Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Human Pathology Reports 27 (2022) 300601

Contents lists available at ScienceDirect

Human Pathology Reports

journal homepage: www.journals.elsevier.com/human-pathology-reports

Case Report

Pulmonary hematoidin deposition in a case of severe COVID19 pneumonia

Nada Shaker [a], Justin P. Rosenheck [b], Bryan A. Whitson [c], Konstantin Shilo [a,*]

[a] Department of Pathology, The Ohio State University Wexner Medical Center, Columbus, OH, USA
[b] Division of Pulmonary, Critical Care & Sleep Medicine, The Ohio State University Wexner Medical Center, Columbus, OH, USA
[c] Division of Cardiac Surgery, The Ohio State University Wexner Medical Center, Columbus, OH, USA

ARTICLE INFO

Keywords:
Coronavirus disease 2019
Lung
Acute respiratory distress syndrome
Diffuse alveolar damage
Infarct
Lung transplantation
Hemosiderin
Hematoidin

ABSTRACT

A 59-year-old male with past medical history significant for hypertension, coronary artery disease, atrial fibrillation, hyperlipidemia, obesity, obstructive sleep apnea and deep vein thrombosis developed severe COVID19 pneumonia. His clinical course was noted for progressive respiratory failure that subsequently resulted in bilateral lung transplantation. Examination of the explanted lungs was notable for the presence of extensive grossly apparent bright yellow discolorations that histologically represented hematoidin deposits. The background lung was affected by diffuse alveolar damage, accompanied by infarcts and organizing thrombi. This case suggests that a combination of acute lung injury and thrombotic complications in severe COVID19 pneumonia can facilitate formation of pockets of anoxic environment leading to hematoidin deposition within lung tissue.

Introduction

A prototypical tissue injury in severe cases of COVID19 infection affecting lung is diffuse alveolar damage (DAD) [1–3]. The DAD as well as in situ thrombi can be seen in association with a variety of infectious agents however the virus associated coagulopathy appears to be an essential part of the disease pathogenesis and in patients with severe COVID19 can histologically manifests as large vessel thrombi and/or fibrin microthrombi with resultant ischemic complications [1,4,5]. While hematoidin deposits have been documented in a wide range of neoplastic and non-neoplastic conditions [6–11] to the best of our knowledge it has not been reported in the setting of COVID19 pneumonia. Here we report a case of severe progressive COVID19 pneumonia that showed prominent deposition of hematoidin in the explanted lungs.

Case presentation

A 59-year-old male never smoker with past medical history significant for hypertension, coronary artery disease, atrial fibrillation, hyperlipidemia, obesity (BMI 34.9), obstructive sleep apnea and deep vein thrombosis developed severe COVID19 pneumonia (Fig. 1A) for which he was treated with Azithromycin, Ceftriaxone, Dexamethasone and Tocilizumab. On day 25 since onset of symptoms, the patient was intubated for worsening hypoxia and ultimately cannulated for veno-venous extracorporeal membrane oxygenation (VV-ECMO). As a part of the pre-transplant evaluation, he was found to have a heterozygous Factor V Leiden mutation (F5 R506Q germline polymorphism). The patient underwent bilateral lung transplantation (day 58) followed by prolonged hospital course and inpatient rehabilitation. Gross examination of the explanted lungs was significant for bilateral consolidations and foci of brightly yellow discolorations (Figure 1B). Histological examination revealed diffuse alveolar damage (DAD), predominantly in proliferative and fibrosing phases, and organizing infarcts (Figure 1C) associated with hemosiderin and hematoidin deposition (Figure 1D). There were occasional organizing thrombi. The hematoidin deposits were seen at the interface of infarcted and viable lung parenchyma, largely within interstitium as well as within alveolar macrophages (Figure 1E). In contrast to the hemosiderin, hematoidin deposits did not change color on Prussian blue stain for iron (Figure 1F).

Discussion

This case documents a unique presentation of a severe COVID19 pneumonia with striking gross and light microscopic features of hematoidin deposition within affected lung parenchyma.

Hematoidin is a product of heme metabolism that is deposited in tissues under low oxygen tension in association with blood extravasation [12,13]. In contrast to hemosiderin, hematoidin is lacking iron and

Abbreviations: COVID19, Coronavirus disease 2019; DAD, diffuse alveolar damage.

* Corresponding author.
E-mail address: konstantin.shilo@osumc.edu (K. Shilo).

https://doi.org/10.1016/j.hpr.2022.300601
Received 27 December 2021; Received in revised form 8 February 2022; Accepted 8 February 2022
Available online 14 February 2022

therefore is not highlighted with conventional histochemical staining methods for iron. Under light microscopic examination it is seen as variable in shape crystals that may or may not yield birefringence under polarized light. The hematoidin deposits also vary in color from brightly yellow or golden to yellow-reddish colors. Hematoidin has been documented in a variety of conditions typically associated with chronic hemorrhage [6–8,10,14]. It has been reported in cytologic specimens of sputum and fine needle aspiration of necrotizing lung lesions; however, it is an unusual finding in cervicovaginal smears [6,15]. Hematoidin was also reported in patients with traumatic and spontaneous cerebral hemorrhages [8], acute gastrointestinal bleeding [7], and in the skin [10]. Alone with hemosiderin it has also been noted in pulmonary infarcts [11].

Due to dual blood supply of lung parenchyma from the pulmonary and bronchial arteries, lung infarcts are relatively rare, nevertheless they do occur in cases where there is significant compromise of either component or if both are compromised. While the observed heterozygous Factor V Leiden mutation increases thrombotic risk approximately 4- to 5-fold [16], the patient's protein C and antithrombin levels preceding lung transplant were within normal range, and therefore this genetic alteration may not have played a significant role in thrombotic complications in the lung. On the other hand, a high frequency of pulmonary arterial thrombosis and lung infarcts has been reported in fatal cases of COVID19 infection [5,17]. In the setting of COVID19 infection, it is likely that a combination of acute lung injury and thrombotic vasculopathy is responsible for propensity to pulmonary infarcts.

Conclusion

While in itself the hematoidin deposition is a non-specific phenomenon that can be seen in variety of conditions, it is a combination of acute lung injury and thrombotic microangiopathy in COVID19 pneumonia that is likely responsible for tissue hypoxia and as in this case can facilitate hematoidin formation in the vicinity of pulmonary infarcts.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

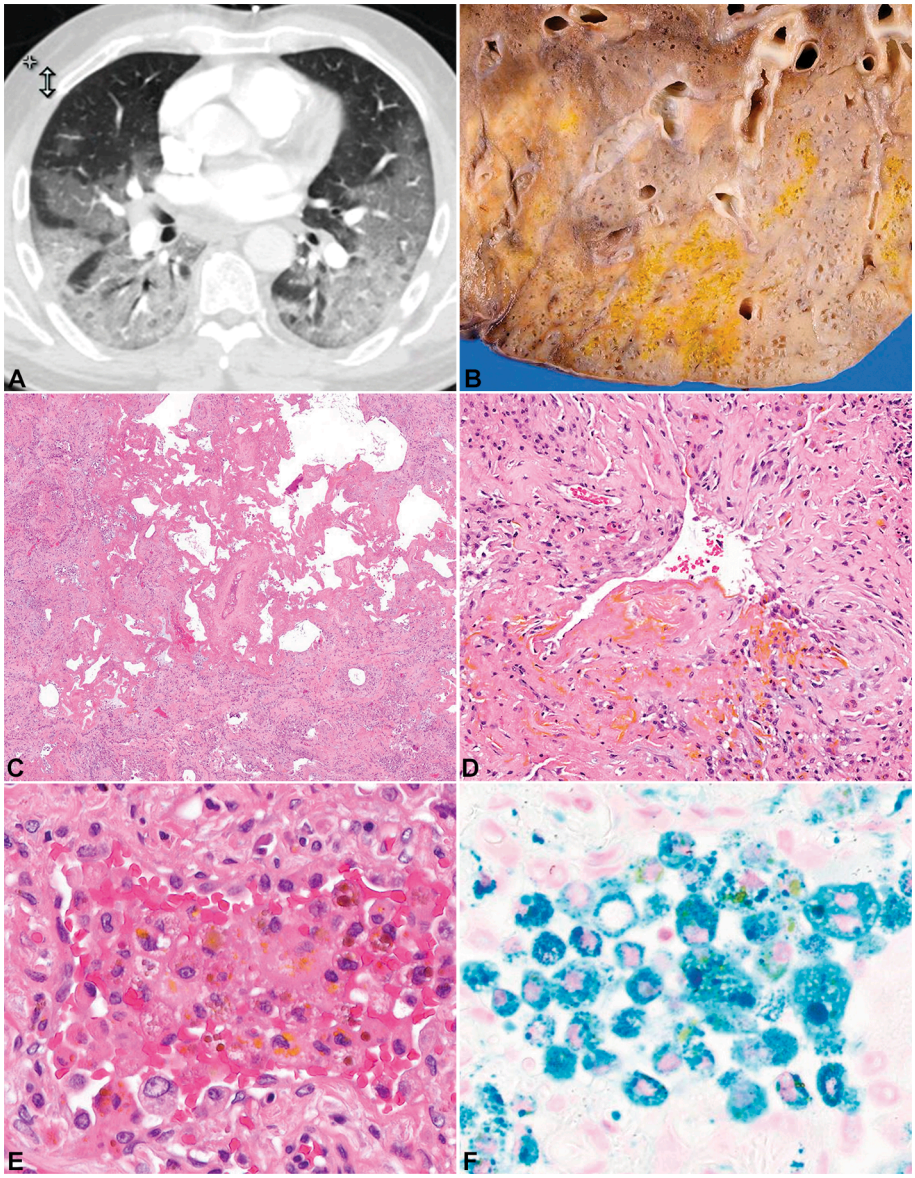

Fig. 1. Imaging and pathological findings. Computed tomography of the chest (A) shows bilateral diffuse groundglass with confluent consolidative opacities in the mid and lower lungs (day 16); (axial plane, lung window image). Gross examination of explanted lungs shows consolidated lung parenchyma with geographic areas of brightly yellow discolorations (B); gross examination following formalin fixation. Light microscopic examination shows area of lung infarct (C), streak-like brightly yellow deposits within area of interstitial organization (D) and granular brightly yellow deposits within alveolar macrophages (E); hematoxylin and eosin, original magnification ×20, ×100 and ×400, respectively. In contrast to hemosiderin (dark blue varying in size granules within macrophages) hematoidin deposits do not change color on Prussian blue stain for iron (F), original magnification ×400.

Patient consent

The patient signed a written consent to the writing of his case summary to be used for educational purposes in training at this facility and/or at local, regional, or national medical conferences. The patient also consented for the use of this summary in medical publications, including medical journals, textbooks, and electronic publications.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

Acknowledgements

The authors are thankful to Shawn Scally for excellent assistance in figures preparation.

References

[1] L.M. Buja, D.A. Wolf, B. Zhao, B. Akkanti, M. McDonald, L. Lelenwa, N. Reilly, G. Ottaviani, M.T. Elghetany, D.O. Trujillo, et al., The emerging spectrum of cardiopulmonary pathology of the coronavirus disease 2019 (COVID-19): report of 3 autopsies from Houston, Texas, and review of autopsy findings from other United States cities, Cardiovasc. Pathol. 48 (2020) 107233.

[2] S.K. Mohanty, A. Satapathy, M.M. Naidu, S. Mukhopadhyay, S. Sharma, L. M. Barton, E. Stroberg, E.J. Duval, D. Pradhan, A. Tzankov, et al., Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and coronavirus disease 19 (COVID-19) - anatomic pathology perspective on current knowledge, Diagn. Pathol. 15 (1) (2020) 103.

[3] K.E. Konopka, T. Nguyen, J.M. Jentzen, O. Rayes, C.J. Schmidt, A.M. Wilson, C. F. Farver, J.L. Myers, Diffuse alveolar damage (DAD) resulting from coronavirus disease 2019 infection is morphologically indistinguishable from other causes of DAD, Histopathology 77 (4) (2020) 570–578.

[4] J. Thachil, N. Tang, S. Gando, A. Falanga, M. Cattaneo, M. Levi, C. Clark, T. Iba, ISTH interim guidance on recognition and management of coagulopathy in COVID-19, J. Thrombosis Haemostasis: JTH 18 (5) (2020) 1023–1026.

[5] S. Elsoukkary, M. Mostyka, A. Dillard, D. Berman, L. Ma, A. Chadburn, R. Yantiss, J. Jessurun, S. Seshan, A. Borczuk, et al., Autopsy findings in 32 patients with COVID-19: a single-institution experience, Pathobiology 88 (1) (2021) 56–68.

[6] R. Martinez-Giron, H.C. van Woerden, L. Pantanowitz, Hematoidin crystals in sputum smears: cytopathology and clinical associations, Ann. Thoracic Med. 15 (3) (2020) 155–162.

[7] K. Hennrick, D. Yang, Hematoidin, Blood 124 (13) (2014) 2158.

[8] G. Strassmann, Formation of hemosiderin and hematoidin after traumatic and spontaneous cerebral hemorrhages, Arch. Pathol. 47 (3) (1949) 205–210.

[9] G. Capaldo, D.P. LeGolvan, J.E. Dramczyk, Hematoidin crystals in cervicovaginal smears. Review of 27 cases seen in one year, Acta Cytol. 27 (3) (1983) 237–240.

[10] A. Fernandez-Flores, Two new forms of hematoidin in the skin, J. Cutan. Pathol. 42 (12) (2015) 1026–1030.

[11] S.A. Yousem, The surgical pathology of pulmonary infarcts: diagnostic confusion with granulomatous disease, vasculitis, and neoplasia, Mod. Pathol. 22 (5) (2009) 679–685.

[12] M.L. Smith, J. Paul, P.I. Ohlsson, K. Hjortsberg, K.G. Paul, Heme-protein fission under nondenaturing conditions, Proc. Natl. Aacd. Sci. 88 (3) (1991) 882–886.

[13] D.S. Brenner, C.B. Drachenberg, J.C. Papadimitriou, Structural similarities between hematoidin crystals and asteroid bodies: evidence of lipid composition, Exp. Mol. Pathol. 70 (1) (2001) 37–42.

[14] H. Minassian, R. Schinella, J.C. Reilly, Crystalline bodies in cervical smears. Clinicocytologic correlation, Acta Cytol. 37 (2) (1993) 149–152.

[15] A. Thakur, H. Sarin, Hematoidin crystals in Pap smear: a revisit, Diag. Cytopathol. 48 (1) (2020) 92.

[16] J.L. Kujovich, Factor V Leiden thrombophilia, Genetics Med. 13 (1) (2011) 1–16.

[17] S.F. Lax, K. Skok, P. Zechner, H.H. Kessler, N. Kaufmann, C. Koelblinger, K. Vander, U. Bargfrieder, M. Trauner, Pulmonary arterial thrombosis in COVID-19 with fatal outcome: results from a prospective, single-center, clinicopathologic case series, Ann. Intern. Med. 173 (5) (2020) 350–361.