HOČKINOV LIMFOM U TRUDNOĆI: PRIKAZ SLUČAJA I PREGLED LITERATURE

PRIKAZ SLUČAJA

CASE REPORT

HODGKIN'S LYMPHOMA IN PREGNANCY: CASE REPORT AND REVIEW OF LITERATURE

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SAŽETAK

Uvod/Cilj: Incidenca Hočkinovog limfoma (HL) je visoka u reproduktivnom periodu tako da problem javljanja ovog maligniteta tokom trudnoće predstavlja značajan problem u svakodnevnoj kliničkoj praksi. Cilj ovog rada je da se kroz prikaz slučaja prikaže karakteristični klinički tok i da se kroz pregled literature analiziraju do sada objavljeni podaci.

Prikaz slučaja: Trudnica, starosne dobi 33 godine, tokom trećeg trimestra trudnoće razvija otok vrata, noćno preznojavanje, svrab uz gubitak telesne mase. Ultrazvučnim pregledom otkrivena je značajna limfadenopatija u supraklavikularnoj regiji. Hirurška ekstirpacija limfnog čvora uz patohistološku verifikaciju potvrdila je dijagnozu Hočkinovog limfoma. S obzirom na trudnoću i ograničenu primenu radiografske dijagnostike, magnetna rezonanca (MR) je urađena i potvrdila je generalizovanu limfadenopatiju s posledičnom hidronefrozom desnog bubrega. Nakon postavljanja dijagnoze uznapredovalog stadijuma HL, odlučeno je da se započne specifično hematološko lečenje primenom citostatske terapije. Porođaj je sproveden u 37. nedelji gestacije prirodnim putem, bez komplikacija po majku i novorođenče. Nakon porođaja, sprovedena je kompletna reevaluacija bolesti, uz odluku da se lečenje nastavi do ukupno šest ciklusa hemioterapije prema ABVD (adriablastin, bleomicin, vinblastin, dakarbazin) protokolu. Nakon šest ciklusa hemioterapije, postignuta je metabolička remisija bolesti.

Zaključak: Lečenje Hočkinovog limfoma tokom trudnoće predstavlja kompleksan izazov koji zahteva koordinisan multidisciplinarni pristup i personalizovani plan lečenja.

Ključne reči: Hočkinov limfom, trudnoća, ABVD

ABSTRACT

Introduction/Objective: The incidence of Hodgkin lymphoma (HL) is high during the reproductive years, making the occurrence of this malignancy during pregnancy a significant issue in everyday clinical practice. The aim is to present a case study demonstrating the characteristics of clinical courses and analyze published data through a literature review.

Case report: A 33-year-old pregnant woman in her third trimester developed neck swelling, night sweats, itching, and weight loss. Ultrasound examination revealed significant lymphadenopathy in the supraclavicular region. Surgical excision of the lymph node and pathological verification confirmed the diagnosis of Hodgkin lymphoma. Given the pregnancy and the limited use of radiographic diagnostics, magnetic resonance imaging (MR) was performed and confirmed generalized lymphadenopathy with resultant hydronephrosis of the right kidney. After diagnosing advanced-stage HL, it was decided to initiate specific hematologic treatment with chemotherapy. Delivery was carried out at 37 weeks of gestation via vaginal delivery, with no complications for the mother or newborn. Following delivery, a complete disease reevaluation was conducted, and it was decided to continue treatment with a total of six cycles of chemotherapy according to the ABVD (adriamycin, bleomycin, vinblastine, dacarbazine) protocol. After six cycles of chemotherapy, metabolic remission of the disease was achieved.

Conclusion: Managing Hodgkin lymphoma during pregnancy presents a complex challenge requiring a coordinated multidisciplinary approach and a personalized treatment plan.

Keywords: Hodgkin lymphoma, pregnancy, ABVD

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UVOD

Hočkinov limfom predstavlja hronično maligno limfoproliferativno oboljenje sa bimodalnom distribucijom javljanja, i to u trećoj deceniji života, kao i u šestoj deceniji [1]. Imajući u vidu da prvi pik obuhvata i žene u reproduktivnom periodu, literaturna incidenca javljanja za vreme trudnoće je oko 3% ukupnih pacijenata. [2]. Prema sistematskom pregledu literature objavljenom 2022. godine gde je cilj ispitivanja bio procena krajnjeg ishoda kod trudnice i ploda nakon postavljanja dijagnoze Hočkinovog limfoma za vreme trudnoće, zaključak je bio da se incidenca kongenitalnih malformacija kao i spontanih pobačaja statistički značajno ne razlikuje kod trudnica sa HL u odnosu na trudnice kod kojih navedena bolest nije bila dijagnostikovana. Od ostalih mogućih ishoda izdvojila se veća učestalost prevremenih porođaja, anemijskog sindroma koji zahteva primenu krvnih komponenata, kao i venskog tromboembolizma [3]. Cilj ovog rada je da se kroz prikaz slučaja prikaže karakteristični klinički tok i da se kroz pregled literature analiziraju do sada objavljeni podaci.

PRIKAZ SLUČAJA

Trudnica, starosne dobi 33 godine, tokom trećeg trimestra treće trudnoće razvija otok vrata, noćno preznojavanje, svrab uz gubitak telesne mase. Ultrazvučnim pregledom mekih tkiva vrata opisana je signifikantna limfadenopatija dominantno u donjem jugularnom spratu i supraklavikualrno levo, promera 30x24 mm i 43x20 mm. Tada se u laboratorijskim analizama u nalazu KKS izdvojila leukocitoza sa neutrofilijom i monocitozom (Le 23,9x10^9/L, Neu 20,3 x10^9/L, Mon 1,6x10^9/L), mikrocitna anemija srednje teškog stepena (Hgb 86 g/L, MCV 72,4 fL), trombocitoza (Tr 626x10^9/L), a u biohemijskim analizama hipoalbuminemija (albumin 30g/L), hipoferemija uz hiperferitinemiju (Fe 4,1 umol/L, TIBC 59,1 umol/L, feritin 798,7 ug/L), povišen nivo alkalne fosfataze (ALP 274 U/L), laktat dehidrogenaze (LDH 674 U/L), beta 2 mikroglobulina (beta 2 M 3,59 mg/L), C reaktivnog proteina (CRP 162,9 mg/L), i u testovima hemostaze hiperfibrinogenemija (fibrinogen 8,1 g/L). Ostali nalazi su bili u granicama referentnih vrednosti. Ginekološki pregled je bio uredan. Odlučeno je da se navedeni limfni nodus supraklavikularne regije levo ekstirpira u celosti. Na osnovu pristiglog histopatološkog nalaza postavljena je dijagnoza HL, tipa nodularne skleroze, sa karakterističnim imunofenotipom: LCA-, CKPAN-, OCT2-, BOB1-, Pax-5-/+, CD79alfa -, CD20-, CD19-, CD15-/+, CD30+, Fascin +, MUM-1+, EBV-, bcl-6+, CD34-, CD3-, CD5-, CD4-, CD8-, ALK-. U okviru dopunske dijagnostike urađen je pregled vrata, grudnog koša, abdomena i male karlice magnetnom rezonan-

INTRODUCTION

Hodgkin's lymphoma is a chronic malignant lymphoproliferative disease with a bimodal distribution of occurrence in the third decade of life as well as in the sixth decade [1]. Considering that the first peak also includes women in the reproductive period, the literature incidence of occurrence during pregnancy is about 3% of total patients. [2]. According to a systematic review of the literature published in 2022, where the study aimed to assess the final outcome of pregnant women and the fetus after the diagnosis of Hodgkin's lymphoma during pregnancy, the conclusion was that the incidence of congenital malformations as well as spontaneous abortions is not statistically significantly different in pregnant women with HL compared to pregnant women in whom the mentioned disease was not diagnosed. Among the other possible outcomes, a higher frequency of premature births, anemic syndrome requiring the use of blood components, and venous thromboembolism [3] were singled out. This paper aims to present a characteristic clinical course through a case report and analyze the data published so far through a literature review.

CASE REPORT

A pregnant woman, aged 33, during the third trimester of her third pregnancy, developed swelling of the neck, night sweats, and itching with loss of body weight, an ultrasound examination of the soft tissues of the neck described significant lymphadenopathy dominantly in the lower jugular floor and supraclavicular left, diameter 30x24mm, and 43x20mm. Then, in the laboratory analysis, leukocytosis with neutrophilia and monocytosis (Le 23.9x10^9/L, Neu 20.3x10^9/L, Mon 1.6x10^9/L), microcytic anemia of medium severity (Hgb 86 g/L, MCV 72.4 fL) were distinguished., thrombocytosis (Tr 626x10^9/L), and in biochemical analyzes hypoalbuminemia (albumin 30g/L), hypoferremia with hyperferritinemia (Fe 4.1 umol/l, TIBC 59.1 umol/L, ferritin 798.7 ug/L), elevated level of alkaline phosphatase (ALP 274 U/L), lactate dehydrogenase (LDH 674 U/L), beta 2 microglobulin (beta 2 M 3.59 mg/L), C reactive protein (CRP 162.9 mg/L), and in hemostasis tests hyperfibrinogenemia (fibrinogen 8.1 g/L). Other findings were within reference values. The gynecological examination was in order. It was decided to extirpate the said lymph node of the left supraclavicular region in its entirety. Based on the received histopathological findings, a diagnosis of HL, a type of nodular sclerosis, with a characteristic immunophenotype: LCA-, CKPAN-, OCT2-, BOB1-, Pax-5-/+, CD79alfa -, CD20-, CD19-, CD15-/+, CD30+, Fascin +, MUM-1+, EBV-, bcl-6+, CD34-, CD3-, CD5-, CD4-, CD8-, ALK-. As part of additional diagnostics, an examination

com (MR), gde je uočena limfadenopatija supraklavikularno (najvećeg promera do 44x22 mm, medijastinalno u svim grupama (najvećeg promera do 28x15 mm), abdominalno u vidu konglomerata dominantno u hilusu jetre (promera 61x28x46 mm), paraaortalno (promera 55x24x39 mm) i parailijačno (promera 31x18x30 mm), sa opisanom hidronefrozom gr. II desnog bubrega. Ehokardiografski pregled je bio uredan uz očuvanu globalnu sistolnu funkciju leve komore (ejekciona frakcija 70%). Odluka o specifičnom hematološkom lečenju je nakon sprovedene dijagnostike bila odložena zbog SARS-CoV-2 pozitivnosti i blaže kliničke slike Covid-19. Pacijentkinja je lečena primenom empirijske antibiotske terapije širokog spektra uz tromboprofilaksu niskomolekularnim heparinom i ostalu simptomatsko - suportivnu terapiju. Po oporavku, kod pacijentkinje sa dijagnozom HL, tipa nodularne skleroze, u IIIB kliničkom stadijumu, EORTC/LYSA i GHSG - "advanced stage", odlučeno je da se započne lečenje osnovne bolesti prema protokolu ABVD, inicijalno primenom dva ciklusa nakon čega je planirana procena interim PET/CT pregledom, uz redovno praćenje sa perinatološke strane (biometrija, cervikometrija i praćenje stanja ploda) neposredno pre primene antineoplastične terapije. Dve nedelje nakon sprovedenog d15 II ciklusa ABVD protokola bio je planiran porođaj carskim rezom u 37. nedelji gestacije, ali se pacijentkinja u tom terminu porodila prirodnim putem, bez pratećih komplikacija. Od strane neonatologa konstatovan je uredan i klinički i laboratorijski nalaz kod ploda. Interim PET/CT pregled je urađen februara 2024. i ukazao je na diskretno povišen metabolizam glukoze u limfnim čvorovima u IV jugularnoj grupi u vratu obostrano, medijastinalnim limfnim čvorovima retrosternalno i limfnim čvorovima hepatogastrično – Deauville skor 3. Imajući u vidu navedeni nalaz, kao i inicijalni stadijum bolesti, odlučeno je da se lečenje nastavi sa još četiri ciklusa hemioterapije prema ABVD protokolu. Terapiju je dobro podnosila i nije bilo pratećih komplikacija niti indikovanih hospitalizacija između ciklusa. Lečenje je kompletirano sa ukupno šest ciklusa ABVD protokola, a po završetku lečenja kontrolni PET/CT je ukazao na metaboličku remisiju osnovne bolesti.

DISKUSIJA

Hočkinov limfom je jedan od najčešćih maligniteta u trudnoći, s obzirom na činjenicu da je incidenca njegovog javljanja najčešća u reproduktivnom periodu. Prema Korkontzelos I. i saradnicima [4], incidence javljanja je 1 slučaj HL na 6000 trudnoća. Karakteristike ovog maligniteta se ne razlikuju kod trudnica, u odnosu na opštu populaciju. Pacijentkinje sa dijagnozom HL u trudnoći imaju trogodišnje preživljavanje od 85% [5].

of the neck, chest, abdomen, and pelvis was performed with magnetic resonance imaging (MR), where lymphadenopathy was observed supraclavicularly (with the largest diameter up to 44x22 mm, mediastinally in all groups (with the largest diameter up to 28x15 mm), abdominally in the form of conglomerates, dominantly in hilus of the liver (diameter 61x28x46 mm), paraaortic (diameter 31x18x30 mm), with described hydronephrosis gr. II of the right kidney. The echocardiographic examination was regular, with a preserved global systolic function (ejection fraction of 70%). Hematological treatment was postponed due to SARS-CoV-2 positivity and a milder clinical picture of COVID-19. The patient was treated with empiric broad-spectrum antibiotic therapy, thromboprophylaxis, low molecular weight heparin, and other symptomatic-supportive therapy. Type of nodular sclerosis, in the IIIB clinical stage, EORTC/LYSA and GHSG - "advanced stage," it was decided to start the treatment of the underlying disease according to the ABVD protocol, initially by applying two cycles, after which an interim PET/CT examination is planned, with regular monitoring from the perinatological side (biometry, cervicometry and monitoring of the condition of the fetus) immediately before the application of antineoplastic therapy. Two weeks after the d15 II cycle of the ABVD protocol, cesarean delivery was planned in the 37th week of gestation, but the patient gave birth naturally at that time without complications. The neonatologist noted that the clinical and laboratory findings of the fetus were normal. An interim PET/CT examination was performed in February 2024 and indicated discretely elevated glucose metabolism in lymph nodes in the IV jugular group in the neck bilaterally, mediastinal lymph nodes retrosternal and hepatogastric lymph nodes - Deauville score 3. Considering the above finding, as well as the initial stage of the disease, it was decided to continue the treatment with four more cycles of chemotherapy according to the ABVD protocol. She tolerated the therapy well, and there were no accompanying complications or indicated hospitalizations between cycles. The treatment was completed with a total of six cycles of the ABVD protocol. At the end of the treatment, the control PET/CT indicated a metabolic remission of the underlying disease.

DISCUSSION

Hodgkin's lymphoma is one of the most common malignancies in pregnancy, considering the fact that the incidence of its occurrence is most common in the reproductive period. According to Korkontzelos I. and colleagues [4], the incidence of occurrence is 1 case of HL per 6000 pregnancies. The characteristics of this

Samo postavljanje dijagnoze HL tokom trudnoće može biti značajno prolongirano, imajući u vidu da simptomi koji ukazuju na postojanje HL mogu biti pripisani tegobama koje se i inače javljaju u trudnoći (zamaranje, malaksalost, dispneja, noćno preznojavanje). Sličan sled događaja se desio i kod naše pacijentkinje, imajući u vidu da je od pojave prvih simptoma do definitivnog postavljanja dijagnoze proteklo nešto manje od dva meseca. Drugi problem predstavlja limitiranost dostupnosti različitih dijagnostičkih procedura. Dok biopsija limfne žlezde ne predstavlja rizik ni za majku, ni za fetus, određene radiografske metode, poput kompjuterizovane tomografije (CT) i pozitronske emisione tomografije (PET) mogu u određenoj meri biti rizične, pre svega za fetus [6]. Bezbednim se smatra primena magnetne rezonance i ultrazvučnih metoda, a eventualna radiografija se može razmotriti u cilju procene proširenosti bolesti ili kod nekih akutnih stanja, uz obaveznu upotrebu zaštitne kecelje. Ipak, od krucijalne važnosti je sprovesti planiranu dijagnostiku i evaluaciju hematološkog statusa, u cilju adekvatne odluke o lečenju. Multidisciplinarni pristup je neophodan radi procene optimalnog trenutka započinjanja specifičnog hematološkog lečenja, uz personalizovan pristup svakom pacijentu i koordinaciju hematologa, ginekologa i neonatologa, gde je potrebno uzeti u obzir potencijalnu korist i rizik od primene ili odlaganja ciljane terapije. Svakako je neophodno poštovati želju pacijentkinje za nastavkom ili prekidom trudnoće u datom trenutku. Ukoliko se pacijentkinja odluči za prekid trudnoće, pristup lečenju je identičan kao i kod opšte populacije.

Kod ranih stadijuma bolesti (IA i IIA po Ann Arbor klasifikaciji), ne postoji zvaničan konsenzus o primeni antineoplastične terapije. Preporuke su da, ukoliko je to moguće, lečenje bude odloženo do porođaja. Thomas, P.R. i saradnici [7] su pokazali na studiji od 19 pacijentkinja da odlaganje terapije do porođaja zaista predstavlja adekvatan izbor, ne ugrožavajući ni majku ni fetus. Sa druge strane, Aviles, A. i saradnici [8] su u svojoj studiji koja je obuhvatila 44 pacijentkinje sa dijagnozom HL tokom trudnoće u ranom stadijumu bolesti, ukazali na značaj primene ABVD protokola, koji predstavlja zlatni standard u lečenju HL. Rezultati studije su pokazali da nije bilo kongenitalnih malformacija, kao i da su PFS (period do progresije bolesti) i OS (ukupno preživljavanje) tokom medijane praćenja od 120,4 meseca iznosili 95%, odnosno 93%, redom.

Kod uznapredovalih stadijuma bolesti, odlaganje primene specifične terapije može, pak, predstavljati veći rizik od započinjanja specifičnog lečenja. I u ovoj grupi pacijenata, ABVD protokol još uvek predstavlja terapiju izbora. Alternativu može predstavljati A-AVD

malignancy do not differ in pregnant women compared to the general population. Patients diagnosed with HL during pregnancy have a three-year survival rate of 85% [5].

Making a diagnosis of HL during pregnancy can be significantly prolonged, bearing in mind that symptoms indicating the existence of HL can be attributed to complaints that also occur during pregnancy (fatigue, weakness, dyspnea, night sweats). A similar sequence of events happened with our patient, bearing in mind that less than two months passed from the appearance of the first symptoms to the definitive diagnosis. Another problem is the limited availability of various diagnostic procedures. While biopsy of the lymph gland poses no risk to either the mother or the fetus, certain radiographic methods, such as computed tomography (CT) and positron emission tomography (PET), can be somewhat risky, primarily for the fetus [6]. The application of magnetic resonance and ultrasound methods is considered safe, and possible radiography can be considered to assess the spread of the disease or, in some acute conditions, with the mandatory use of a protective apron. Nevertheless, it is crucial to carry out planned diagnostics and evaluation of the hematological status to make an adequate decision on treatment. A multidisciplinary approach is necessary to assess the optimal moment of starting a specific hematological treatment, with a personalized approach to each patient and the coordination of hematologists, gynecologists, and neonatologists, where it is necessary to take into account the potential benefits and risks of applying or delaying targeted therapy. It is certainly essential to respect the patient's wish to continue or terminate the pregnancy at a given moment. If the patient decides to terminate the pregnancy, the approach to treatment is identical to that of the general population.

In the early stages of the disease (IA and IIA, according to the Ann Arbor classification), there is no official consensus on the use of antineoplastic therapy. Recommendations are that, if possible, treatment should be delayed until childbirth. Thomas, P.R. et al. [7] showed in a study of 19 patients that postponing therapy until childbirth really represents an adequate choice without endangering either the mother or the fetus. On the other hand, Aviles, A. et al. [8] in their study, which included 44 patients diagnosed with HL during pregnancy in the early stages of the disease, pointed out the importance of applying the ABVD protocol, which represents the gold standard in the treatment of HL. The study's results showed no congenital malformations and that PFS (period to disease progression) and OS (overall survival) during a median follow-up of 120.4 months were 95% and 93%, respectively.

protokol (brentuksimab vedotin, adriablastin, vinblastin, dakarbazin), ali za sada ne postoji dovoljno podataka o potencijalnom teratogenom efektu brentuksimaba [9,10]. Alkilirajući agensi su poznati kao izuzetno teratogeni, te njih svakako treba izbegavati kod trudnica, posebno u prvom trimestru trudnoće [11]. Imajući u vidu činjenicu da se tokom prvog trimestra odvija organogeneza i da je tada fetus izuzetno vulnerabilan, ne preporučuje se primena bilo kakve antineoplastične terapije u ovom periodu. U većem broju studija, primena ABVD protokola u drugom i trećem trimestru trudnoće kod trudnica sa HL pokazala se bezbednom, ne izazivajući komplikacije kako kod majke, tako ni kod fetusa [12-18]. Ipak, Cotteret, C. i saradnici su došli do zaključka da primena doksorubicina tokom trudnoće može dovesti do prolazne disfunkcije leve komore kod novorođenčeta, uz kompletnu restituciju mesec dana nakon porođaja [19]. Studija [20] koja je obuhvatila 405 pacijentkinja sa dijagnozom HL lečenih BEACOPP (bleomicin, etopozid, doksorubicin, ciklofosfamid, vinkristin, prokarbazin, prednison) protokolom, došla je do zaključka da je čak 51,4% pacijentkinja razvilo permanentnu amenoreju, s višom stopom kod pacijentkinja lečenih eskalirajućim BEACOPP protokolom u odnosu na standardni. Zbog svega navedenog, ABVD protokol se smatra relativno bezbednim za lečenje HL u trudnoći.

Radioterapija nosi sledstveni rizik od kongenitalnih anomalija kod odojčadi i adolescenata koji su bili izloženi zračenju *in utero*, i to uglavnom ako uzmemo u obzir doze veće od 50 Gy. Samim tim, primena radioterapije u trudnoći ne predstavlja apsolutnu kontraindikaciju, posebno kada se radi o supradijafragmalnoj lokalizaciji tumora, ali i ovo je jedna od odluka koja mora biti multidisciplinarno sagledana zbog potencijalnih rizika koje nosi [21].

Još jedan od izazova predstavlja i izmenjena farmakokinetika tokom trudnoće. Hipoalbuminemija, koja se može javiti u trudnoći, povećava slobodnu frakciju lekova u plazmi, te tako menja njihovu distribuciju. Treba imati u vidu da se brojni citostatici izlučuju putem mleka, te je dojenje tokom primene citostatika kontraindikovano. Određeni antineoplastični lekovi mogu perzistirati u mleku određeni period nakon primene leka, te se savetuje da se dojenje odloži minimum 3-6 nedelja po kompletiranju lečenja.

Prilikom odluke o idealnom terminu porođaja neophodan je personalizovan pristup. Ukoliko je to moguće, porođaj treba odložiti najmanje do 35. nedelje gestacije. Takođe, zbog mijelosupresivnog efekta određenih citostatika i potencijalne jatrogene aplazije koštane srži, porođaj treba planirati minimum tri nedelje po kompletiranju terapije, odnosno, kada se postigne

In advanced stages of the disease, delaying the application of specific therapy may, on the other hand, represent a greater risk than starting specific treatment. Even in this group of patients, the ABVD protocol is still the therapy of choice. An alternative may be the A-AVD protocol (brentuximab vedotin, adriablastine, vinblastine, dacarbazine), but for now, there is not enough data on the potential teratogenic effect of brentuximab [9,10]. Alkylating agents are known to be highly teratogenic and should be avoided in pregnant women, especially in the first trimester of pregnancy [11]. Given the fact that organogenesis takes place during the first trimester and that then the fetus is highly vulnerable, it is not recommended to use any antineoplastic therapy during this period. In a large number of studies, the application of the ABVD protocol in the second and third trimesters of pregnancy in pregnant women with HL has been shown to be safe without causing complications in either the mother or the fetus [12-18]. Nevertheless, Cotteret, C., and co-workers concluded that the administration of doxorubicin during pregnancy can lead to transient left ventricular dysfunction in the newborn, with complete restitution one month after delivery [19]. A study [20] that included 405 patients diagnosed with HL treated with BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone) protocol concluded that as many as 51.4% of patients developed permanent amenorrhea, with a higher rate in female patients treated with an escalating BEACOPP protocol compared to the standard one. Because of all the above, the ABVD protocol is considered relatively safe for the treatment of HL in pregnancy.

Radiotherapy carries a consequent risk of congenital anomalies in infants and adolescents who were exposed to radiation in utero, especially if we consider doses higher than 50 Gy. Therefore, the use of radiotherapy during pregnancy does not represent an absolute contraindication, especially when it comes to supradiaphragmatic tumor localization, but this is also one of the decisions that must be considered multidisciplinary because of the potential risks it carries [21].

Another challenge is the altered pharmacokinetics during pregnancy. Hypoalbuminemia, which can occur in pregnancy, increases the free fraction of drugs in plasma, thus changing their distribution. Many cytostatics are excreted through milk, so breastfeeding during the use of cytostatics is contraindicated. Certain antineoplastic drugs can persist in milk for a certain period after the drug is administered, so it is advised to postpone breastfeeding for at least 3-6 weeks after completing the treatment.

odgovarajući oporavak hematoloških parametara. Porođaj je kod naše pacijentkinje planiran prema aktuelnim preporukama, tri nedelje nakon primene d15 drugog ciklusa ABVD protokola, u 37. nedelji gestacije, kada je po uvidu u klinički i laboratorijski status završen prirodnim putem, bez pratećih komplikacija.

Sistematski pregled Houlihana i saradnika [3] je ukazao da ne postoji statistički značajna razlika u stepenu javljanja kongenitalnih malformacija i spontanih pobačaja kod trudnica sa dijagnozom HL u odnosu na trudnice u opštoj populaciji. Ipak, kod pacijentkinja sa dijagnozom HL češće se javljaju prevremeni porođaji, što može biti povezano sa planiranim preterminskim završavanjem trudnoće, češće nego spontanim, bilo kao odluka tima lekara ili odluka same pacijentkinje kako bi se izbegla primena terapije tokom trudnoće. Takođe, češći su venski tromboembolijski događaji (VTE), što je očekivano, s obzirom na činjenicu da sama trudnoća doprinosi hiperkoagulabilnosti i venskoj stazi. Kod naše pacijentkinje je po započinjanju lečenja primenjivana i profilaktička doza niskomolekularnog heparina, imajući u vidu i dobro poznat pojam tromboza udruženih sa kancerom, gde aktivni malignitet i primena antineoplastične terapije dodatno povećavaju rizik od VTE.

ZAKLJUČAK

Hočkinov limfom predstavlja hematološki malignitet sa dobrom prognozom i visokom stopom izlečenja. Lečenje pacijentkinja sa HL tokom trudnoće nosi sa sobom brojne izazove, polazeći od dijagnostike, preko izbora odgovarajuće terapije i momenta započinjanja lečenja, do donošenja odluke o terminu završavanja trudnoće. Kompleksnost lečenja potvrđuje i činjenica o neophodnosti prisustva multidisciplinarnog tima u cilju razmatranja prethodno navedenih odluka. Studije ukazuju na obećavajuće rezultate kod trudnica lečenih ABVD protokolom. Ipak, dodatna istraživanja su neophodna za dalja saznanja, kao i dugoročno praćenje potencijalnih postterapijskih posledica kod dece rođene od majki sa dijagnozom HL koje su lečene tokom trudnoće.

Sukob interesa: Nije prijavljen.

A personalized approach is necessary when deciding on the ideal date of birth. If possible, childbirth should be postponed until at least the 35th week of pregnancy. Also, due to the myelosuppressive effect of certain cytostatics and potential iatrogenic bone marrow aplasia, childbirth should be planned at least three weeks after the completion of therapy; that is when appropriate recovery of hematological parameters is achieved. The birth of our patient was planned according to current recommendations, three weeks after the application of d15 of the second cycle of the ABVD protocol, in the 37th week of gestation, when, according to the clinical and laboratory status, it was completed naturally, without accompanying complications.

A systematic review by Houlihan et al. [3] indicated that there is no statistically significant difference in the incidence of congenital malformations and spontaneous abortions in pregnant women diagnosed with HL compared to pregnant women in the general population. However, in patients diagnosed with HL, premature births occur more often, which may be related to planned premature termination of pregnancy, more often than spontaneous, either as a decision of the medical team or the decision of the patient herself to avoid the use of therapy during pregnancy. Also, venous thromboembolic events (VTE) are more common, which is expected, given the fact that pregnancy itself contributes to hypercoagulability and venous congestion. Our patient was given a prophylactic dose of low-molecular-weight heparin after the start of treatment, bearing in mind the well-known concept of thrombosis associated with cancer, where active malignancy and the use of antineoplastic therapy additionally increase the risk of VTE.

CONCLUSION

Hodgkin's lymphoma is a hematological malignancy with a good prognosis and a high cure rate. Treatment of patients with HL during pregnancy brings with it numerous challenges, starting from diagnosis, through the selection of appropriate therapy and the moment of starting treatment, to deciding on the date of termination of pregnancy. The complexity of the treatment confirmed the fact of the necessity of the presence of a multidisciplinary team to review the aforementioned decisions. Studies indicate promising results in pregnant women treated with the ABVD protocol. However, additional research is necessary for further knowledge, as well as long-term monitoring of potential post-therapy consequences in children born to mothers diagnosed with HL who were treated during pregnancy.

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