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CASE REPORT PRIKAZ BOLESNIKA

LONG TERM MANAGEMENT OF COMPLEX PATIENT WITH COMMON VARIABLE IMMUNODEFICIENCY – A CASE REPORT

DUGOTRAJNO PRAĆENJE KOMPLEKSNOG PACIJENTA S OBIČNOM VARIJABILNOM IMUNODEFICIJENCIJOM – PRIKAZ BOLESNIKA

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Abstract

Common variable immunodeficiency (CVID) is a primary immune disorder that results from insufficient immunoglobulin (IG) secretion. Hypogammaglobulinemia is currently treated with substitute IGs, however, the substantial variation of post-application IG levels, as well as the development of complex clinical manifestations in patients set up a significant challenge for their physicians. A 33-year-old male patient has been followed-up with the diagnosis of CVID. From early childhood, he presented with recurrent respiratory infections. In 2010, he was diagnosed with CVID. Treatment was started with substitute intravenous (IV) IG. During a 9-year follow-up in day care and stationary University Hospital Centre (UHC) departments, the patient experienced a total of 14 respiratory and 2 digestive system complications of the disease. Eventually, he developed a non-infectious pulmonary complication – granulomatous-lymphocytic interstitial lung disease (GLILD). In 2015, treatment was altered to accomplish satisfactory IG levels from IV to conventional subcutaneous (SC) IG therapy. Due to easier application and greater volume of subcutaneously inserted IG, the patient was switched to a new generation of SCIG therapy in 2019. Additionally, corticosteroids and mesalazine were also administered, and with current treatment the patient is stable. In the 9-year period, he never reached the preferable reference levels of IGs presumed for healthy individuals. Respiratory infections are common CVID complications, but it is necessary to consider the autoimmune and neoplastic manifestations of the disease. A multidisciplinary approach, regular follow-up, and regular application of IG therapy are the key factors in decreasing morbidity and mortality in these patients.

Keywords: common variable immunodeficiency, CVID, complications, therapy

Sažetak

Obična varijabilna imunodeficijencija (CVID) oblik je primarne imunodeficijencije koja nastaje kao posljedica smanjene proizvodnje imunoglobulina (IG). Posljedična hipogamaglobulinemija trenutačno se liječi nadomještanjem

IG-a, a značajne varijacije u postaplikacijskim vrijednostima IG-a kao i razvoj komplikacija osnovne bolesti predstavljaju značajan izazov u liječenju ovih pacijenata. Prikazujemo 33-godišnjeg muškarca koji se više godina prati s dijagnozom CVID-a. Od ranog djetinjstva pokazivao je podložnost opetovanim respiratornim infekcijama. Pacijentu je 2010. godine dijagnosticiran CVID te započinje liječenje intravenskim (IV) nadomjestkom IG-a. Tijekom devetogodišnjeg praćenja putem dnevne bolnice i stacionara Kliničkoga bolničkog centra pacijent je razvio ukupno 14 respiratornih i dvije probavne komplikacije osnovne bolesti. Razvio je i neinfektivnu plućnu komplikaciju: granulomatoznu limfocitnu intersticijsku plućnu bolest (GLILD). Bolesnik je 2015. godine sa svrhom postizanja poboljšanih vrijednosti IG-a prešao s IV na konvencionalnu supkutanu terapiju (SC) IG-a. Uslijed lakše primjene i povećanog volumena supkutanog unosa IG-a, 2019. godine dotadašnja terapija zamijenjena je novom generacijom SCIG pripravaka. Kao dodatak, propisani su mu kortikosteroidi i mesalazin te je pacijent s trenutačnom terapijom stabilno. U posljednjih devet godina nikada nije postigao referentne vrijednosti za zdrave osobe. Respiratorne infekcije česta su komplikacija CVID-a, ali je potrebno razmatrati i autoimune te neoplastične manifestacije ove bolesti. Multidisciplinarni pristup, redovito praćenje i redovita primjena imunoglobulina ključni su čimbenici u smanjenju morbiditeta i mortaliteta u pacijenata s CVID-om.

Ključne riječi: obična varijabilna imunodeficijencija, CVID, komplikacije, terapija

INTRODUCTION

Common variable immunodeficiency (CVID) is a primary immunodeficiency with an estimated prevalence ranging from 1:10 000 to 1:50 000 (1). The highest prevalence of CVID has been detected in North America, followed by Europe and Australia (2). Many cases are sporadic; however, 5–25% of them can be familial (3). Characteristic findings include reduced serum levels of immunoglobulin G (IgG), immunoglobulin M (IgM), and/or immunoglobulin A (IgA) by two or more standard deviations from the normal mean (4). The knowledge of the pathogenesis of CVID is increasing, but the disease is still unknown. Patients are usually diagnosed between the age of 20 and 40, however, the time interval between the first symptoms and diagnosis is 6–8 years (4). Patients with the diagnosis of CVID present with various clinical manifestations: recurrent infections, autoimmune manifestations, lymphoproliferative disorders, chronic lung disease, gastrointestinal disease, lymphoma, and other selected cancers. Encapsulated bacteria such as *Streptococcus pneumoniae, and Haemophilus influenzae are often causing diverse infections (2). The aim of this* case report was to provide a summary of the patient's CVID symptoms and complications, to point out the importance and difficulties of the patient's regular follow-up, and to present the advantages of subcutaneous (SC) immunoglobulin (IG) therapy.

CASE PRESENTATION

We present a case report of a 33-year-old male patient who has been followed up with the diagnosis of CVID. He had no significant disorders in his family history. From early childhood, he experienced numerous recurrent respiratory infections (cases of pneumonia, acute sinusitis, bronchitis, streptococcal pharyngitis) and presented with clubbed fingers. In 2010, the patient was admitted to General Hospital (GH) with

UVOD

Obična varijabilna imunodeficijencija (CVID) jest primarna imunodeficijencija s procijenjenom prevalencijom u rasponu od 1:10.000 do 1:50.000 (1). Najveća prevalencija CVID-a otkrivena je u Sjevernoj Americi, a zatim u Europi i Australiji (2). Mnogi su slučajevi ove bolesti sporadični, no, 5 – 25% njih može biti rezultat obiteljske povijesti (3). Karakteristični nalazi uključuju smanjene serumske razine imunoglobulina G (IgG), imunoglobulina M (IgM) i/ili imunoglobulina A (IgA) za dvije ili više standardnih devijacija od normalne srednje vrijednosti (4). Sve se više znanja i informacija saznaje o patogenezi CVID-a, ali je bolest još uvijek nepoznata. Bolesnicima se obično bolest dijagnosticira između 20. i 40. godine života, no vremenski je razmak od pojave prvih simptoma do dijagnoze šest do osam godina (4). Bolesnici s dijagnozom CVID-a imaju različite kliničke manifestacije: rekurentne infekcije, autoimune manifestacije, limfoproliferativne poremećaje, kronične bolesti pluća, gastrointestinalne bolesti, limfome i druge vrste raka. Inkapsulirane bakterije kao što su *Streptococcus pneumoniae i Haemophilus influenzae često uzrokuju različite infekcije (2). Cilj ovog* prikaza slučaja bio je dati sažetak bolesnikovih simptoma i komplikacija CVID-a, ukazati na važnost i poteškoće redovitog praćenja bolesnika te prikazati prednosti supkutane (SC) terapije imunoglobulinima (IG).

PRIKAZ BOLESNIKA

Prikazujemo slučaj 33-godišnjeg muškarca koji se više godina prati s dijagnozom CVID-a. U obiteljskoj povijesti nije imao značajnih poremećaja. Od ranog djetinjstva pokazivao je podložnost rekurentnim respiratornim infekcijama (upale pluća, akutni sinusitis, bronhitis, streptokokni faringitis) i imao je batićaste prste. Bolesnik je 2010. primljen u opću bolnicu sa simptomima druge bronhopneumonije, a nalazi dija-

Table 1 List of patient's CVID complications from 2011 to 2020.
Tablica 1. Popis bolesnikovih komplikacija CVID-a od 2011. do 2020.

Year / Godina	Diagnosis / Dijagnoza	Signs and symptoms / Znakovi i simptomi
2011	Acute sinusitis / Akutni sinuitis	purulent nose secretion / gnojni iscjedak iz nosa
2012 / 2012.	Simultaneous acute sinuitis and right sided pneumonia / Istovremeni akutni sinusitis i desnostrana upala pluća	fever – 38˚C, purulent nose secretion, productive cough / vrućica: 38˚C, gnojni iscjedak iz nosa, produktivni kašalj
	Acute sinuitis, acute exacerbation of chronic bronchitis / Akutni sinusitis, pogoršanje kroničnog bronhitisa	purulent nose secretion, productive cough, inspiratory and expiratory wheezing / gnojni iscjedak iz nosa, produktivni kašalj, udisajni i izdisajni hropci
2013 / 2013.	Left-sided pneumonia / Lijevostrana upala pluća	fever – 39˚C, productive cough, chills and shivering, sore throat, inspiratory wheezing / vrućica: 39˚C, produktivni kašalj, zimice i tresavice, grlobolja, udisajni hropci
	Acute exacerbation of chronic bronchitis / akutno pogoršanje kroničnog bronhitisa	productive cough, left-sided basally impaired respiratory sound / produktivni kašalj, lijevostrano bazalno smanjeni zvuk disanja
2014 / 2014.	No complications / Bez komplikacija	–
2015 / 2015.	Acute sinusitis / Akutni sinuitis	fever – 39˚C, purulent nose secretion, frontal sinus pain / vrućica: 39˚C, gnojni iscjedak iz nosa, bol u području frontalnog sinusa
	Pneumonia / Upala pluća	fever – 38˚C, dry cough, chest pain / vrućica: 38˚C, suhi kašalj, bol u prsištu
2016 / 2016.	Two episodes of right-sided pneumonia / Dvije epizode desnostrane upale pluća	productive cough, dyspnea, palpitations, right basal crackles / produktivni kašalj, otežano disanje, desno bazalno krepitacije
	Acute sinusitis / Akutni sinuitis	purulent nose secretion, painful maxillary sinus; positive sputum on *Klebsiella pneumoniae* / gnojni iscjedak iz nosa, bol u području maksilarnog sinusa; pozitivan iskašljaj na *Klebsiella pneumoniae*
2017 / 2017.	Left-sided pneumonia / Lijevostrana upala pluća	productive cough with greenish sputum, chills, fever – 38˚C, and chest pain; swabs of the nasopharynx were positive for *H. influenzae* / produktivni kašalj sa zelenkastim iskašljajem, tresavica, vrućica: 38˚C i bol u prsištu; bris nazofarinksa je bio pozitivan na *H. influenzae*
2018 / 2018.	Right-sided pneumonia / Desnostrana upala pluća	productive cough with greenish sputum, fever – 38.5˚C and chest pain / produktivni kašalj sa zelenkastim iskašljajem, vrućica: 38,5˚C i bol u prsištu
2019 / 2019.	Chronic gastritis, IBD-like colitis / Kronični gastritis, IBD-u sličan kolitis	diarrhea, loss of body weight, abdominal cramps, and bloating / proljev, gubitak na tjelesnoj težini, grčevi u trbuhu i napuhnutost
2020 / 2020.	Granulomatous-lymphocytic interstitial lung disease (GLILD) / Granulomatozno-limfocitička intersticijska plućna bolest (GLILD)	no symptoms, presented on thoracic CT scan / bez simptoma, prikazano na CT-u toraksa

symptoms of another bronchopneumonia and during disease evaluation results showed severe hypogammaglobulinemia. Subsequently, the patient was diagnosed with CVID. According to the guidelines, the patient started his treatment with substitute intravenous (IV) IGs. During the follow-up in day care and stationary University Hospital Center (UHC) departments from 2011 to 2020, the patient experienced a total of 14 respiratory (7 pneumonias, 5 acute sinusitis, 2 acute exacerbations of chronic bronchitis) and 2 digestive system (chronic gastritis, colitis) complications of CVID.

In 2011, while hospitalized in UHC, patient had significantly decreased levels of IgG – 1.9 g/L (healthy individuals 7–16 g/L), IgA <0.05 g/L (0.7–4 g/L), IgM <0,05 g/L (0.4–2.3 g/L). The timeline of the patient's CVID complications is presented in Table 1 and the

gnostičke evaluacije bolesti pokazali su tešku hipogamaglobulinemiju. Nakon toga je bolesniku dijagnosticiran CVID. Prema smjernicama, bolesnik je započeo liječenje intravenskim (IV) nadomjeskom IG-a. Tijekom praćenja putem dnevne bolnice i stacionara Kliničkog bolničkog centra (KBC) od 2011. do 2020. bolesnik je razvio ukupno 14 respiratornih (sedam pneumonija, pet akutnih sinusitisa, dvije akutne egzacerbacije kroničnog bronhitisa) i dvije probavne komplikacije (kronični gastritis, kolitis) CVID-a.

Godine 2011., dok je bio hospitaliziran u KBC-u, bolesnik je imao značajno snižene razine IgG – 1,9 g/L (zdrave osobe 7 – 16 g/L), IgA < 0,05 g/L (0,7 – 4 g/L), IgM < 0,05 g/L (0,4 – 2,3 g/L). Vremenski prikaz bolesnikovih komplikacija povezanih s CVID-om prikazan je u tablici 1, a najčešće su respiratorne infekcije, obič-

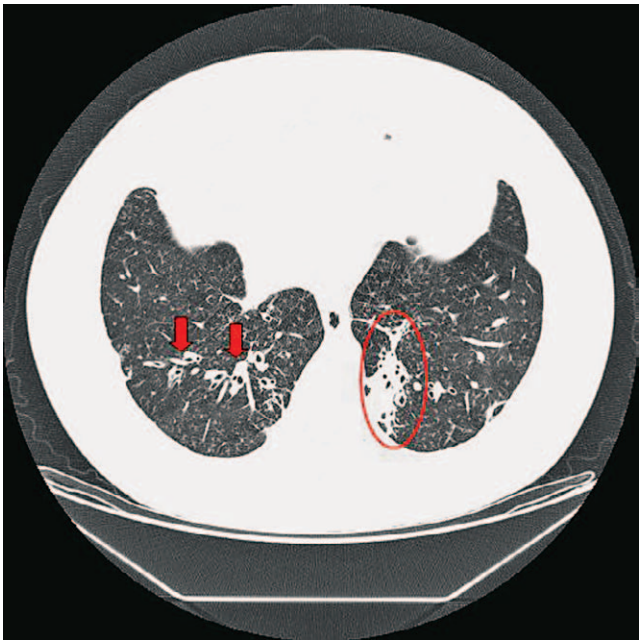

Figure 1 Thoracic CT scan (transversal view) with indicated peribronchial infiltration (red arrows) and pneumonia-like consolidation (red circle) – in 2017.
Slika 1. CT toraksa (transverzalni presjek) s istaknutim peribronhalnim infiltratom (crvene strjelice) i konsolidacijom pluća nalik na pneumoniju (crveni krug): 2017. godine

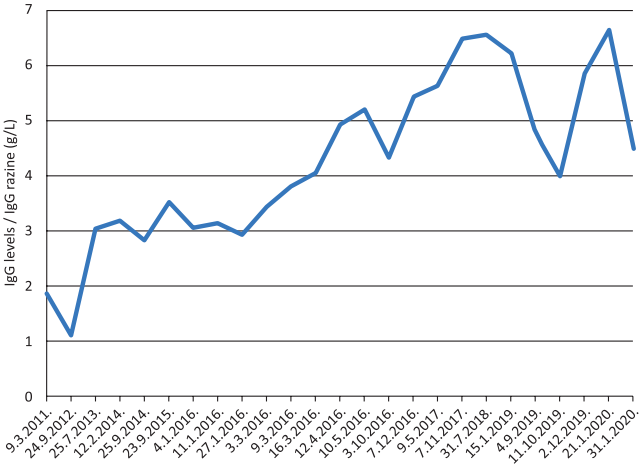

Figure 2 Levels of IgG during patient's follow up from 2011 to 2020.
Slika 2. Vrijednosti IgG-a tijekom praćenja pacijenta od 2011. do 2020.

most common ones are respiratory infections, usually pneumonia (Figure 1). In August 2019 patient presented with a new set of symptoms such as diarrhea, loss of weight, abdominal cramps, and bloating. Stool samples tested negative for bacteria and parasites and, even though a broad spectrum of antibiotics was given, he was not feeling better. In December 2019, he was diagnosed with chronic gastritis (*Helicobacter pylori*-negative). Gastrointestinal symptoms continually persisted, and he was admitted to UHC in 2020 for a thorough evaluation. Stool microbiology tests were positive for *Clostridium difficile* toxin and oral Vancomycin therapy was administered. Despite temporary improvement in clinical features of the disease, a few days later fecal calprotectin levels were high (86 µg). During a colonoscopy, biopsy specimens were taken and eventually showed inflamed bowel mucosa and epithelial granulocyte penetration with cryptal abscesses. Histopathological findings were consistent with inflammatory bowel disease (IBD)-like colitis. Besides standard treatment, corticosteroids and mesalazine were also administered, and currently patient is stable. During the above-mentioned evaluation, the patient underwent computed tomography (CT) scan of the thorax, abdomen, and pelvis. Thoracic images showed peribronchovascular thickening with mild deformations of bronchi and sporadic mucoid impactions with bilateral lung consolidations. Moreover, small lymph nodules with non-specific morphology were found. Selected

no pneumonije (slika 1). U kolovozu 2019. bolesniku su se pojavili novi simptomi kao što su proljev, gubitak težine, grčevi u trbuhu i nadutost. Uzorci stolice bili su negativni na bakterije i parazite te se bolesnik nije osjećao bolje iako je dobio širok spektar antibiotika. U prosincu 2019. godine dijagnosticiran mu je kronični gastritis (*Helicobacter pylori* – negativan). Gastrointestinalni simptomi neprestano su se manifesirali i bolesnik je 2020. primljen u KBC na temeljitu evaluaciju. Mikrobiološki testovi stolice bili su pozitivni na toksin *Clostridium difficile* i primijenjena je oralna terapija vankomicinom. Unatoč privremenom poboljšanju kliničke slike bolesti, nekoliko dana kasnije razine fekalnog kalprotektina bile su visoke (86 µg). Tijekom kolonoskopije uzeti su biopsijski uzorci koji su na kraju pokazali upalu crijevne sluznice i prodiranje epitelnih granulocita s kriptalnim apscesima. Patohistološki nalazi bili su u skladu s kolitisom sličnim upalnoj bolesti crijeva (UBC). Uz standardnu terapiju primijenjeni su i kortikosteroidi i mesalazin, a bolesnik je trenutno stabilno. Tijekom gore navedene evaluacije bolesnik je podvrgnut kompjutoriziranoj tomografiji (CT) toraksa, abdomena i zdjelice. Snimke toraksa pokazale su peribronhovaskularno zadebljanje s blagim deformacijama bronha i sporadične mukoidne impakcije s bilateralnim plućnim konsolidacijama. Uz to, pronađeni su mali limfni čvorići nespecifične morfologije. Odabrani nalazi pokazali su da je razvio i neinfektivnu plućnu komplikaciju: granulomatoznu intersticijsku plućnu bolest (GLILD).

Od 2011. do 2020. značajno su se promijenile mogućnosti liječenja oboljelih od CVID-a, a time i kvaliteta njihovog života. Naš bolesnik je 2010. godine započeo liječenje IV nadomjestkom IG-a (normalni humani imunoglobulin za IV infuziju – 30g/mjesečno). Nakon višestrukih nuspojava (crvenilo lica, dispneja,

findings were indicative of non-infectious pulmonary complication – granulomatous-lymphocytic interstitial lung disease (GLILD).

From 2011 to 2020, treatment options for CVID patients considerably changed and consequently their quality of life. Our patient started his treatment with substitute IV IG in 2010 (Human Normal Immunoglobulin for IV infusion – 30g/month). After multiple adverse effects (face redness, dyspnea, palpitations, sweating, tinnitus, hypertensive reactions) and to accomplish satisfactory IG levels, the patient was transferred from IV to conventional SCIG therapy in 2015. Initially, the dose of Human Normal Immunoglublin for IV injection was 50 mL/week but from 2015 to 2017 dosage changed from 80 mL/week (2015) to 100 mL/week (2016) and finally to 140 mL/2x week (2017). Due to easier application and greater volume of subcutaneously inserted IG, the patient was switched to Human Normal Immunoglobulin with Recombinant Human Hyaluronidase for SC injection in 2019. Starting dose was 400 mL/month, changed to 800mL/month and at beginning of 2020 dose was corrected to 1000 mL/month. The patient's IgG levels in the last 9 years are displayed in Figure 2. Retrospectively, IgG levels varied from the mean lowest of 1.12 g/L (2012) to the mean highest of 6.55 g/L (2018) and never reached the lower limit of 7g/L for healthy individuals.

DISCUSSION

Even though CVID is a rare condition, it has a broad clinical spectrum, it may present at any age, and it may be difficult to recognize. In this report, we presented the long-term management of a complex patient with CVID and his infectious, pulmonary, autoimmune, and gastrointestinal complications.

The majority of CVID patients present with numerous acute and recurrent infections, mostly recurrent sinusitis, bronchitis, and otitis media (2). A study has shown that approximately 84% of CVID patients have experienced pneumonia at least once in their lifetime but, before the initial diagnosis, most of them have suffered multiple episodes (5). In a retrospective study, Thickett et al. (6) reported that bronchiectases occur in 70% of patients. A study by Bates et al. (7) divided 69 patients with CVID into 3 groups based on the type of pulmonary disease present. In approximately 19% of cases, authors detected GLILD and, in comparison to other groups, these patients had worse outcomes. A systematic review by Lamers et al. (8) reported that adult CVID patients with GLILD have a reduction in life expectancy by more than 50%. Despite the radiological findings of GLILD in our patient, that diagnostic suspicion must be taken with precaution. In 2020, the patient underwent a thoracic CT scan where lung alterations associated with GLILD were detected but

palpitacije, znojenje, tinitus, hipertenzivne reakcije) i postizanja zadovoljavajuće razine IG-a bolesnik je 2015. prebačen s IV na konvencionalnu supkutanu (SC) IG terapiju. U početku je doza normalnoga humanog imunoglobulina za IV injekciju bila 50 mL/tjedno, ali od 2015. do 2017. doza se promijenila s 80 mL/tjedno (2015.) na 100 mL/tjedno (2016.) i konačno na 140 mL / 2x tjedno (2017.). Uslijed lakše primjene i povećanog volumena supkutanog unosa IG-a, 2019. godine dotadašnja terapija zamijenjena je normalnim humanim imunoglobulinom s rekombinantnom humanom hijaluronidazom za supkutanu (SC) injekciju. Početna doza bila je 400 mL/mjesečno, promijenjena je na 800 mL/mjesečno, a početkom 2020. godine doza je korigirana na 1000 mL/mjesečno. Bolesnikove razine IgG-a u posljednjih devet godina prikazane su na slici 2. Retrospektivno, razine IgG-a varirale su od najniže srednje vrijednosti od 1,12 g/L (2012.) do najviše prosječne vrijednosti od 6,55 g/L (2018.) i nikada nisu dosegle donju granicu od 7 g/L za zdrave osobe.

RASPRAVA

Iako je CVID rijetko stanje, ima širok klinički spektar, može se pojaviti u bilo kojoj dobi i može ga biti teško prepoznati. U ovom slučaju prikazali smo dugotrajno liječenje bolesnika s raznim komplikacijama, CVID-om i njegovim infektivnim, plućnim, autoimunim i gastrointestinalnim komplikacijama.

Većina bolesnika s CVID-om ima brojne akutne i rekurentne infekcije, uglavnom rekurentne sinusitise, bronhitise i upale srednjeg uha (2). Istraživanja su pokazala da je približno 84% bolesnika s CVID-om doživjelo upalu pluća barem jednom u životu, ali je većina njih prije prve dijagnoze imala višestruke epizode (5). U retrospektivnoj studiji koju su proveli Thickett i suradnici (6) navedeno je da se bronhiektazije javljaju u 70% bolesnika. U studiji koju su proveli Bates i suradnici (7) 69 bolesnika s CVID-om podijeljeno je u tri skupine na temelju vrste plućne bolesti koja je kod njih prisutna. U približno 19% slučajeva autori su otkrili prisutnost GLILD-a i, u usporedbi s drugim skupinama, ti su bolesnici imali lošije ishode. U sustavnom pregledu Lamersa i suradnika (8) navodi se da odrasli bolesnici s CVID-om i GLILD-om imaju kraći očekivani životni vijek za više od 50%. Unatoč radiološkim nalazima GLILD-a kod našeg bolesnika, tu dijagnostičku sumnju treba uzeti s dozom opreza. Godine 2020. bolesnik je podvrgnut CT-u toraksa na kojem su otkrivene plućne promjene povezane s GLILD-om, ali one nisu histološki verificirane. Ipak, ove nalaze je potrebno pratiti budući da se limfoproliferativna bolest može pojaviti u 31% bolesnika s GLILD-om (7). Uz respiratorne komplikacije postoji i velik broj upalnih i infektivnih gastrointestinalnih poremećaja, koji se

they were not histologically verified. Nevertheless, these findings must be monitored since the lymphoproliferative disease can occur in 31% of patients with GLILD (7). In addition to respiratory complications, there is also a great number of inflammatory and infectious gastrointestinal disorders, mainly presenting in form of acute or chronic diarrhea (2). A study by Muşabak et al. (9) provided evidence of an association between chronic diarrhea, low body weight, and deterioration of B and T cell immunity. Studies have also shown that there are no significant discrepancies in the prevalence rates of *H. pylori* between CVID patients and healthy controls (2). Although the presence of *H. pylori* often results in chronic gastritis (1), our patient presented with *H. pylori*-negative chronic gastritis. Individuals with CVID are more prone to malignancy and most cancer cases include the digestive system and the lymphoid tissues (usually extranodal non-Hodgkin B cell in type) (2, 10–12). An interesting fact is that selected CVID patients showed evidence of radiosensitivity and should be protected from unnecessary radiographic diagnostic and therapeutic procedures (13).

Our patient has increased body weight (BMI 34.0 kg/m^2 – 2019) and a more difficult trajectory for him to reach the reference levels of IGs was expected. He never reached the desired IG levels which were one of the main reasons for him to be transferred to the newest therapy. The newest generation of SCIG therapy has 2 components: immunoglobulin and recombinant human hyaluronidase. It allows SC administration of 10–15 times greater volume of IG than conventional SCIG therapy (up to 600 mL of IG) (14). The key improvement in CVID therapy was the addition of human hyaluronidase which disintegrates SC fat and ensures a greater volume of inserted IG. Therefore, it offers increased bioavailability, need for fewer needle sticks, reduced frequency of treatment sessions, lower peak than IGIV with the same 4-week dosing interval and it also provides lesser systematic adverse effects and home-self administration (15). In recent years, hematopoietic stem cell transplantation is emerging as a potential therapeutic option for severe, conventional therapy-resistant cases of CVID with some form of immune system dysregulation (2, 3).

CONCLUSION

Patient with common variable immunodeficiency (CVID) is a group of patients that may be quite demanding for treatment, follow-up, and remission accomplishment due to recurrent complications. Although respiratory infections are common CVID complications, it is also necessary to expand the diagnostic evaluation to identify the autoimmune and neoplastic manifestations of the disease. Frequent infections, structural lung damage, and the presence of autoimuglavnom manifestiraju u obliku akutnog ili kroničnog proljeva (2). U studiji koju su proveli Muşabak i suradnici (9) navedeni su dokazi o povezanosti između kroničnog proljeva, niske tjelesne težine i pogoršanja imuniteta B-stanica i T-stanica. Istraživanja su također pokazala da nema značajnih odstupanja u stopama prevalencije *H. pylori* između bolesnika s CVID-om i zdravih osoba (2). Iako prisutnost *H. pylori* često rezultira kroničnim gastritisom (1), naš je bolesnik imao *H. pylori*-negativni kronični gastritis. Bolesnici s CVID-om skloniji su zloćudnim bolestima, a većina slučajeva raka uključuje probavni sustav i limfna tkiva (obično ekstranodalni ne-Hodgkinov limfom B-stanica) (2, 10–12). Zanimljiva je činjenica da su odabrani bolesnici s CVID-om pokazali simptome radiosenzibilnosti te ih treba zaštititi od nepotrebnih radiografskih dijagnostičkih i terapijskih postupaka (13).

Naš bolesnik ima povećanu tjelesnu težinu (BMI 34,0 kg/m^2: 2019.) i očekivan je teži način postizanja referentnih razina IG-a. Nikada nije postigao željene razine IG-a, što je bio jedan od glavnih razloga da se prebaci na najnoviju terapiju. Najnovija generacija SCIG terapije ima dvije komponente: imunoglobulin i rekombinantnu humanu hijaluronidazu. Takva terapija omogućuje SC primjenu 10–15 puta većeg volumena IG-a od konvencionalne SCIG terapije (do 600 mL IG) (14). Ključno poboljšanje u CVID terapiji bio je dodatak humane hijaluronidaze koja razgrađuje potkožno (SC) masno tkivo i osigurava veći volumen ubrizganog IG-a. Stoga nudi povećanu bioraspoloživost, potrebu za manjim brojem uboda iglama, smanjenu učestalost tretmana, niži vršni učinak od IGIV-a s istim četverotjednim intervalom doziranja, a također omogućuje manje sustavne nuspojave i primjenu kod kuće (15). Posljednjih se godina transplantacija hematopoetskih matičnih stanica pojavljuje kao potencijalna terapijska opcija za teške slučajeve CVID-a otporne na konvencionalnu terapiju s određenim oblikom disregulacije imunološkog sustava (2, 3).

ZAKLJUČAK

Bolesnici s običnom varijabilnom imunodeficijencijom (CVID) skupina su bolesnika koja može biti vrlo zahtjevna za liječenje, praćenje i postizanje remisije zbog ponavljajućih komplikacija. Iako su respiratorne infekcije česta komplikacija CVID-a, također je potrebno proširiti dijagnostičku evaluaciju te razmatrati i autoimune te neoplastične manifestacije ove bolesti. Česte infekcije, strukturna oštećenja pluća i prisutnost autoimune bolesti ili karcinoma određuju prognozu bolesnika. Štoviše, razina oštećenja ciljnih organa i uspjeh profilakse protiv infekcija također mogu utjecati na prognozu. Stoga su multidisciplinarni pristup, redovito praćenje i redovita primjena imunoglobulina

mune disease or cancer determine the prognosis for patients. Moreover, the extent of end-organ damage and the success of prophylaxis against infections may also influence the prognosis. Therefore, a multidisciplinary approach, regular follow-up, and application of immunoglobulins are the key factors in decreasing the disability and mortality in patients with CVID.

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ključni čimbenici u smanjenju invaliditeta i mortaliteta u bolesnika s CVID-om.

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