³/mm³ at Day 78.

The complete resolution of hyper-eosinophilia occurred as kidney function recovered, allowing for weaning from IHD and thereby adding further support to the hypothesis of dialysis membrane-related hypersensitivity.

Lessons for the clinical nephrologist

Eosinophilia is not a rare event in patients requiring hemodialysis, and has been described since the 70s [1, 2], either isolated or associated with minor symptoms such as abdominal pain or moderate hypotension during dialysis sessions. These clinical manifestations have been indiscriminately clustered as “reaction to dialyzer membrane materials” [3]. Some rare cases of major hypereosinophilia presenting as part of a so-called allergy to hemodialysis material have been reported in the last decades in the chronic dialysis setting [3, 4].

Multiple components of the extra corporeal circuit (dialysis membrane, catheters, dialysate, etc.) have been implicated in the occurrence of eosinophilia [5, 6]. Chapelet-Debout et al. recently reported 6 cases of major hypereosinophilia attributed to the tunneled central venous catheter [6], but in our case, the catheter was not tunneled and consisted in a classical percutaneous double lumen dialysis catheter used in intensive care units in emergency dialysis settings. The dialysate was also taken into consideration in our etiologic investigation, but in our
ICU we have a central water treatment system integrated into the dialysis loop, and the purified osmosis water is tested monthly. During our patient’s ICU stay, bacterial cultures were < 100 UFC/ml, and testing for endotoxins was < 0.25 UI/ml, as required. Moreover, at the time of our diagnosis, no other patient undergoing dialysis from this loop developed any adverse effects, including eosinophilia (approximately 40 patients were treated during the time interval of our patient’s stay). Yet, the onset of eosinophilia 3 days after implementation of IHD and 20 days after the patient was started on CVVHD pointed to the dialyzer membrane as the culprit since eosinophilia typically develops within a couple of days following exposure to the dialysis membrane.

In the era of modified cellulose or synthetic membranes, as used in our ICU, severe symptomatic allergic reactions are infrequent. Thus, in recent years, hypereosinophilia (> 1.10^9 G/L) has been reported in an estimated 5% of patients on chronic hemodialysis [5]. It is therefore important, in the case of hypereosinophilia in a patient undergoing dialysis, to have an exhaustive, step-by-step, etiological diagnostic approach before blaming the dialysis equipment (Fig. 2).

Treatment with ACE-inhibitors is the major known factor associated with hypereosinophilia in this setting [5], potentially due to enhanced bradykinin release during allergic episodes, but our patient never received any.

The pathophysiology of hypereosinophilia and allergic reaction related to the hemodialysis circuit is unclear, although cytokine release following eosinophil activation by the membrane components has been hypothesized [7]. Direct and alternative complement pathways might also be involved, with C3a and C5a fractions potentially participating in eosinophil activation [8]. In the setting of long-term hemodialysis patients, resolution of eosinophilia has been achieved through treatment with systemic corticosteroids (0.5–1 mg/kg) and/or changing the membrane [9]. In our case, immunosuppression induced by the prolonged ICU stay, the absence of vital organ damage and the gradual but consistent resolution of eosinophilia following dialysis weaning discouraged us from using corticosteroids.

Hypereosinophilia linked to dialyzer membrane should be taken into consideration when dealing with critically ill patients after all competing causes have been carefully ruled out.
Funding None.

Declarations

Conflict of interest The authors have no conflicts of interest.

Consent to publication The results presented in this paper have not been published previously in whole or part.

References

1. Agarwal R, Light RP (2011) Patterns and prognostic value of total and differential leukocyte count in chronic kidney disease. Clin J Am Soc Nephrol CJASN 6:1393–1399. https://doi.org/10.2215/CJN.10521110
2. Higuchi T, Yamazaki T, Ohnishi Y et al (2007) A case report of hemodialysis intolerance with eosinophilia. Ther Apher Dial Off Peer-Rev J Int Soc Apher Jpn Soc Apher Jpn Soc Dial Ther 11:70–73. https://doi.org/10.1111/j.1744-9987.2007.00457.x
3. Röckel A, Kline B, Herlet J et al (1989) Allergy to dialysis materials. Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc Eur Ren Assoc 4:646–652
4. Kanda E, Kida Y, Suzuki H et al (2004) Role of cytokines in anaphylactoid reaction with marked eosinophilia in a hemodialysis patient. Clin Exp Nephrol 8:384–387. https://doi.org/10.1007/s10157-004-0300-4
5. Hildebrand S, Corbett R, Duncan N, Ashby D (2016) Increased prevalence of eosinophilia in a hemodialysis population: longitudinal and case control studies. Hemodial Int Int Symp Home Hemodial 20:414–420. https://doi.org/10.1111/hdi.12395
6. Chapelet-Debout A, Couvel S, de Geyer DG et al (2021) Eosinophilia due to central venous catheter in hemodialysis patients. Kidney Int Rep 6:1189–1191. https://doi.org/10.1016/j.ekir.2020.12.033
7. Hertel J, Kimmel PL, Phillips TM, Bosch JP (1992) Eosinophilia and cellular cytokine responsiveness in hemodialysis patients. J Am Soc Nephrol JASN 3:1244–1252. https://doi.org/10.1681/ASN.198410043111403
8. Hakim RM, Breillatt J, Lazarus JM, Port FK (1984) Complement activation and hypersensitivity reactions to dialysis membranes. N Engl J Med 311:878–882. https://doi.org/10.1056/NEJM198410043111403
9. Mutsuyoshi Y, Hirai K, Morino J et al (2021) Idiopathic hypereosinophilic syndrome in hemodialysis patients: case reports. Medicine (Baltimore) 100:e25164. https://doi.org/10.1097/MD.0000000000025164

Publisher’s Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.