LEČENJE COVID-19 PRIMENOM LEKA CASIRIVIMAB/INDEVIMAB KOD PACIJENTA SA POVREDOM VRATNOG DELA KIČME: PRIKAZ SLUČAJA

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CASE REPORT

TREATMENT OF COVID-19 WITH CASIRIVIMAB/INDEVIMAB IN A PATIENT WITH CERVICAL SPINE INJURY: A CASE REPORT

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SAŽETAK

Uvod/Cilj: Prikazujemo pacijenta obolelog od COVID-19 sa povredom vratne kičme koji je lečen primenom antivirusnog leka casirivimab/indevimab (Regen-CoV), monoklonskih antitela za COVID-19, u toku bolničkog lečenja u Kovid bolnici Batajnica Univerzitetskog kliničkog centra Srbije.

Prikaz slučaja: Primena leka casirivimab/indevimab (Regen-CoV) sprečila je razvoj teže slike Covida-19 i dovela je do brze negativizacije nazofaringealnog brisa na SARS-CoV-2 kod našeg pacijenta koji je imao povredu vratne kičme. Pacijentu je uspešno izvršena operacija vratne kičme u Institutu za ortopedsko-hirurške bolesti Banjica, koja je dovela do povlačenja neuroloških deficita koje je imao ranije.

Zaključak: Pokazali smo još jednu veoma važnu indikaciju za primenu leka casirivimab/indevimab (Regen-CoV) u bolničkim uslovima, koja je, po terapijskim Protokolima, bila *off-label*.

Ključne reči: COVID-19, casirivimab/indevimab, terapija monoklonskim antitelima, povreda vratne kičme

ABSTRACT

Introduction/Aim: We present a patient suffering from COVID-19 with a cervical spine injury who was treated with the antiviral drug casirivimab/indevimab (Regen-CoV), monoclonal antibodies for COVID-19, during hospital treatment at the Batajnica Hospital of the University Clinical Center of Serbia.

Case report: The administration of the drug casirivimab/indevimab (Regen-CoV) prevented the development of a more severe picture of Covid-19 and led to the rapid negativization of the nasopharyngeal swab for SARS-CoV-2 in our patient who had a cervical spine injury. The patient underwent successful cervical spine surgery at the Institute for Orthopedic-Surgical Diseases in Banjica, which led to the recovery of the neurological deficits he had previously.

Conclusion: We showed another significant indication for using casirivimab/indevimab (Regen-CoV) in hospital conditions, which was off-label according to therapeutic protocols.

Keywords: COVID-19, casirivimab/indevimab, monoclonal antibody therapy, cervical spine injury

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UVOD

Tokom pandemije COVID-19, svetska naučna zajednica intenzivno je radila na pronalaženju inovativnih terapijskih pristupa koji bi efikasno pomogli u borbi protiv SARS-CoV-2. Jedan od njih je i lek Regen-CoV®, mešavina monoklonskih antitela (casirivimab (REGN10933) / indevimab (REGN10933)), koji se pokazao efikasnim u smanjenju opterećenja organizma virusom (engl. *virus load*) što se posledično manifestuje blažom kliničkom slikom i smanjenom potrebom za lečenjem pacijenata u bolničkim uslovima i smrću [1].

Lek casirivimab/indevimab (Regen-CoV®), prema preporukama Američke agencije za hranu i lekove (FDA), primenjuje se samo kod pacijenata koji se leče u vanbolničkim uslovima [2], imaju blagu kliničku sliku COVID-19 i kojima nije potrebna hospitalizacija i bolničko lečenje. Primena ovog leka ne savetuje se kod hospitalizovanih pacijenata, kao i kod pacijenata koji imaju potrebu za primenom oksigenoterapije [2], s obzirom na to da primena ovog leka kod ovih pacijenata može dovesti do deterioracije kliničke slike i pogoršanja opšteg stanja sa mogućim posledičnim fatalnim ishodom.

Tokom lečenja pacijenata u prvom talasu COVID-19 pandemije 2020. godine, postavljena je hipoteza da kod pacijenata koji razviju hiperreaktivni imunski odgovor [3] dolazi do posledičnog razvoja hipoksemije, koja zahteva hospitalizaciju i primenu oksigenoterapije. Iz tog razloga započeta je primena imunomodulatorne terapije u lečenju SARS-CoV-2 infekcije, nakon čega je sprovedeno naučno istraživanje koje je navedenu hipotezu potvrdilo [4]. Dokazano je da SARS-CoV-2 ulazi u ćelije preko ACE2 receptora za koji se vezuje S (engl. *spike*) protein na površini virusa [5]. Lek casirivimab/indevimab predstavlja kombinaciju dva humana monoklonska antitela koja deluju tako što se vezuju za navedeni S protein, ispoljavajući snažan inhibitorni efekat na sposobnost vezivanja virusa za ćelije domaćina, samim tim neutrališući SARS-CoV-2 [6,7]. Zbog učestalih mutacija spike proteina i posledične rezistencije na terapiju pojedinačnim antitelima, započeta je primena kombinacija antitela u cilju prevencije nastanka novih mutacija i razvoja dalje rezistencije virusa [8,9].

U ovom radu prikazaćemo slučaj pacijenta kome je u bolničkim uslovima aplikovan lek casirivimab/indevimab radi sprečavanja dalje progresije COVID-19 i postizanja brze negativizacije RT-PCR testa nazofaringealnog brisa na SARS-CoV-2, s ciljem omogućavanja daljeg lečenja osnovne bolesti pacijenta. Ovaj slučaj je naročit ne samo zbog primene leka van dotadašnjih zvaničnih preporuka, prema kojima se on primenjivao isključivo u vanbolničkim uslovima, već i zbog kompleksnosti samog slučaja, koji je zahtevao multidisciplinarni pristup lečenju i omogućavanje što ranijeg

INTRODUCTION

During the COVID-19 pandemic, the global scientific community worked intensively to find innovative therapeutic approaches that would effectively aid in the fight against SARS-CoV-2. One of them is the drug Regen-CoV®, a combination of monoclonal antibodies (casirivimab (REGN10933) / indevimab (REGN10987)), which has proven effective in reducing the viral load in the body, consequently resulting in a milder clinical presentation, a decreased need for hospitalization, and lower mortality rates [1].

According to the recommendations of the U.S. Food and Drug Administration (FDA), casirivimab/indevimab (Regen-CoV®) is intended exclusively for use in outpatients with mild COVID-19 who do not require hospitalization or inpatient treatment [2]. The use of this drug is not advised for hospitalized patients or those requiring oxygen therapy [2], as its administration in these cases may lead to a deterioration in clinical status and a possible fatal outcome.

During the treatment of patients in the first wave of the COVID-19 pandemic in 2020, the hypothesis was proposed that patients who develop a hyperreactive immune response [3] consequently experience hypoxemia, necessitating hospitalization and oxygen therapy. This led to the initiation of immunomodulatory therapy in the treatment of SARS-CoV-2 infection, followed by scientific research that confirmed this hypothesis [4]. It has been proven that SARS-CoV-2 enters cells through the ACE2 receptor, to which the S protein on the viral surface binds [5]. Casirivimab/indevimab is a combination of two human monoclonal antibodies that bind to this S protein, exerting a strong inhibitory effect on the virus's ability to attach to host cells, thereby neutralizing SARS-CoV-2 [6,7]. Due to frequent mutations of the spike protein and the subsequent development of resistance to single-antibody therapy, combinations of antibodies have been introduced to prevent the emergence of new mutations and further viral resistance [8,9].

In this paper, we present a case of a patient who received casirivimab/indevimab in a hospital setting to prevent further progression of COVID-19 and achieve rapid RT-PCR test negativization of the nasopharyngeal swab for SARS-CoV-2, enabling further treatment of the patient's underlying condition. This case is noteworthy not only because the drug was used outside the existing official recommendations, which restricted its use to outpatient settings, but also due to the complexity of the case itself. It required a multidisciplinary treatment approach and the earliest possible hospital management, including surgical treatment outside the COVID-19 care system.

hospitalnog zbrinjavanja, odnosno hirurškog lečenja pacijenta van COVID-19 sistema.

PRIKAZ SLUČAJA

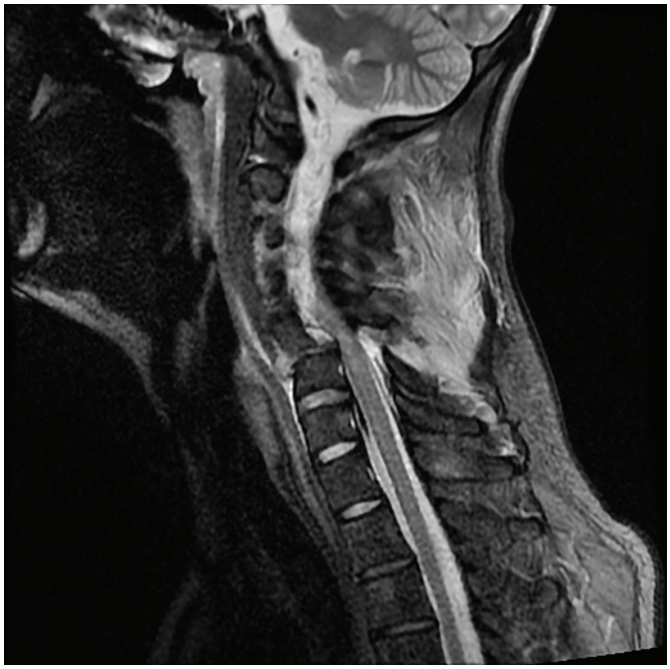
Naš pacijent, starosti 23 godine, zadobio je povrede dva vratna kičmena pršljena (C5 i C6) u saobraćajnoj nesreći pet dana pre prijema u Kovid bolnicu Batajnica Univerzitetskog kliničkog centra Srbije u Beogradu. Zbog ove povrede, shodno terapijskim protokolima, bilo je indikovano strogo mirovanje uz imobilizaciju vratnog dela kičme pomoću Šancovog okovratnika, kao i hitno operativno lečenje u specijalizovanoj tercijarnoj ustanovi. U objektivnom nalazu, neposredno po povređivanju, pacijent je imao potpunu slabost sva četiri ekstremiteta, da bi se nekoliko sati posle povređivanja povratila delimična funkcija desne strane tela, a kasnije i leve noge, dok je zaostajala slabost leve ruke. Sprovedena je radiološka dijagnostika, pri čemu je u nalazu Magnetne rezonancije vratnog dela kičme opisana spondilolisteza na nivou C5-C6, gradus II/III, zatim leva dorzolateralna ekstruzija intervertebralnog diska C5-C6, kao i stenoza spinalnog kanala uz kompresiju medule i znake mijelopatije, uz prisustvo fraktura leve lamine C5 i levog transverzalnog nastavka C6 (Slika 1). Na radiografskom snimku glave opisana je fraktura medijalnog dela krova desne orbite. Na urađenom ultrazvučnom pregledu trbuha nisu viđeni znaci traume unutrašnjih organa, a radiografski snimci grudnog koša, karlice i levog ramena su bili urednog nalaza.

Pacijent je primarno zbrinut u regionalnom zdravstvenom centru. Tada je od tegoba imao bol u vratu, koji se širio duž leve ruke i kičmenog stuba, uz prisutnu slabost leve ruke. Petog dana hospitalizacije, zbog nemogućnosti operativnog lečenja u toj ustanovi, preveden je u Institut za ortopedsko-hirurške bolesti Banjica u Beogradu koji se specijalizovano bavi lečenjem bolesti i povreda koštano-zglobnog sistema. Prilikom hospitalizacije u ovu ustanovu, pacijentu je rutinski učinjen brzi antigenski test nazofaringealnog brisa na SARS-CoV-2 čiji je nalaz bio pozitivan. Tada je od strane spinalnog hirurga indikovano hiruško lečenje čim se za to steknu uslovi u smislu negativizacije testa na SARS-CoV-2, kao i strogo mirovanje u postelji, a pacijent je preveden u Kovid bolnicu Batajnica Univerzitetskog kliničkog centra Srbije u Beogradu, najveću Kovid bolnicu u Srbiji, radi lečenja COVID-19.

U trenutku prvog pregleda u našoj ustanovi, pacijent je mogao da pokreće donje ekstremitete, uz prisutnu izraženu slabost leve ruke, kao i blagu slabost leve noge, i intenzivne bolove u vratu, koji su se propagirali duž kičmenog stuba i leve ruke. Ostali somatski nalaz je bio uredan, uz održavanje dobrih vitalnih parametara. Anamnestički, pacijent je negirao prisustvo hroničnih bolesti, prethodne operacije i primenu lične terapije.

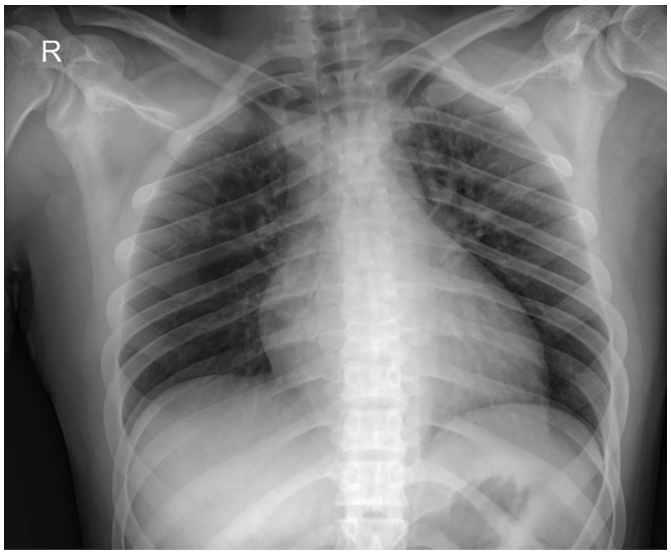
CASE REPORT

Our patient, a 23-year-old male, sustained injuries to two cervical vertebrae (C5 and C6) in a traffic accident five days before being admitted to the COVID Hospital Batajnica at the University Clinical Center of Serbia in Belgrade. Due to the nature of the injury, therapeutic protocols dictated strict immobilization of the cervical spine using a Schanz collar, as well as urgent surgical intervention at a specialized tertiary facility. Upon initial examination following the injury, the patient exhibited complete weakness in all four extremities. However, a few hours later, partial function returned to the right side of his body, followed by his left leg, while weakness in his left arm persisted. Radiological diagnostics, including MRI of the cervical spine, revealed spondylolisthesis at the C5-C6 level, grade II/III, left dorsolateral extrusion of the C5-C6 intervertebral disc, spinal canal stenosis with medullary compression and signs of myelopathy, as well as fractures of the left lamina of C5 and the left transverse process of C6 (Figure 1). A skull X-ray revealed a fracture of the medial roof of the right orbit. Abdominal ultrasound showed no signs of internal organ trauma, and radiographs of the chest, pelvis, and left shoulder were unremarkable.



Slika 1. NMR vratne kičme: spondilolisteza na nivou C5–C6, gradus II/III, leva dorzolateralna ekstruzija intervertebralnog diska C5–C6, kao i stenoza spinalnog kanala uz kompresiju medule i znake mijelopatije, i prisustvo fraktura leve lamine C5 i levog transverzalnog nastavka C6

Picture 1. MRI of the cervical spine: spondylolisthesis at the C5–C6 level, grade II/III, left dorsolateral extrusion of the C5–C6 intervertebral disc, as well as spinal canal stenosis with medullary compression and signs of myelopathy, along with fractures of the left lamina of C5 and the left transverse process of C6



Slika 2. RTG snimak pluća na dan prijema u Kovid bolnicu Batajnica, uredan nalaz

Picture 2. Chest X-ray on the day of admission to the COVID hospital Batajnica, normal findings

Tokom hospitalizacije, pacijent je pregledan od strane ortopeda, neurohirurga i neurologa, kada je indikovana MDCT angiografija glave i vrata, koja je bila urednog nalaza, a zatim i CT glave i vrata, gde je na nivou pršljenova C5–C6 viđen nalaz identičan prethodnom, uz preostali uredan nalaz. U neurološkom nalazu je sve vreme bila prisutna monopareza leve ruke srednje teškog stepena.

Pri prijemu u Kovid Bolnicu Batajnica UKCS pacijent je imao blagu kliničku sliku COVID-19, uredan radiografski nalaz snimka pluća (Slika 2), i uredan nalaz laboratorijskih analiza krvi (Tabela 1 i 2). U objektivnom nalazu je bio respiratorno i hemodinamski stabilan, urednog auskutatornog nalaza nad plućima. Konzilijarno je odlučno da se pacijentu u bolničkim uslovima, u izolaciji od drugih bolesnika, jednokratno parenteralno (intravenski) primeni lek casirivimab/indevimab u jednoj preporučenoj dozi. Odluka o primeni ovog leka

The patient was initially treated at a regional healthcare center. At that time, his primary complaints included neck pain radiating down his left arm and spine, along with weakness in his left arm. On the fifth day of hospitalization, due to the facility's inability to provide surgical treatment, he was transferred to the Institute for Orthopedic-Surgical Diseases Banjica in Belgrade, a specialized center for musculoskeletal conditions and injuries. Upon admission to this facility, a routine rapid antigen test for SARS-CoV-2 was performed on a nasopharyngeal swab, yielding a positive result. The spinal surgeon then indicated surgical treatment as soon as conditions permitted, specifically upon achieving a negative SARS-CoV-2 test. Meanwhile, the patient was advised to remain on strict bed rest and was transferred to the COVID Hospital Batajnica at the University Clinical Center of Serbia, the largest COVID hospital in Serbia, for COVID-19 management.

Upon initial examination at our institution, the patient was able to move his lower extremities but had significant weakness in his left arm, mild weakness in his left leg, and intense neck pain radiating along the spine and left arm. The remaining somatic examination findings were unremarkable, and his vital parameters were stable. His medical history was negative for chronic diseases, previous surgeries, or any long-term medication use.

During hospitalization, the patient was assessed by an orthopedic surgeon, a neurosurgeon, and a neurologist. MDCT angiography of the head and neck was performed, yielding normal results. A subsequent CT scan of the head and neck confirmed findings consistent with the previous imaging at the C5-C6 level, with no additional abnormalities. Neurological examination consistently revealed moderate left-arm monoparesis.

Upon admission to the COVID Hospital Batajnica, the patient had a mild clinical presentation of COVID-19, a normal chest X-ray (Figure 2), and unremarkable blood test results (Tables 1 and 2). He was respiratory and hemodynamically stable, with normal pulmonary auscultation. A multidisciplinary team de-

Tabela 1. Vrednosti kompletne krvne slike, parametara koagulacije i parametara zapaljenja u toku lečenja pacijenta u Kovid bolnici Batajnica UKCS

Table 1. Values of complete blood count, coagulation parameters, and inflammation markers during the patient's treatment at the COVID hospital Batajnica UKCS.

Labora-torijske analize krvi / *Blood Laboratory Analyses*	**Le**	**Ly**	**Er**	**Hgb**	**Tr**	**CRP**	**PCT**	**INR**	**D-dimer**
Refere-ntne vrednosti / *Reference Values*	3.4–9.7 x 10^9/L	1.2–3.4 x 10^9/L	4.34–5.72 x 10^{12}/L	138–175 g/L	158–424 x 10^9/L	0.0–3.0 mg/L	> 0.5 ng/L		cut off 0.5 mg/L
Pri prijemu / *On Admission*	7.7	2.17	5.45	164	252	2.0	0.05	1.0	0.43
Pri otpustu / *On Discharge*	11.4	2.77	5.29	161	266	2.0	0.03	0.99	0.44

Tabela 2. Vrednosti biohemijskih analza krvi u toku lečenja pacijenta u Kovid bolnici Batajnica UKCS

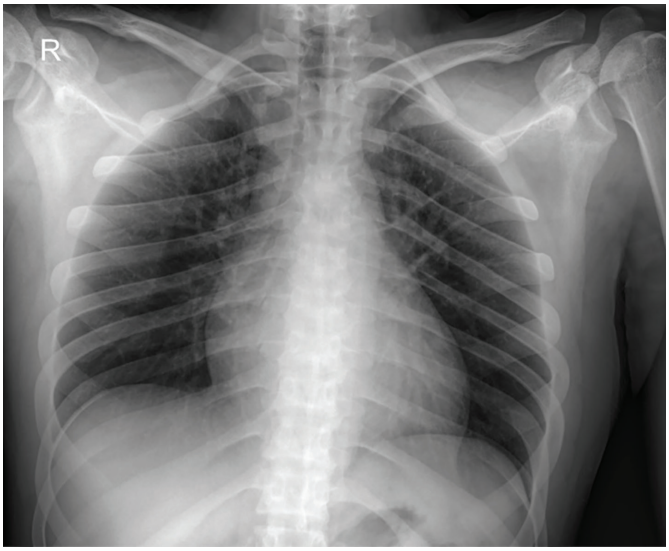
Table 2. Blood Biochemistry Values During the Treatment of the Patient at the COVID Hospital Batajnica UKCSBatajnica UKCS.

Biohemijske analize / Blood Laboratory Analyses Referentne vrednosti / Reference Values	Glucose 3.9–6.1 mmol/L	eGFR > 60mL/min/1.73m²	Proteins 62/81 g/L	Albumin 34–55 g/L	Na^+ 135–148 mmol /L	K^+ 3.5–5.1 mmol /L	AST U/L	ALT U/L
Pri prijemu / *On Admission*	5.1	> 60	69	41	137	3.6	18	20
Pri otpustu / *On Discharge*	4.2	> 60	67	41	135	3.6	18	19

je doneta u cilju sprečavanja razvoja teže kliničke slike koja bi mogla ugroziti opšte stanje pacijenta i dovesti do daljih komplikacija primarne bolesti. Takođe, primenom ove terapije omogućila bi se brža negativizacija testa na SARS-CoV-2, što bi ubrzalo neophodno i hitno hiruško lečenje u što kraćem roku.

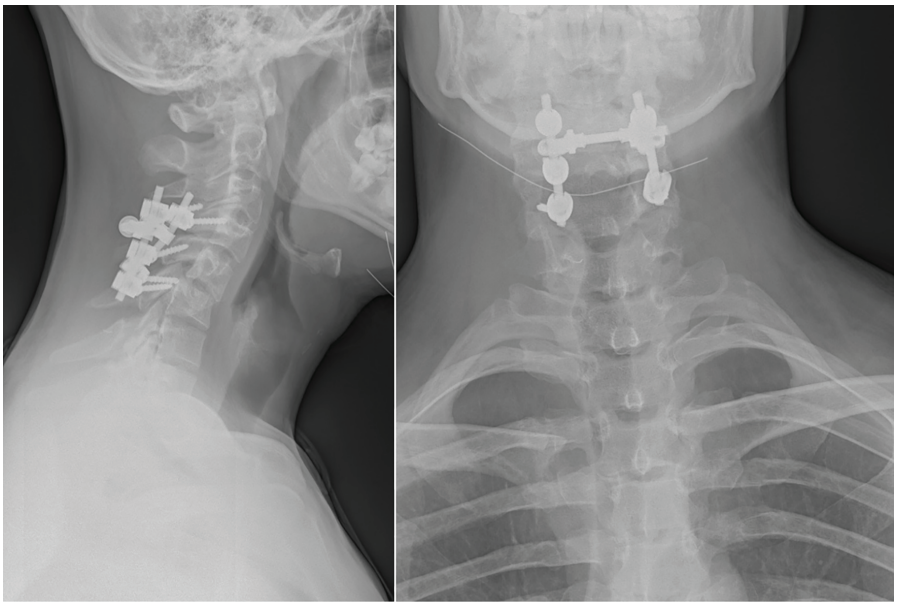
Sedam dana nakon primene leka casirivimab/imdevimab pacijent je testiran na SARS-CoV-2 pomoću Real Time PCR testa nazofaringealnog brisa, i rezultat testa je bio negativan. U tom trenutku pacijent je bio stabilnog, dobrog opšteg stanja, bez simptoma vezanih za COVID-19, uz uredan nalaz RTG snimka pluća (Slika 3) i urednih vrednosti laboratorijskih analiza krvi (Tabela 1 i 2). Preveden je na dalje lečenje u Institut za ortopedsko-hirurške bolesti Banjica u Beogradu radi neophodnog hirurškog lečenja.

Pacijent je po prevodu operisan, 18 dana nakon inicijalnog povređivanja, kada je urađena repozicija C5 vratnog pršljena uz unutrašnju spinalnu stabilizaciju C4–C6 (Slike 4 i 5). U postoperativnom toku došlo je do daljeg neurološkog oporavka. Na kontrolnom pregledu



Slika 3. Kontrolni RTG snimak pluća pred otpust iz Kovid bolnice Batajnica UKCS, uredan nalaz

Picture 3. Follow-up chest X-ray before discharge from the COVID hospital Batajnica UKCS, normal findings



Slika 4 i 5. RTG snimak vratne kičme posle uspešne operacije i stabilizacije vratnih pršljenova

Picture 4 i 5. X-ray of the cervical spine after successful surgery and stabilization of cervical vertebrae

četiri meseca kasnije, pacijent je imao uredan neurološki nalaz na svim ekstremitetima. Ponovljeno testiranje RT-PCR testom nazofaringealnog brisa na SARS-CoV-2 mesec dana nakon primene casirivimab/indevimab dalo je negativan rezultat, uz odsustvo uobičajenih tegoba vezanih za COVID-19 u kliničkom nalazu.

DISKUSIJA

Lečenje COVID-19 je od početka pandemije bio pravi izazov za zdravstvene sisteme svih država širom sveta. U pokušajima da na što bezbedniji i brži način pomognemo pacijentima, u praksi smo primenjivali različite oblike terapije. Primena imunomodulatorne antivirusne terapije činila se kao izuzetno dobra opcija za lečenje nekomplikovanog oblika COVID-19 kod pacijenata koji ne zahtevaju hospitalizaciju, a koji imaju rizik za razvoj teškog oblika ove bolesti. Međutim, usled izuzetno dobre efikasnosti leka casirivimab/indevimab, koji je inicijalno bio namenjen samo za primenu u vanbolničkim uslovima kod pacijenata sa blagom kliničkom slikom, počinje se sa prvim pokušajima lečenja ovim lekom u hospitalnim uslovima, uz pozitivne rezultate [10]. U skladu sa ovim rezultatima, u novembru 2021. godine objavljene su zvanične preporuke za primenu leka casirivimab/indevimab u hospitalnim uslovima [11].

Indikacije za primenu antivirusne terapije monoklonskim antitelima su ambulantni pacijenti sa blagom ili umereno teškim oblikom COVID-19 koji imaju visok rizik za progresiju i hospitalizaciju, ili za fatalan ishod.

Monoklonska antitela se primenjuju jednokratno, nakog čega je potrebna izolacija bolesnika kako ne bi došlo do ponovne zaraze. Ova terapija se može primeniti i kod hospitalizovanih bolesnika ukoliko postoje isti rizici i ukoliko se radi o asimptomatskim ili pacijentima sa blagom i umereno teškom formom bolesti, a koji su hospitalizovani iz nekog drugog razloga koji nije COVID-19 [2,12].

Tokom primene antitela u terapiji COVID-19 primećena je učestala pojava rezistencije virusa prilikom primene jednog antitela, zbog čega je pribegnuto primeni kombinacije dva antitela u vidu leka casirivimab/indevimab [13], uz odlične rezultate u lečenju, ali i u izbegavanju razvoja rezistencije. Kombinacija casirivimaba i indevimaba predstavlja kombinaciju visokoafinitetnih humanih monoklonskih IgG antitela, koja se vezuju direktno za S protein na površini SARS-CoV-2 i na taj način sprečavaju ulazak virusa u ćelije domaćina [2].

Lek casirivimab/indevimab, prema preporukama, primenjuje se u vanbolničkim uslovima kod pacijenata u ranoj fazi zaražavanja, kod kojih nije potrebna primena oksigenoterapije, ali sa prisutnim visokim rizikom za razvoj teškog oblika COVID-19. Cilj ove terapije je

cided to administer a single intravenous dose of casirivimab/indevimab in a hospital setting, in isolation from other patients. The rationale for this decision was to prevent disease progression, which could compromise the patient's overall condition and lead to complications related to his primary injury. Additionally, this therapy was expected to accelerate the negativization of the SARS-CoV-2 test, thereby facilitating the urgent surgical intervention required.

Seven days after receiving casirivimab/indevimab, the patient underwent RT-PCR testing for SARS-CoV-2 via a nasopharyngeal swab, which returned a negative result. At this point, he was in stable condition, free of COVID-19 symptoms, with a normal chest X-ray (Figure 3) and unremarkable blood test results (Tables 1 and 2). He was subsequently transferred back to the Institute for Orthopedic-Surgical Diseases Banjica in Belgrade for the necessary surgical treatment.

The patient underwent surgery 18 days after the initial injury, during which C5 vertebral repositioning and internal spinal stabilization of C4–C6 were performed (Figures 4 and 5). Postoperatively, he exhibited further neurological improvement. At a follow-up examination four months later, he had a normal neurological status in all extremities. Repeat RT-PCR testing for SARS-CoV-2 one month after casirivimab/indevimab administration remained negative, and he showed no clinical signs of COVID-19.

DISCUSSION

The treatment of COVID-19 has been a major challenge for healthcare systems worldwide since the beginning of the pandemic. In an effort to help patients as safely and quickly as possible, various therapeutic approaches have been implemented in practice. The use of immunomodulatory antiviral therapy appeared to be an extremely beneficial option for treating mild COVID-19 cases in outpatients at risk of developing severe disease. However, due to the exceptional efficacy of casirivimab/imdevimab, initially intended for outpatient use in patients with mild disease, the first attempts at hospital treatment with this drug began, yielding positive results [10]. Based on these findings, official recommendations for the administration of casirivimab/imdevimab in hospitalized patients were published in November 2021 [11].

The indications for monoclonal antibody antiviral therapy include ambulatory patients with +mild to moderate COVID-19 who are at high risk of progression, hospitalization, or fatal outcome.

Monoclonal antibodies are administered as a single dose, followed by patient isolation to prevent reinfection. This therapy can also be used in hospitalized

postizanje adekvatnog imunološkog odgovora na infekciju kod onih pacijenata koji nisu postigli adekvatan odgovor na infekciju, odnosno kod onih koji su imali visok titar virusa [8,14].

Naš pacijent je imao blagu kliničku sliku, uredan nalaz RTG pluća i tokom hospitalizacije nije zahtevao primenu oksigenoterapije. Pacijent nije imao rizik za tešku formu COVID-19, ali uzimajući u obzir njegovo stanje i povredu vratne kičme, kao i neophodnost strogog mirovanja, gde bi i kašalj mogao dodatno da iskomplikuje tok osnovne bolesti, spadao je u pacijente sa visokim rizikom. Tokom njegovog lečenja bilo je važno sprečiti razvoj težih simptoma ove bolesti, koji bi mogli da otežaju i dodatno prolongiraju njegovo operativno lečenje.

Ovaj mladi čovek imao je povredu vratnih pršljenova, sa posledičnom stenozom kičmenog kanala i znacima mijelopatije, kao i prisustvom spinalne nestabilnosti (engl. *spinal instability*), što se smatra indikacijom za urgentno hiruško lečenje [15-20]. Iz tog razloga, još jedan važan cilj koji smo imali tokom lečenja ovog pacijenta lekom casirivimab/indevimab bio je postizanje brze negativizacije nazofaringealnog brisa na SARS-CoV-2, koja je potvrđena u literaturi [10,11], a postignuta je i u ovom slučaju. Uz primenu svih dostupnih modaliteta lečenja i nege koji su nam bili dostupni, uspešno su izbegnute potencijalne komplikacije odlaganja hiruškog lečenja povreda kičme, za koje je zabeleženo učestalije javljanje tokom COVID-19 pandemije [21]. Kod povreda kičme sa prisutnom kompresijom savetuje se hiruško lečenje u vremenskom periodu od 8 do 24 sata od povređivanja kako bi se postigli najbolji rezultati u oporavku neurološke funkcije [22,23]. Iako je pacijent operisan nekoliko dana kasnije, njegov oporavak je protekao uredno, sa neurološkim nalazom koji ne ukazuje na zaostale neurološke ispade.

U literaturi postoji mali broj studija u kojima je lek casirivimab/indevimab primenjivan kod hospitalizovanih pacijenata sa prisutnom blagom kliničkom slikom [24], među kojima i jedna koja se bavi primenom leka casirivimab/indevimab kod pacijenata koji su bili na niskim dozama kiseonične potpore [14], uz ohrabrujuće rezultate, što se slaže sa ishodom lečenja koji je postignut kod našeg pacijenta.

ZAKLJUČAK

Kroz ovaj slučaj uspešno je prikazano da je uz multidisciplinarni pristup lečenju pacijenta, kao i primenu imunomodulatorne terapije, postignuto brzo izlečenje COVID-19 i negativizacija nazofaringealnog brisa na SARS-CoV-2, a zatim i urgentno hiruško lečenje akutne povrede vratnog dela kičme, koje je pretilo da permanentno ugrozi kvalitet života našeg mladog pacijenta.

patients who meet the same risk criteria and who are asymptomatic or have mild to moderate disease but are hospitalized for reasons unrelated to COVID-19 [2,12].

During the use of monoclonal antibodies in COVID-19 treatment, frequent viral resistance was observed when a single antibody was used, prompting the introduction of combination therapy with casirivimab/imdevimab [13]. This approach has demonstrated excellent treatment efficacy and prevented resistance development. Casirivimab and imdevimab are high-affinity human monoclonal IgG antibodies that bind directly to the SARS-CoV-2 spike (S) protein, preventing the virus from entering host cells [2].

According to recommendations, casirivimab/imdevimab is used in outpatient settings for patients in the early phase of infection who do not require oxygen therapy but are at high risk for severe COVID-19. The goal of this therapy is to achieve an adequate immune response in patients who have not mounted a sufficient response to the infection or who have a high viral load [8,14].

Our patient had a mild clinical presentation, normal chest X-ray findings, and did not require oxygen therapy during hospitalization. Although he was not at risk for severe COVID-19, considering his cervical spine injury and the necessity for strict immobilization-where even coughing could complicate his primary condition-he was classified as a high-risk patient. Preventing the progression of severe symptoms was crucial to avoid further delays in the necessary surgical treatment.

This young man sustained cervical spine injuries, resulting in spinal canal stenosis, myelopathy, and spinal instability, which are indications for urgent surgical intervention [15-20]. Therefore, another important goal of administering casirivimab/imdevimab was to achieve rapid SARS-CoV-2 clearance from the nasopharyngeal swab, as documented in the literature [10,11], and successfully achieved in this case. By utilizing all available treatment modalities and care strategies, we successfully avoided complications associated with delaying spinal surgery, which had been more frequently reported during the COVID-19 pandemic [21]. For spinal injuries with compression, surgery is recommended within 8 to 24 hours of injury to achieve the best neurological recovery outcomes [22,23]. Although our patient underwent surgery several days later, his recovery progressed favorably, with no residual neurological deficits.

The literature contains few studies on the use of casirivimab/imdevimab in hospitalized patients with mild clinical presentation [24], including one study in-

Pokazali smo i da je *off-label* primena imumodulatorne antivirusne terapije monoklonskim antitelima kod obolelih od COVID-19 delotvorna i spasonosna, ali i indikovana kod pacijenata koji su hospitalizovani iz nekog drugog medicinskog razloga, a ne zbog COVID-19, kod kojih nije prošlo više od 5 dana od pojave prvih simptoma, kod pacijenata koji zahtevaju dalju hospitalizaciju i lečenje ili kod pacijenata koji mogu biti otpušteni na dalje kućno lečenje.

Ovi zaključci su veoma važni i za ubuduće, u cilju daljeg pristupa lečenja pacijenata sa različitim virusnim infekcijama, a za koje ne postoji specifična antivirusna ili preventivna terapija.

Sukob interesa: Nije prijavljen.

volving patients receiving low-dose oxygen therapy [14], which showed promising results. These findings align with the positive treatment outcome observed in our patient.

CONCLUSION

This case successfully demonstrates that a multidisciplinary approach, combined with immunomodulatory therapy, enabled rapid COVID-19 recovery and SARS-CoV-2 clearance, followed by urgent surgical treatment of an acute cervical spine injury that threatened the young patient's quality of life.

We have also shown that the off-label use of monoclonal antibody-based immunomodulatory therapy for COVID-19 is both effective and life-saving. It is particularly indicated for patients hospitalized for reasons other than COVID-19, provided that no more than five days have elapsed since symptom onset, for those requiring ongoing hospitalization and treatment, or for patients who can be discharged for home care.

These findings are highly significant for future treatment strategies in patients with various viral infections for which no specific antiviral or preventive therapy exists.

Conflict of interest: None declared.

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