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Spontaneous bilateral pectoralis major hematoma secondary to therapeutic dose of enoxaparin in elderly Covid-19 patient

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Abstract
Type 1 respiratory failure secondary to ventilation-perfusion mismatch by micro-thrombus in the pulmonary vasculature and subsequent damage to the endothelial cells is by far the most typical presentation of Covid-19 pneumonia. Computed tomography pulmonary angiogram remains the investigation of choice to diagnose pulmonary embolism or micro-thrombi; however, it is not possible due to extreme hemodynamic instability or oxygen requirements in patients, making the transfer to the scanner a precarious affair. Therefore, clinicians worldwide use anticoagulant treatment doses based on clinical features, blood investigations, or echocardiography following local or national guidelines. In this report, we describe a case of bilateral pectoralis major hematoma due to treatment dose of enoxaparin in an elderly Covid-19 patient admitted in our ICU. This case report emphasises the need for extra precaution and vigilance while using treatment dose of anticoagulants for suspected pulmonary embolism in Covid-19 patients.

Keywords: anticoagulant therapy, covid-19, intensive care, pectoralis hematoma, thromboembolism

Introduction
Anticoagulants are essential components of therapy for critically ill patients in intensive care (ICU) for preventing thromboembolism unless contraindicated. Anticoagulants can cause life-threatening haemorrhage, particularly in renal and liver failure or severe drug interactions. Covid-19 patients are at risk of developing micro-thrombus or pulmonary embolism (PE). At times, in severely ill unstable Covid-19 patients, clinical diagnosis and investigations are the only guides to initiate anti-coagulation treatment for a suspicious/probable thromboembolic episode. This report describes a patient who developed bilateral pectoralis major hematoma secondary to treatment dose of anticoagulant. Despite having normal renal and liver functions and no known drug interactions, the patient developed massive bilateral pectoralis major hematomas, which we managed conservatively.

Case report
An 81-year-old gentleman (76 kg, BMI 31.2) presented to the emergency department with a four-day history of dry cough, fever and malaise, and six hours of shortness of breath. He was tachypnoeic (respiratory rate 40), tachycardic (heart rate 121) and requiring 15 L oxygen/min. His arterial blood gas showed type 1 respiratory failure (T1RF). We started him on continuous positive airway pressure (CPAP). Chest X-ray showed peripheral ground-glass opacities involving both lower lobes, typical for Covid-19 pneumonia (Figure 1). Reverse-Transcription Polymerase Chain Reaction for Covid-19 returned positive. In ICU, we continued with CPAP. He was too unstable (high oxygen requirements and tachypnoeic) for a computed tomography-pulmonary angiogram (CTPA). Following hospital protocol, we started dexamethasone 6.6 mg intravenous (IV) daily for ten days.

He had high d-dimer (>ten times of normal range), high ferritin (1635 microgram/L) and creatine phosphokinase. Echocardiography showed mild right ventricular (RV) dilatation. As per national guidelines [1], we counselled him for self-proning on CPAP and high flow nasal oxygen (HFNO). Because of the high d-dimer and high Wells score, we started therapeutic dosing of enoxaparin (1mg/kg, subcutaneous, twice daily). Over the next 48 hours, he responded well to self-proning and CPAP. On the fourth day in ICU, we changed CPAP to HFNO. We noticed painless ecchymosis over his right pectoral region. There was no trauma history; his blood results (haemoglobin, coagulation profile, anti-factor Xa) were normal. Our initial impression was that minor trauma associated with proning/CPAP might have caused ecchymosis. Therefore, we decided to avoid self-proning, discontinue enoxaparin, use mechanical thromboprophylaxis, and mobilisation. He was not receiving any other drugs which interacted with enoxaparin. We marked the site of ecchymosis and closely observed haemoglobin and haemodynamics.

His ecchymosis increased over the next 12 hours; haemoglobin fell to 98 g/L (baseline 122 g/L), but he remained hemodynamically stable. After an ultrasound scan of the hematoma, the radiologist advised CTPA for any deterioration. Within 24 hours, the ecchymosis and haematoma increased significantly, extending over the right flank, left lateral and pectoral regions (Figures 2). Haemoglobin dropped to 78 g/L; platelets to 125 (baseline 189x10^9); blood pressure fell by 20% from baseline. Coagulation and renal function were normal. He received IV fluids, two units of blood and noradrenaline for blood pressure support. Noradrenaline was tapered and discontinued

within a day. Throughout this period, his T1RF gradually improved. We performed a CTPA, which revealed a large hematoma (10 x 5.5 cm) in the tissue plane between the right pectoralis major and minor muscles (Figure 3) and a similar haematoma on the left side. The axillary artery traversed through the hematoma, but there was no vascular abnormality (Figure 4). Vascular input advised continuing conservative management given haemodynamic stability and no active bleeding point but planned for intervention if any deterioration. For 48 hours, he remained hemodynamically stable with unchanged ecchymosis and haemoglobin. We transferred him to the ward after three more monitoring days in ICU.

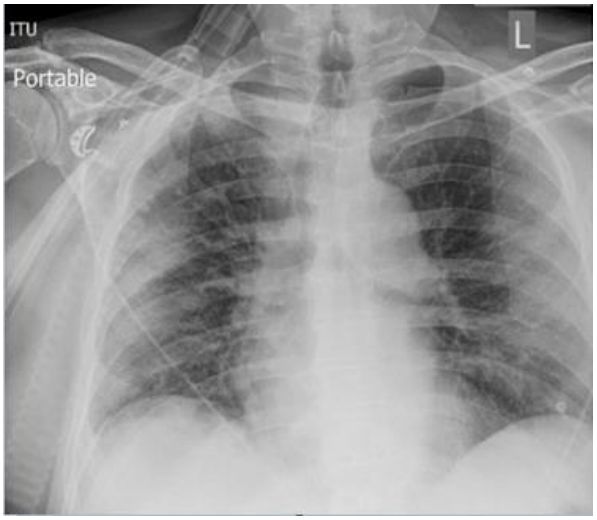

Fig 1: Chest X-ray showing peripheral ground-glass opacities involving both lower lobes

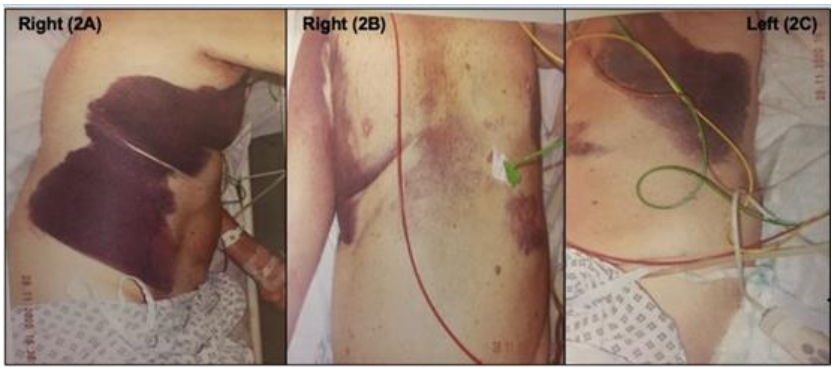

Fig 2: 2A: Ecchymosis and the haematoma extending to the right flank, 2B: Ecchymosis and the haematoma extending bilateral pectoral region, 2C: Ecchymosis and the haematoma extending to left lateral and pectoral regions

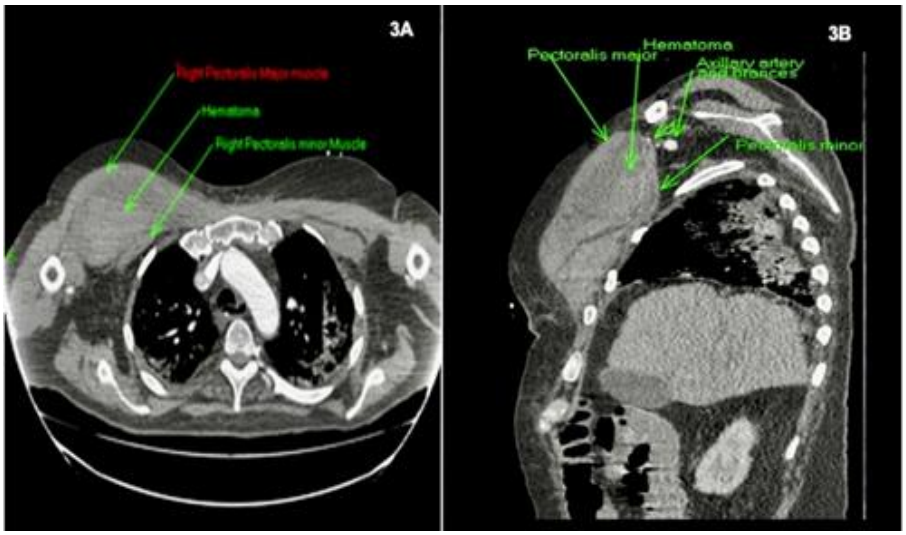

Fig 3: Hematoma (10 x 5.5 cm) in the tissue plane between the right pectoralis major and minor muscles.

Discussion

Acute severe pneumonia in Covid-19 is occasionally very intense and involves most organs [2, 3]. Covid-19 infection can cause a severe inflammatory reaction and hypercoagulable stage. One of the causes of hypercoagulability is direct damage to endothelial cells, thereby releasing pro-inflammatory cytokines [2, 4, 5]. Abnormal activation of the coagulation system could result in a generalised small vessel vasculitis and extensive micro thrombosis [6]. Thromboembolic events are common in patients admitted to ICU and carry a poor prognosis [7]. The ventilation-perfusion mismatch explains profound hypoxia in severe Covid-19 pneumonia due to thromboembolic episodes [8]. In April 2020, the International Society on Thrombosis and Haemostasis developed guidelines for thromboprophylaxis with enoxaparin for patients with Covid-19 [9].

Mauhat B *et al*. found that PE is ubiquitous in Covid-19 patients with high d-dimer in the absence of anticoagulant therapy. They noticed that when the d-dimer level is >2590 ng/mL, a 17-fold increase in PE risk and absence of anticoagulation increases PE risk by a 4-fold [10].

Our patient had T1RF secondary to Covid-19 pneumonia, initially haemodynamically unstable with high oxygen requirements. He had RV dilatation, a common finding in massive pulmonary embolism [11]. He was not safe enough for transfer for immediate CTPA. Based on hospital and national guidelines [12], we started enoxaparin treatment dose (d-dimer was > six times normal). His T1RF improved in the initial 72 hours; however, he developed a pectoralis hematoma on day four.

Multivariate analysis in an observational study revealed serum creatinine elevations by increments of 20 μmol/l is predictive of significant bleeding (OR: 1.44, 95% CI: 0.96–2.16, P = 0.079) [13]. Other predictors for spontaneous hematoma include chronic liver damage, chronic renal failure and obesity.

Pectoral hematomas are rarely reported in the literature. Ozpolat *et al*. described massive subpectoral hematoma and haemorrhage in an 81-year-old man treated for deep vein thrombosis with enoxaparin that ultimately needed surgical evacuation [14]. Our patient had a slightly high BMI, normal hepatic and renal profile, and no other anticoagulant and antiplatelet medicines. We are not sure about the cause of the bilateral pectoral hematoma. No vascular abnormality was evident in CTPA, and no intervention was needed.

Although Covid-19 infection causes microthrombus formation, there is controversy about the dose of enoxaparin; as per NICE and national guidelines, we gave a treatment dose of anticoagulant in high d-dimer. However, given this unanticipated complication in our patient, we suggest in future to use extra caution with anticoagulant dosing in similar patients.

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