Hemorrhagic complications in COVID-19: three women with pectoral hematoma and a review

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ABSTRACT

Patients hospitalized with COVID-19 pneumonia are at risk for thrombotic complications. At the same time, they need respiratory support, and they frequently require nursing in a prone position. From March to May 2020, 57 patients with acute respiratory distress syndrome were admitted to our departments. Our therapeutic protocol included anticoagulant treatment and prone positioning. We have treated three obese women affected by severe pneumonia and pectoral hematoma with post-hemorrhagic anemia. We have already described two of these cases in our previous publication; in this new article, we describe a third similar case and review clinical reports from 2020 to 2022 about hemorrhagic complications during COVID-19. Reports confirm that pectoral hematomas and bleeding in unusual sites are a complication of COVID-19. Pectoral hematomas are likely to be related to COVID-19 severity, heparin dosage, and traumatism due to cough and pronosupination.

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Introduction

There is evidence that patients hospitalized with COVID-19 pneumonia have hyperactive coagulation status, and they are at risk for thrombotic complications, including deep vein thrombosis, pulmonary embolism, ischemic stroke, and myocardial infarction. Thrombosis is associated with critical illness and all-cause mortality, and one of the main causes of death is pulmonary embolism.[1-7] At the same time, these patients suffer from hypoxia; therefore, they need respiratory support with high-flow oxygen via face mask and/or non-invasive positive pressure ventilation (NIPPV).[8]

Frequently, patients suffering from acute respiratory distress syndrome (ARDS) require nursing in a prone position. In fact, this strategy takes advantage of different pathophysiological mechanisms: a better expansion of the posterior lung fields, optimization of the ventilation-perfusion ratio due to fluids' redistribution, improvement of ventilation of the dorsal lung fields and reduction of the amount of parenchyma compressed by the heart muscle.[9-13]

In 2020, from March 19 to May 30, the Urgency Medicine ward of the Emergency Department and a large section of the Internal Medicine department were transformed into COVID wards. During this period, 75 patients with SARS-CoV-2 were admitted: 57 had pneumonia with ARDS.

We adopted a therapeutic protocol shared with the Infectious diseases and Respiratory departments,[14] which consisted of the administration of an association

of drugs, according to the severity of clinical features, and respiratory physiotherapy management, such as pronation: i) antibiotic therapy with azithromycin (500 mg daily), sometimes associated with ceftriaxone (2 g daily) or levofloxacin (500 mg daily); ii) antiviral therapy with hydroxychloroquine and/or protease inhibitors (darunavir + ritonavir or lopinavir + ritonavir); iii) immunomodulatory therapy with methylprednisolone or dexamethasone in severe cases and tocilizumab in selected cases; iv) enoxaparin sodium (prophylactic dosage or, in severe cases, anticoagulant dosage); v) high-flow oxygen therapy delivered by a Venturi mask and/or NIPPV; vi) alternation of supine and prone position in bed (prone positioning).

We have analyzed three cases in which hemorrhagic complications endangered life: three cases of women affected by severe ARDS, due to COVID-19 pneumonia, and pectoral hematoma with post-hemorrhagic secondary acute anemia. We have already described two of these clinical cases in our previous publication.[15]

In this new article, we describe a third similar case: she was obese as the other two women, and she had a pectoral hematoma, a problem that was very rare before this pandemic. We have also reviewed clinical reports from 2020 to 2022 about hemorrhagic complications during COVID-19 (PubMed and online reviewed publications).

Case report

An 82-year-old woman, suffering from obesity (weight 84 Kg, BMI 31), arterial hypertension, type II diabetes mellitus, dyslipidemia, vascular encephalopathy with epilepsy, and hypomobility, came to the Emergency Department on the 2nd of May 2020 because of dyspnea and fever.

Chest x-ray on admission: widespread accentuation of the peribronchovasal plot with bilateral parenchymal thickening strips; cardiomediastinal shadow in axis.

Bioumoral tests: leucocytes 13910/ul, erythrocytes 3530000/ul, hemoglobin 10 g/dl, PT 1.00, creatinine 0,67 mg/dl, C-reactive protein 2,4 mg/dl. Her nasal swab was positive for COVID-19.

Arterial blood gas analysis during NIPPV: pH 7.45, pO_2 59 mmHg, pCO_2 32 mmHg, O_2 saturation 94% with inspired fraction of O_2 (FiO_2) 35%, pO_2/FiO_2 169, PEEP 5 cmH_2O (moderate ARDS according to Berlin definition).[16]

Treatment: ceftriaxone 2 g and azithromycin 500 mg daily, high flow oxygen via Venturi mask (6 l/min) alternating with NIPPV, methylprednisolone 40 mg daily, enoxaparin 6000 U bid, respiratory physiotherapy and alternating supine and prone position in bed.

On the 6th of May, a swelling in the right mammary-pectoral site was noticed. A thoracic computed tomography (CT) scan without contrast medium was performed (Figure 1): right pectoral hematoma (8.2 x 5.3 x 11 cm) with multiple arterial spreads, likely coming from the lateral thoracic artery.

She underwent arterial embolization (branches from the lateral thoracic artery have been treated with hemostatic material). Moreover, she received a blood transfusion with 2 bags of packed red cells due to acute anemia (hemoglobin 7.2 g/dl, hematocrit 23%).

Pectoral muscle hematoma is a rare condition. It is generally caused by traumas to the chest wall or invasive medical procedures. The spontaneous pectoral hematoma is even rarer, and it is reported in five cases related to blood thinner medication.[17,18] Despite it is rare, the pectoral hematoma was a life-threatening complication in a significant number of cases of COVID-19 in our departments (4%).

Our three patients have similar characteristics: they are females with high BMI, treated with pronosupination and sodium heparin at a higher dosage than prophylactic dosage. A consistent large hematoma developed and led to severe acute anemia. In two cases, embolization was necessary to stop bleeding. In the less dramatic case, a CT scan was performed without contrast (due to chronic renal failure), and it did not allow us to identify which vessels were involved, but the morphological-anatomical characteristics of the hematoma suggested that it also may have been determined by an arterial injury from lateral thoracic or collateral branches. In one case, the CT scan showed not only the pectoral hematoma, but also the presence of pulmonary embolism in a subsegmental branch.

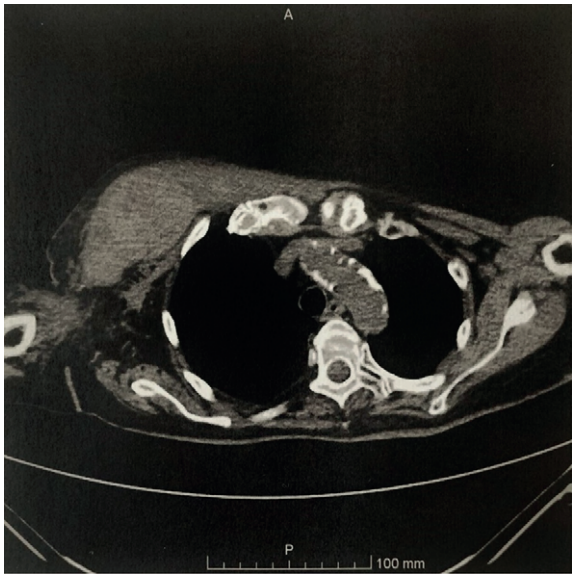

Figure 1. Image from the thoracic computed tomography scan of the patient showing a severe right wall hematoma.

Discussion

The lateral thoracic artery is a branch of the axillary artery that follows the pectoralis minor muscle's margin towards the thoracic lateral wall, vascularizing the anterior pectoral and sub-scapular muscles. It is anastomosed with the internal mammary artery, with the subscapular artery and the intercostal arteries.

In women, the lateral thoracic artery is particularly large and emits lateral mammary branches that reach the breast. In obese women, the breast is bigger and more prone to traumas during passive postural changes.

Bargellini *et al*. reported four COVID-19 patients with spontaneous bleedings underwent endovascular embolization. The first case was a woman with a large left pectoral muscle hematoma due to rupture of the superior thoracic artery, probably occurring during patient's mobilization while she was on the respirator in the prone position. The second case was a large hematoma of left ileopsoas. The third case was a rectus sheath hematoma. The last case was a hematoma of the left thigh. All these four patients were treated with low-molecular-weight heparin (LMWH) at a therapeutic dosage.[19]

Abate *et al*. evaluated the local prevalence of spontaneous muscular hematoma (SMH) retrospectively analyzing the medical records of all COVID-19 patients referring from March 11th 2020 to February 22nd 2021. The study identified ten patients with COVID-19 complicated by SMH (2.1%). In five cases, the hematoma appeared in the ileopsoas muscle, in three cases in the vastus intermedius, in one case in the large pectoral muscle and in one case in the gluteus. All patients had been mobilized with pronosupination and treated with LWMH.[20]

Taleja *et al*. reported four COVID-19 patients on anticoagulation therapy complicated by spontaneous hematomas (one in the gastrocnemius muscle, the second in the retroperitoneum anterolateral to the left psoas muscle, the third in the vastus medialis and the fourth in the pectoral muscle).[21]

Okuturlar *et al*. have described a single case of a 70-year-old man with a pectoral muscle hematoma as a complication of COVID-19 treatment. He was treated with favipiravir, levofloxacin, enoxaparin 8000 U bid, dexamethasone, and oxygen.[22]

Lopez-Martinez *et al*. have described treatments by embolization in nine patients with spontaneous hematomas and COVID-19. One of them had a pectoral hematoma.[23]

Singh *et al*. have reported four cases of COVID-19-associated pneumonia complicated by bleeding at an unusual location. In two cases patients were female, treated with heparin at anticoagulation dosage: they developed chest wall hematomas.[24]

Sottilotta *et al*. have described two cases of iliopsoas hematoma in male patients with COVID-19 being treated with enoxaparin 6000 U bid.[25]

Clinical reports show that coagulopathy is a prominent feature of COVID-19. A high incidence of thromboembolic complications has been reported (*e.g.*, pulmonary embolism).[3,4,26] This is why patients are treated with heparin (LMWH) at a prophylactic or therapeutic dosage.

We have described pectoral hemorrhagic complications during prone positioning and non-invasive ventilation in patients affected by COVID-19. It should also be noted that one of our patients' treatments with enoxaparin not only probably contributed to the onset of the bleeding complication, but also did not prevent pulmonary embolism.

It can be hypothesized that the pro-inflammatory endovascular bioumoral condition in severe forms of COVID-19 pneumonia and the anticoagulant treatment with enoxaparin sodium have determined the condition of fragility of the vascular wall.[4,2,27] In addition, cough and the continuous changes of posture, applied according to the respiratory therapeutic protocol, have probably led to a repeated breast-pectoral traumatism and the rupture of blood vessels.[8,10,11]

Conclusions

In conclusion, clinical researchers confirm our initial hypothesis: severe cases of COVID-19 are related to rare major hematomas or bleeding in unusual sites and consequent severe acute anemia.

Bleeding diathesis is likely multifactorial, related to COVID-19 illness severity, heparin dosage, traumatism due to cough and pronosupination.

The practice of pronosupination in patients with respiratory failure affected by COVID-19 should be personalized, considering the characteristics of the patients, in particular BMI, and the dosage of enoxaparin sodium.

Bleeding can be life-threatening, so it is important to monitor patients carefully and limit therapeutic anticoagulation to appropriate indications.

References

1. Marietta M, Ageno W, Artoni A, et al. COVID-19 and haemostasis: a position paper from Italian Society on Thrombosis and Haemostasis (SISET). Blood Transfus 2020;18:167-9.
2. Lodigiani C, Iapichino G, Carenzo L, et al. Venous and arterial thromboembolic complications in COVID-19 patients admitted to an academic hospital in Milan, Italy. Thromb Res 2020;191:9-14.
3. Al-Samkari H, Karp Leaf RS, Dzik WH, et al. COVID-19 and coagulation: bleeding and thrombotic manifestations of SARS-CoV-2 infection. Blood 2020;136: 489-500.

4. McFadyen JD, Stevens H, Peter K. The emerging threat of (micro)thrombosis in COVID-19 and its therapeutic implications. Review. Circ Res 2020;127:571-87.
5. Miesbach W, Makris M. COVID-19: coagulopathy, risk of thrombosis, and the rationale for anticoagulation. Clin and Appl Thromb Hemost 2020;26:1-7.
6. Connors JM, Levy JH. COVID-19 and its implications for thrombosis and anticoagulation. Blood 2020;135: 2033-40.
7. Xu Z, Shi L, Wang Y, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med 2020;8:420-2.
8. Duca A, Memaj I, Zanardi F, et al. Severity of respiratory failure and outcome of patients needing a ventilator support in the Emergency Department during Italian novel coronavirus SARS-CoV2 outbreak: preliminary data on the role of helmet CPAP and non-invasive positive pressure ventilation. EClinicalMedicine 2020;24: 100419.
9. Gattinoni L, Busana M, Giosa L, et al. Prone positioning in acute respiratory distress syndrome. Semin Respir Crit Care Med 2019;40:94-100.
10. Longhini F, Bruni A, Garofalo E, et al. Helmet continuous positive airway pressure and prone positioning: a proposal for an early management of COVID-19 patients. Pulmonology 2020;26:186-91.
11. Bastoni D, Poggiali E, Vercelli A, et al. Prone positioning in patients treated with non-invasive ventilation for COVID-19 pneumonia in an Italian emergency department. Emerg Med J 2020;37:565-6.
12. Guérin C, Reignier J, Richard JC, et al. Prone positioning in severe acute respiratory distress syndrome. N Engl J Med 2013; 368:2159-68.
13. Scaravilli V, Grasselli G, Castagna L, et al. Prone positioning improves oxygenation in spontaneously breathing nonintubated patients with hypoxemic acute respiratory failure: a retrospective study. J Crit Care 2015;30:1390-4.
14. SIMIT (Società Italiana di Malattie Infettive e Tropicali). Vademecum per la cura delle persone con malattia da COVID-19, ed 2.0. 13th March 2020. Available from: http://www.simit.org/simit/sezioni-regionali/lombardia/comunicazioni/214-vademecum-COVID-19.
15. Benazzi D, Antonicelli V, Presciuttini B, et al. COVID-19 and hemorrhagic complications: pectoral hematoma. Ital J Emerg Med 2021;10:6-10.
16. The ARDS Definition Task Force (2012). Acute Respiratory distress syndrome: the Berlin definition. JAMA 2012;307: 2526-33.
17. Koklu H, Koklu NO, Khurami FA, et al. Therapy-related spontaneous pectoral muscle hematoma: a case report and review of the literature. J Am Geriatr Soc 2016;64: 1135-7.
18. Yang JC, Makaryus AN. Warfarin anticoagulation and spontaneous pectoral haematoma. Heart Lung Circ 2016;25:e81-4.
19. Bargellini I, Cervelli R, Lunardi A, et al. Spontaneous bleedings in COVID-19 patients: an emerging complication. Cardiovasc Intervent Radiol 2020;43:1095-6.
20. Abate V, Casoria A, Rendina D, et al. Spontaneous muscle hemathoma in patients with COVID-19: a systematic literature review with description of an additional case series. Semin Thromb Hemost 2022; 48:100-8.
21. Taleja H, Nair VV, Yadav S, et al. Spontaneous hematomas in COVID-19 patients on low-molecular-weight heparin. Dubai Med J 2021;4:285-90.
22. Okuturlar Y, Gurleyik D, Ramoglu N, et al. Pectoral muscle hematoma as a complication of COVID-19 treatment: a case report. Turk J Int Med 2021;3:S79-S81.
23. Lopez-Martinez L, Molina-Nuevo JD, Pedrosa-Jimenez MJ, Julia-Molla E. Spontaneous haematomas in anticoagulated COVID-19 patients: diagnosis and treatment by embolization. Cardiovasc Intervent Radiol 2022;45:1001-6.
24. Singh B, Mechineni A, Kaur, et al. COVID-19 and bleeding at unusual locations: report of four cases. Hematol Transfus Cell Ther 2021;43:214-218.
25. Sottilotta G, Mangano C, Basile R, et al. Iliopsoas hematoma in patients with COVID-19 on low-molecular-weight heparin treatment. SAGE Open Med Case Rep 2021;9:1-4.
26. Scarduelli C, Inglese F, Beccaria M, et al. Pulmonary embolism in patients with severe COVID-19 treated with intermediate-to full-dose enoxaparin: a retrospective study. Monaldi Arch Chest Dis 2021;91:1758.
27. Bikdeli B, Madhavan MV, Jimenez D, et al. COVID-19 and Thromboembolic Disease: Implications for Prevention Antithrombotic Therapy and Follow-up. J Am Coll Cardiol 2020; 75:2950-73.