PLEURALNI IZLIV KOD PACIJENTKINJE OBOLELE OD KOVID-19 INFEKCIJE

PRIKAZ SLUČAJA

CASE REPORT

PLEURAL EFFUSION IN A COVID-19 PATIENT

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SAŽETAK

Uvod/Cilj: Pleuralni izlivi se retko beleže na snimcima grudnog koša kompjuterizovanom tomografijom *(CT)* i radiografijom (RTG), kod bolesti izazvane koronavirusom 2019 (KOVID-19). Kada su prisutni, najčešće se javljaju kasno u toku bolesti, uglavnom su unilateralni, ali mogu biti i bilateralni, i apsorbuju se nakon dvodnevnog praćenja. Istraživanja su pokazala i da se pleuralni izlivi javljaju prevashodno kod starijih osoba i osoba sa osnovnom respiratornom bolešću, ali i da su incidencija respiratorne insuficijencije, incidencija sindroma akutnog respiratornog distresa, kao i stopa smrtnosti, više kod pacijenata sa pleuralnim izlivom nego kod pacijenata kod kojih do njega nije došlo. Cilj rada je da se prikaže slučaj koji se razlikuje od najčešće opisanih slučajeva u dostupnoj literaturi.

Prikaz bolesnika: Prikazujemo bolesnicu staru 49 godina, bez komorbiditeta, obolelu od KOVID-19 oboljenja, kod koje se pleuralni izliv razvio desetog dana hospitalizacije; bio je unilateralan i nije ga bilo na ponovljenom snimku nakon četiri dana. Osim povećanja broja trombocita, krvna slika je bila u referentnim vrednostima, dok je vrednost CRP-a bila umereno povišena. Bolesnica je šesnaestog dana hospitalizacije otpuštena u dobrom opštem stanju.

Zaključak: Ovaj slučaj nam pruža uvid u tok i prognozu KOVID-19 bolesti, koji se razlikuje od onog što je opisano u do sada objavljenim radovima, ukazujući na to da se pleuralni izliv ne javlja samo kod starijih bolesnika sa komorbiditetima i teškom kliničkom slikom KOVID-19 infekcije.

Ključne reči: KOVID-19, pleuralni izliv, radiografija grudnog koša

ABSTRACT

Introduction/Aim: Pleural effusions are rarely seen on computerized tomography (CT) or radiography (X-ray) images of the chest, in coronavirus disease of 2019 (COVID-19). When present, they usually occur late in the course of the disease; they are mostly unilateral but can also be bilateral, and are absorbed after two days. Studies have also shown that pleural effusions occur primarily in the elderly and individuals with underlying respiratory disease. The incidence of respiratory failure and acute respiratory distress syndrome, as well as the mortality rates are higher in patients with pleural effusion than in patients without it. Our aim is to report a case that is different from the most commonly described cases in available literature.

Patient presentation: We present a 49-year-old, comorbidity-free COVID-19 patient, who developed pleural effusion on the 10th day of hospitalization. The pleural effusion was unilateral and did not appear on a repeat lung radiography after four days. Except an elevated platelet count, the blood count parameters were in the reference ranges, while the value of CRP was slightly elevated. The patient was discharged with a good general health status, after 16 days of hospitalization.

Conclusion: This case provides insight into the course and prognosis of the COVID-19 disease that is different from what has been reported in previously published papers and shows that pleural effusions do not occur only in elderly patients with comorbidities and a severe clinical presentation of the COVID-19 infection.

Key words: COVID-19, pleural effusions, chest radiography

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UVOD

Kako globalna pandemija bolesti izazvane koronavirusom 2019 (KOVID-19) napreduje, mnoge specijalnosti i dalje imaju ključnu ulogu u postavljanju dijagnoze i lečenju. U radiologiji, većina literature se fokusira na kompjuterizovanu tomografiju (*CT*) grudnih manifestacija KOVID-19 oboljenja [1,2]. Međutim, zbog kontrole infekcije, koja se odnosi na transport pacijenta i dekontaminaciju, kao i zbog nedostatka dostupnosti *CT*-a u različitim delovima sveta, radiografija grudnog koša (RTG) se najčešće koristi za identifikaciju i praćenje plućnih promena. Američki koledž za radiologiju (engl. *American Radiology College - ACR*) navodi da potrebna dekontaminacija CT-a, nakon skeniranja pacijenata sa KOVID-19 oboljenjem, može poremetiti dostupnost radiološke usluge, te sugeriše da se može primeniti prenosna radiografija grudnog koša (RTG), i time minimizovati rizik od unakrsne infekcije [3]. Dalje, u slučajevima značajne kliničke sumnje na KOVID-19 infekciju, pozitivan RTG može ukloniti potrebu za CT-om. Pored toga, upotreba RTG-a za rano otkrivanje bolesti takođe može igrati važnu ulogu u područjima širom sveta u kojima je ograničen pristup pouzdanom testiranju na KOVID-19 oboljenje pomoću reakcije lančane polimerizacije (engl. *polymerase chain reaction - PCR*) [4]. Najčešći opisi RTG i *CT* nalaza kod KOVID-19 oboljenja uključuju neprozirnost mlečnog stakla uz pojavu konsolidacije [4,5]. Pleuralni izlivi se retko beleže na *CT*-u i RTG-u kod KOVID-19 oboljenja, a kada su prisutni, najčešće se javljaju kasnije u toku bolesti [6,7,8]. Pleuralni izlivi su uglavnom unilateralni [9], ali mogu biti i bilateralni, a apsorboju se nakon dvodnevnog praćenja [10].

S obzirom da se radi o retkoj manifestaciji KOVID-19 oboljenja, samo na osnovu pleuralnog izliva, a bez promena u plućima, možda ne bi bila postavljena ispravna dijagnoza. Pored toga, istraživanja su pokazala i da su incidencija respiratorne insuficijencije i incidencija sindroma akutnog respiratornog distresa, kao i stopa smrtnosti, više kod pacijenata sa pleuralnim izlivom nego kod pacijenata bez pleuralnog izliva [11].

Predstavljamo *PCR*-om potvrđen slučaj KOVID-19 oboljenja, od ukupno 331 hospitalizovanog pacijenta, u periodu oktobar - decembar 2020. godine, na Infektivnoj klinici KBC „Priština - Gračanica", kod kojeg se u toku bolesti razvio pleuralni izliv, a koji se razlikuje od do sada najčešće opisivanih slučajeva pleuralnog izliva.

PRIKAZ BOLESNIKA

Bolesnica stara 49 godina hospitalizovana je sedmog dana od početka prvih tegoba, zbog uporno prisutne povišene telesne temperature koja se kretala do 38,6 °C, suvog kašlja, malaksalosti i bolova u mišićima i zglobovima. Bolesnica je prethodno bila zdrava, bez komorbiditeta, bez alergija na lekove. Nije bila pušač i nije konzumirala

INTRODUCTION

As the global pandemic of the coronavirus disease of 2019 (COVID-19) progresses, many medical specialties still have a key role in establishing diagnosis and treatment. In radiology, most of the literature is focused on computerized tomography (CT) findings of COVID-19 manifestations in the chest [1,2]. However, due to infection control, which relates to the transportation of patients and decontamination, and because in different parts of the world there is a lack of availability of CT imaging, the chest X-ray, i.e., radiography (RTG) is most commonly used for the identification and monitoring of pulmonary lesions. The American Radiology College (ACR) states that the necessary decontamination of CT machines, after they are used for scanning COVID-19 patients, may negatively affect the availability of radiological diagnostics and suggests the possibility of applying mobile X-rays, thereby minimizing the risk of cross infection [3]. Furthermore, in cases of significant clinical suspicion of COVID-19, a positive RTG finding may render the CT scan unnecessary. Also, application of RTG for early detection of the disease may play an important role in those parts of the world where access to reliable polymerase chain reaction (PCR) testing for COVID-19 is limited [4]. The most common X-ray and CT findings include ground glass opacity with consolidations [4,5]. Pleural effusion is rarely found on CT and X-ray images of COVID-19 patients, and when they *are* registered, it is most commonly in the later course of the disease [6,7,8]. Pleural effusions are mostly unilateral [9], but may be bilateral, and are absorbed after two days of monitoring [10].

As this is a rare finding in COVID-19, based only on pleural effusion, and without a finding of pulmonary lesions, the correct diagnosis may not be established. Also, studies have shown that the incidence of respiratory insufficiency and the incidence of acute respiratory distress syndrome, as well as the mortality rate, are higher in patients with pleural effusion than in patients without pleural effusion [11].

We present the case of a PCR-confirmed COVID-19 patient, out of a total of 331 patients hospitalized in the period October – December 2020, at the Clinic for Infectious Diseases of the Medical Center *Priština - Gračanica*, where pleural infusion developed during the course of the disease, but which is different from the cases of pleural effusion most commonly described so far.

CASE REPORT

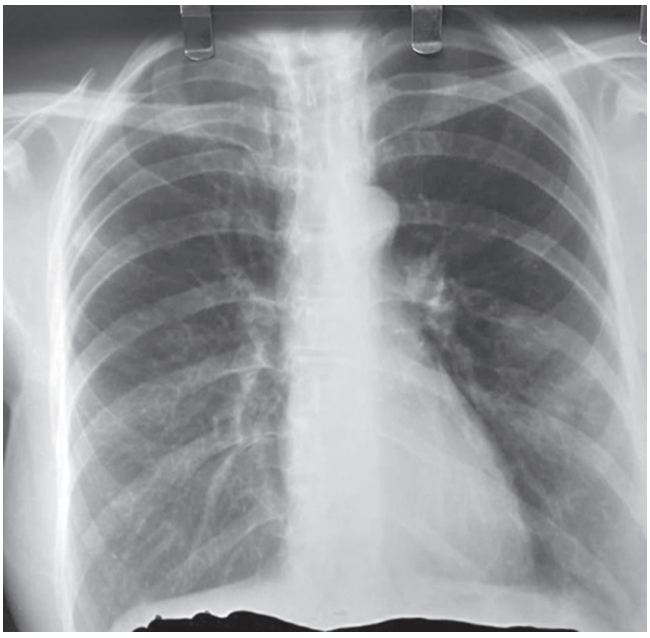
A 49-year-old female patient was hospitalized on the 7th day of the onset of symptoms, due to persistent elevated body temperature of approximately 38.6 °C, dry cough, malaise and weakness, and pain in the muscles and joints. The patient was previously healthy, without comorbidities and without allergies to medication.

alkohol. Na prijemu je bila svesna, orijentisana, afebrilna, sa vrednostima: SpO2 89,0%, TA 110/70mmHg. Površinski limfni čvorovi nisu bili palpabilni, tonzile i ždrelo su bili urednog nalaza. Auskultatorno nad plućima, desno bazalno su bili čujni slabi pukoti. Trbuh je bio mek, palpatorno bolno neosetljiv, jetra i slezina se nisu palpirale ispod rebarnih lukova. Na donjim ekstremiteta nije bilo edema. Neurološki nalaz je bio uredan.

Rezultati laboratorijskih analiza su bili sledeći: Er 4,25...5,02 (referentna vrednost: 3,7 - 5,8 x 10^{12}/L); Le 4,73...5,5 (referentna vrednost: 4 - 10 x 10^{9}/L); Ne 0,55...0,75 (referentna vrednost: 0,50 - 0,75); *Ly* 0,41...0,22 (referentna vrednost: 0,20 - 0,40); Mo 0,04...0,02 (referentna vrednost: 0,02 - 0,10); Tr 171...480...563 (referentna vrednost: 150 - 350 x 10^{9}/L); CRP 6...18...30...12 (referentna vrednost: < 6 IU/ml); ukupni proteini 72...67...77 (referentna vrednost: 65 - 87 g/L); albumini 45...35...38 (referentna vrednost: 38 - 51 g/L), ALT 19...61...46 (referentna vrednost: <32 U/L); AST 34...87...29 (referentna vrednost: < 31 U/L); *ALP* 89...95...88 (referentna vrednost: 64 - 306 U/L); LDH 473...721...419 (referentna vrednost: 225 - 450 U/L); CK 209...89...29 (referentna vrednost: 24 - 170 U/L). *PCR* test je pokazao da je pacijentkinja bila pozitivna na virus SARS KoV-2. Na inicijalnom RTG-u, u plućnom parenhimu je bila naglašena bronhovaskularna šara, sa obostrano smanjenom transparencijom bazalno. Hilusi su bili primerene veličine i položaja. Frenikokostalni (FK) sinusi su bili oštri i transparentni. Obe hemidijafragme su bile oštro konstruisane i lučno svedene (Slika 1).

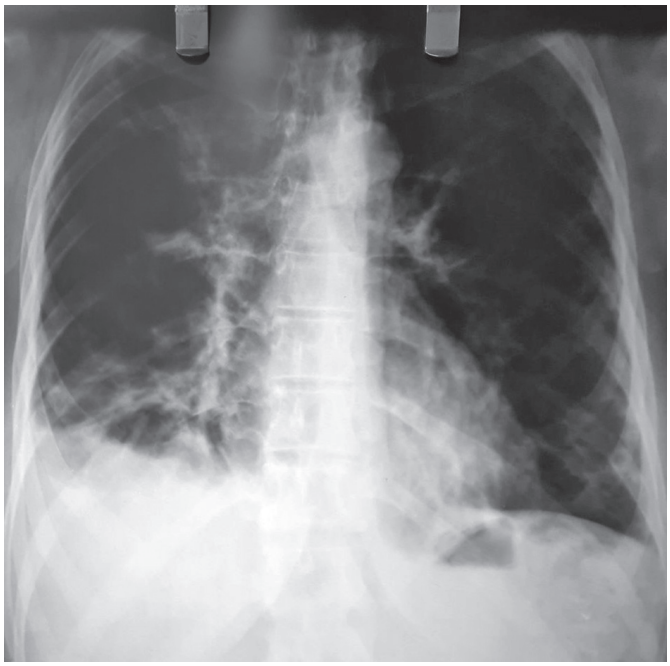
She did not smoke nor drink alcohol. At admission, the patient was conscious, oriented, afebrile, with the following vitals: SpO2 89.0%, TA 110/70mmHg. Superficial lymph nodes were not palpable, the clinical presentation of the tonsils and pharynx was normal. Auscultation of the lungs, basally on the right, revealed fine crackles. The abdomen was soft and was not tender on palpation, the liver and spleen were not palpable below the costal margins. There was no edema in the lower extremities. The neurological finding was normal.

The laboratory test results were as follows: RBC 4.25...5.02 (reference range: 3.7 – 5.8 x 10^{12}/L); WBC 4.73...5.5 (reference range: 4 - 10 x 10^{9}/L); ANC 0.55...0.75 (reference range: 0.50 – 0.75); Lymphs 0.41...0.22 (reference range: 0.20 – 0.40); Mo 0.04...0.02 (reference range: 0.02 – 0.10); PLT 171...480...563 (reference range: 150 - 350 x 10^{9}/L); CRP 6...18...30...12 (reference range: < 6 IU/ml); TP 72...67...77 (reference range: 65 - 87 g/L); Alb 45...35...38 (reference range: 38 - 51 g/L), ALT 19...61...46 (reference range: <32 U/L); AST 34...87...29 (reference range: < 31 U/L); ALP 89...95...88 (reference range: 64 - 306 U/L); LDH 473...721...419 (reference range: 225 - 450 U/L); CK 209...89...29 (reference range: 24 - 170 U/L). The PCR test showed that the patient was positive for SARS CoV-2. The initial lung X-ray revealed prominent bronchovascular marking in the pulmonary parenchyma, with bilaterally reduced transparency, basally. The position and size of the hiluses was normal. The costophrenic angles were sharp and transparent. Both hemidiaphragms were sharp and well defined (Figure 1).



Slika 1. Naglašena bronhovaskularna šara, sa obostrano smanjenom transparencijom bazalno

Figure 1. Prominent bronchovascular marking, with bilaterally reduced basal transparency



Slika 2. Pleuralni izliv sa fibroadhezivnim promenama bazalno, desno

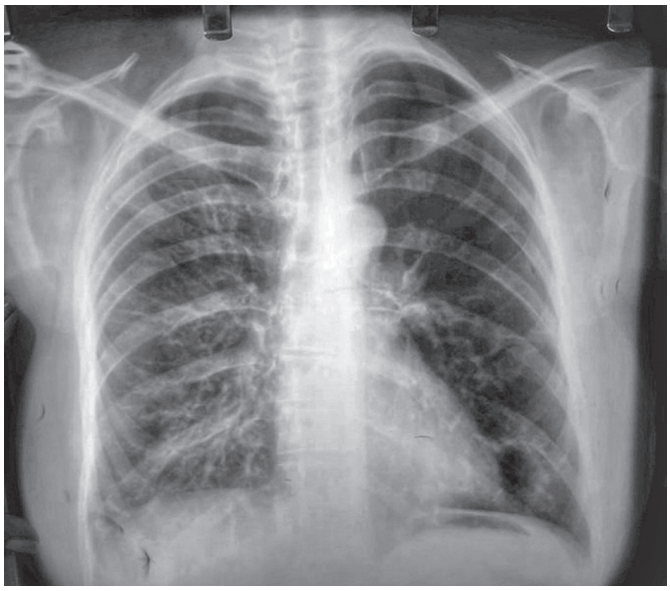
Figure 2. Pleural effusion with fibroadhesive lesions basally, on the right

Bolesnica je u toku hospitalizacije lečena po protokulu za lečenje pacijenata sa KOVID-19 oboljenjem, uz postepeno poboljšanje, povlačenje simptoma bolesti i oslobađanje od kiseoničke potpore. Desetog dana hospitalizacije razvio se pleuralni izliv (Slika 2), koji se vrlo brzo povlačio i nije bio prisutan na RTG-u ponovljenom nakon četiri dana (Slika 3). Bolesnica je šesnaestog dana hospitalizacije otpuštena u dobrom opštem stanju.

DISKUSIJA

Prikazujemo slučaj pleuralnog izliva kod bolesnice obolele od KOVID-19 oboljenja kod koje se pleuralni izliv javio kasnije u toku progresije bolesti (Slika 2), što je u skladu sa izveštajem Salehija i saradnika [6], dok su Žang i saradnici prikazali slučaj KOVID-19 oboljenja sa pleuralnim izlivom kao inicijalnim simptomom [12]. Song i saradnici izveštavaju da se pleuralni izliv apsorbuje već nakon dva dana [10]. Takođe, kod naše bolesnice, na ponovljenom snimku načinjenom nakon četiri dana, nije bilo pleuralnog izliva (Slika 3). Neka istraživanja ukazuju na to da učestalost pleuralnih izliva varira sa godinama [11,13]. U svom istraživanju na 552 pacijenta, Madžidi i saradnici su pokazali da se pleuralni izliv češće stvara kod osoba starosti pedeset godina i više [13]. I Vei i saradnici su u svom istraživanju pokazali da su pacijenti, koji su u toku bolesti razvili pleuralni izliv, bili značajno starije životne dobi (60,8 ± 15,4 godina) i imali su u istoriji bolesti osnovnu respiratornu bolest [11]. Naša bolesnica je imala 49 godina i bila je bez komorbiditeta, što može ukazivati na to da starost ispod 60 godina, kao i odsustvo komorbiditeta nužno ne znači i odsustvo rizika od pleuralnog izliva.

U literaturi, laboratorijska ispitivanja su pokazala razlike među pacijentima sa i bez pleuralnog izliva. Pacijenti sa pleuralnim izlivom imali su viši nivo leukocita, neutrofila, trombocita, te više vrednosti CRP-a i sedimentacije eritrocita, u poređenju sa pacijentima bez pleuralnog izliva. To ukazuje na tešku upalu kod pacijenata sa pleuralnim izlivom [11], što nije bio slučaj kod naše bolesnice. U našem slučaju je bolesnica sve vreme hospitalizacije imala vrednosti leukocita i neutrofila u referentnim vrednostima. Inače, povećane vrednosti CRP-a i trombocita su pokazatelji loše prognoze kod pacijenata sa KOVID-19 oboljenjem [14]. Vei i saradnici navode veći broj pacijenata sa pleuralnim izlivom kod kojih su vrednosti CRP-a bile povišene u odnosu na broj pacijenata koji nisu imali pleuralni izliv, ali su imali povišene vrednosti CRP-a [11]. Naša bolesnica je takođe imala vrednosti CRP-a iznad referentnih, dok je broj trombocita na prijemu bio u referentnim vrednostima, a u daljem toku hospitalizacije se kretao iznad referentnih vrednosti. I obimno istraživanje na 476 pacijenata



Slika 3. Lako smanjena transparencija plućnog parenhima desno, najpre pozicione. U plućnom parenhimu nema konsolidacije. Difuzno naglašen intersticijalni crtež. Hilusne senke normalne širine, vaskularne. Radiografski bez sigurnih znakova pleuralnog izliva. Obostrano bazalno, izraženije desno, pleuralne adhezije

Figure 3. Slightly reduced transparency of the pulmonary parenchyma on the right, first positionally. There is no consolidation in the pulmonary parenchyma. Diffusely accentuated interstitial pattern. Hilar shadows of normal width, vascular. Radiographically without definitive signs of pleural effusion. Pleural adhesions, bilaterally basally, more pronounced on the right

During hospitalization, the patient was treated according to the protocol for treating COVID-19 patients. Gradually, her status improved, her symptoms subsided, and she was taken off oxygen therapy. On the 10th day of hospitalization, pleural effusion developed (Figure 2), which subsided very quickly and was not visible on repeat X-ray, after four days (Figure 3). On the 16th day of hospitalization, the patient was discharged with a good general health status.

DISCUSSION

We present a case of pleural effusion in a COVID-19 female patient, in whom pleural effusion developed at a later stage of the progression of disease (Figure 2), which coincides with what Salehi et al. reported in their study [6], while Zhang et al. reported on a case of COVID-19 with pleural effusion as an initial symptom [12]. Song et al. found that pleural effusion resolved after two days [10]. In our patient, as well, a repeat X-ray, four days later, showed that the pleural effusion had disappeared (Figure 3). Some studies show that the frequency of pleural effusions varies depending on age [11,13]. In their study involving 552 patients, Majidi et al. showed that pleural effusion developed more often in patients aged 50 years and older [13]. In their study, Wei et al. also

obolelih od KOVID-19 oboljenja, koje su sproveli Feng i saradnici, pokazalo je da je incidencija pleuralnih izliva bila značajno viša kod pacijenata sa teškom kliničkom slikom, u odnosu na pacijente sa lakšom kliničkom slikom [15]. Slična zapažanja su zabeležena i u još nekim istraživanjima koja su pokazala da je učestalost pleuralnih izliva bila značajno viša kod pacijenata sa teškom kliničkom slikom KOVID-19 oboljenja u odnosu na pacijente sa lakšom kliničkom slikom [7,8,16,17,18]. Međutim, ovo nije bio slučaj sa našom bolesnicom, koja nije imala tešku kliničku sliku i otpuštena je izlečena, šesnaestog dana hospitalizacije.

ZAKLJUČAK

Iako ovaj slučaj ima svoja ograničenja, u pogledu nedostatka dodatne radiološke i laboratorijske dijagnostike, ipak pruža uvid u tok i prognozu bolesti, koji se razlikuje od do sada objavljenih radova u ovoj oblasti. Naše iskustvo pokazuje da se pleuralni izliv može javiti i kod mlađih pacijenata bez komorbiditeta i sa lakšom kliničkom slikom KOVID-19 infekcije.

SPISAK SKRAĆENICA

Er – Eritrociti
Le – Leukociti
Ne – Neutrofili
Ly – Limfociti (engl. *Lymphocytes*)
Mo – Monociti
Tr – Trombociti
CRP – C-reaktivni protein
ALT – Alanin aminotransferaza
AST – Aspartat aminotransferaza
ALP – Alkalna fosfataza (engl. *alkaline phosphatase*)
LDH – Laktat dehidrogenaza
CK – Kreatin kinaza (engl. *creatinine kinase*)

Sukob interesa: Nije prijavljen.

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demonstrated that patients who had developed pleural effusion during COVID-19 were significantly older (60.8 ± 15.4 years) and that they had an underlying respiratory disease registered in their medical history [11]. Our patient was 49 years old, without comorbidities, which may indicate that if a patient is younger than 60 years and without comorbidities, this does not necessarily mean that they are completely without risk of pleural effusion.

Studies have shown that laboratory findings demonstrate differences between patients with pleural effusion and those without pleural effusion. Patients with pleural effusion had a higher white blood cell count, neutrophil count, platelet count, as well as higher values of CRP and the erythrocyte sedimentation rate, as compared to patients without pleural effusion. This indicates severe inflammation in patients with pleural effusion [11], which was not the case with our patient. Our patient had a white blood cell count and neutrophil count within the reference ranges, throughout her hospital treatment. Normally, increased levels of CRP and an elevated platelet count are indicators of poor prognosis in COVID-19 patients [14]. Wei et al. report a greater number of patients with pleural effusion whose CRP levels were elevated as compared to the number of patients without pleural effusion but with elevated CRP levels [11]. Our patient also had CRP values above the reference range, while the thrombocyte count at admission was within the reference range, while further, during hospitalization, this value was above the reference range. A large study including 476 COVID-19 patients, carried out by Feng et al., also showed that the incidence of pleural effusion was significantly higher in patients with severe clinical presentation, as compared to patients who presented with a milder form [15]. Similar findings were recorded in some other studies, which showed that the frequency of pleural effusion was significantly higher in patients with severe clinical presentation of COVID-19 than in patients with milder presentation [7,8,16,17,18]. However, this was not the case with our patient, who did not have a severe clinical presentation and was discharged on the 16th day of hospitalization, cured of disease.

CONCLUSION

Although this case has its limitations, regarding the lack of additional radiological and laboratory diagnostics, it nevertheless offers insight into the course and prognosis of disease that is different from what has been reported so far in the studies related to this field. Our experience has shown that pleural effusion may develop even in younger patients who have no comorbidities and whose clinical presentation of COVID-19 is not severe.

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LIST OF ABBREVIATIONS AND ACRONYMS

RBC – Red blood cell count (erythrocyte count)
WBC – White blood cell count (leukocyte count)
ANC – Absolute neutrophil count
Lymphs – Lymphocytes
Mo – Monocytes
PLT – Platelets (thrombocytes)
CRP – C-reactive protein
TP – Total protein
Alb – Albumin
ALT – Alanine aminotransferase
AST – Aspartate aminotransferase
ALP – Alkaline phosphatase
LDH – Lactate dehydrogenase
CK – Creatinine kinase

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