Managing Lymphoma During Pregnancy

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Introduction

Lymphoma is one of the most common cancers that occur during pregnancy. Primarily due to its typical peak onset in the reproductive years, Hodgkin lymphoma (HL) occurs more often than non-Hodgkin lymphoma (NHL) during pregnancy. Several recently published series on lymphoma during pregnancy indicate that the majority of patients present with advanced-stage disease and that the occurrence of extranodal disease is relatively common and that it may occur in unique sites (e.g., reproductive organs), especially in NHL.

The evaluation and treatment of lymphoma in pregnant patients is highly individualized based in part on the clinical scenario as well as patient and family wishes. Furthermore, overarching objectives for the diagnosis and treatment of pregnant mothers are to optimize maternal survival and minimize treatment-related fetal toxicity and prematurity. This is maximized by involvement of high-risk maternal–fetal medicine as part of the multidisciplinary team and also promoting the goal of continuing the pregnancy to full term. This review details available information on staging of lymphoma, disease characteristics, gestational data, treatment (including targeted therapeutics), maternal and fetal complications, and additional special considerations of patients diagnosed with NHL and HL during pregnancy.

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Staging, Disease Characteristics, and Gestational Data

Staging

The diagnosis of lymphoma in the pregnant patient is no different than the typical patient requiring a lymph node biopsy, which can usually be safely done, including in the first trimester, utilizing either local or general anesthesia. Staging of a pregnant patient with lymphoma includes a detailed history and physical, laboratory testing, bone marrow biopsy, and shielded chest X-ray. For further imaging, the use of nonionizing ultrasound and MRI are preferred to abdominal/pelvic CT imaging (0.02 Gy). There is no evidence of harmful fetal effects with MRI; however, some regulatory bodies discourage the use of gadolinium during pregnancy in part due to potential acoustic damage and systemic fibrosis [1, 2]. Gadoterate meglumine and gadobenate dimeglumine may be safer than gadolinium and can be considered for use antepartum. PET scan should be avoided during pregnancy as it results in pelvic irradiation and ^{18}F-FDG crosses the placenta, which is considered fetotoxic [3].

Disease Characteristics

There are several important considerations regarding the presentation of lymphoma occurring during pregnancy. Lymphomas often occur later in gestation (i.e., second and third trimester), are typically an aggressive subtype, involve the reproductive organs, and the majority are diagnosed at a more advanced stage. Delay in diagnosis may occur as symptoms related to lymphoma may mimic pregnancy-related symptoms (e.g., fatigue, nausea, anemia, etc.). A systematic review of 121 published NHL cases [4] occurring during pregnancy described 48 % of NHLs as aggressive, DLBCL and T-cell lymphoma, and 47 % as highly aggressive, Burkitt lymphoma; 76 % of all patients had stage IV disease and 49 % had reproductive organ involvement. In addition, a recent multicenter retrospective analysis studied 90 patients with lymphoma (NHL and HL) that occurred during pregnancy [5]. Fifty patients in that series had NHL; the most common subtype was DLBCL, which constituted 56 % of all NHLs and 73 % of B-cell NHLs. The vast majority of patients had newly diagnosed disease. NHL patients more likely had advanced-stage disease compared with HL, and extranodal involvement was common in NHL patients with one-quarter of patients having >1 extranodal site (e.g., breast, gastrointestinal tract, gynecologic (i.e., uterine, cervical, placental), bone marrow, and central nervous system (CNS)) [6]. For patients in this series, HL patients more commonly had bulky disease compared with NHL (30 % vs. 17 %, respectively) [5].

Gestational Data

In the aforementioned series, the diagnosis of lymphoma occurred at a median of 24 weeks gestation (range, 5–38 weeks) with no difference based on lymphoma

subtype [5]. Pregnancy was terminated in only 7 % of patients in order to enable immediate multi-agent chemotherapy (5 in first trimester and 1 patient early second trimester who required high-dose methotrexate). Among other patients, 33 % had therapy deferred until postpartum; these patients had lymphoma diagnosed at a median of 30 weeks gestation compared with all other patients who received treatment during pregnancy, the latter group diagnosed at a median gestation of 22 weeks ($P < 0.0001$).

Treatment

Goals in the treatment of lymphoma during pregnancy can be divided into maternal outcomes, fetal outcomes, and obstetric outcomes. Maternal outcomes of interest include overall survival and progression-free survival. Fetal outcomes of interest include fetal demise, NICU admission, malformations, and low gestational age (defined as below tenth percentile for age and sex). Obstetric outcomes impact both the mother and the fetus and include preterm delivery (defined as delivery prior to 37 weeks gestation), spontaneous preterm delivery (such as premature rupture of membranes (PROM) or preterm labor), postpartum hemorrhage (>500 mL for vaginal delivery, >1000 mL for cesarean), preeclampsia, gestational diabetes, endometritis, and route of delivery.

The decision on whether to administer therapy antepartum and moreover when, which, and how much treatment to recommend is highly individualized and based on the clinical scenario and patients' wishes. General precautions in administering chemotherapy in pregnant patients include renal clearance and third spacing (from amniotic fluid) that may decrease active drug concentrations (including chemotherapy) in the first trimester [3, 7]. Given their low molecular weight, chemotherapeutic drugs have the potential to cross the placenta (Table 14.1). During the organogenesis of the first trimester, especially weeks 2–8, there is a significant increased risk of drug-related teratogenicity, including fetal death [3].

This risk is highly reduced during the second and third trimesters (i.e., beginning week 12), but there remains risk of palate and ear anomalies after 10 weeks gestation [8]. In the second trimester, the risk shifts from that of malformations to low birth weight or intrauterine growth retardation (IUGR) and impact on delivery such as stillbirth and preterm births. Overall, however, most therapeutics are safer for the mother and fetus during the second and third trimesters [8]. There are a handful of chemotherapy agents that are proven human teratogens and contraindicated throughout pregnancy (e.g., older-generation alkylators (i.e., procarbazine and busulfan), thalidomide and lenalidomide, and the antimetabolite, aminopterin) [9].

The decision to administer radiotherapy antepartum is controversial as fetal exposure may cause malformations, growth retardation, and death. Further, long-term side effects such as mental retardation, sterility, and cataracts may occur resulting from cell death due to irreparable DNA damage. The occurrence and severity of these effects depend strongly on fetal dose and gestational stage, with the highest risk during the embryonic, organogenesis, and early fetal phases. Thus,

Table 14.1 Chemotherapy in NHL and its effects on pregnancy

Chemotherapy	Distribution	Maternal Patient	Fetus (first trimester)	Fetus (second and third trimester)
Cytoxan	Liver cytochrome P450; found in the brain, cerebrospinal fluid, milk, saliva, and amniotic fluid	Myelosuppression	First trimester: Malformations: oculofacial malformations, missing digits and nail abnormalities, coronary artery defects, umbilical hernia, hemangioma, imperforate anus, rectovaginal fistula, cleft palate, microcephaly, growth restriction, and developmental delays	Second and third trimester: Growth restriction, microcephaly (rare), and possibly, neonatal pancytopenia
Chlorambucil		Myelosuppression	First trimester: Malformations: renal and ureter agenesis, cardiac defects	
Cisplatin	Highest in the liver and kidneys	Myelosuppression; nephrotoxicity and neurotoxicity	No congenital defects reported; unknown late-term effects	
Bleomycin	Intra-/extracellular fluid	Pneumonitis (caution with supplemental oxygen)	No congenital defects reported	
Methotrexate	Fluid spaces; amniotic fluid	Myelosuppression; acute renal failure	Malformations: cephalic and skull, widened nasal bridge, mandible, cardiac defects (less prominent after 20 weeks)	
Etoposide	All body fluids and tissue	Myelosuppression; prolonged PT/INR	Intrauterine growth restriction and pancytopenia	
Doxorubicin	Wide distribution	Myelosuppression; cardiotoxicity	Anal malformation; rectovaginal fistula, microcephaly	
Vincristine	Wide distribution; poor penetration of blood–brain barrier	Neurotoxicity (peripheral neuropathy, CN palsies; CNS dysfunction, seizures, coma)	ASD; renal hypoplasia, pancytopenia; absent radii	
Vinblastine	Wide distribution; poor penetration of blood–brain barrier	Myelosuppression; neurotoxicity (less than vincristine)	Unclear teratogenicity	

radiotherapy is usually contraindicated prior to week 16, except for rare clinical scenarios [10]. If radiotherapy is administered, a medical physicist should be closely involved in the patient care. Exposure to doses ≥100 mSv (especially ≥500 mSv) is associated with increased risks of malformation and mental retardation, while after 25 weeks, 1 Sv (1000 mSv) or less is considered relatively safe depending on the radiation site. Altogether, if used, radiotherapy should be involved-field or involved-site and used primarily for locations distant from the fetus with additional protection against leakage and room scatter [11].

Collectively, there should be strong consideration to have all treatment delayed until after the first trimester and in select scenarios (e.g., indolent lymphomas, diagnoses in late third trimester, etc.) held until after delivery. It is important to highlight that labor should not be induced to expedite therapy. An overarching goal in the care of all pregnant patients diagnosed with lymphoma is to have delivery at full term (i.e., beyond 37 weeks). A therapeutic abortion should primarily be considered if urgent multi-agent chemotherapy is warranted during the first trimester (especially before week 8), owing to the heightened risk of teratogenicity. Intermediate-to-high-dose corticosteroids may be used as "bridging" therapy, providing symptom management for lymphoma, especially in the first trimester. Steroids that cross the placenta in the smallest amounts, such as prednisolone and methylprednisolone, should be considered.

Treatment of NHL

For asymptomatic patients with indolent NHL (e.g., follicular) and low tumor burden, clinical observation without therapy is an option. Additionally, patients diagnosed later in the third trimester (i.e., beyond 35 weeks) without life-threatening disease, including ones with aggressive histology (e.g., diffuse large B-cell lymphoma (DLBCL)), may have therapy delayed until postpartum. Furthermore, steroids may be used as a "bridge" to allow maturation from the first to second trimester or from late third trimester to delivery.

If antenatal chemotherapy is warranted, therapeutic choices are guided in part by NHL subtype and extent of disease (Fig. 14.1). For patients with DLBCL, rituximab, cyclophosphamide, doxorubicin, Oncovin, and prednisone (R-CHOP) may be considered during the second and third trimesters. Patients treated with 3–6 cycles of R-CHOP prior to delivery have been shown to have overall good outcomes, although with increased incidence of preterm births [5, 8, 12].

The use of anthracyclines is somewhat controversial [9]; transient and permanent cardiomyopathy has been diagnosed in neonates, while other studies have found no link to myocardial damage [13–15]. Despite the known effects in adults, the use of bleomycin or vinca alkaloids has not been associated with pulmonary or neurologic complications of the fetus (Table 14.1) [7, 9]. There remains risk of these drug-specific toxicities, however, in the mother. This includes caution with the use of supplemental oxygen in patients exposed to bleomycin. Antimetabolites are the most teratogenic agents and should be used with caution, especially before 20 weeks. Methotrexate interferes with organogenesis and should be prohibited before 20 weeks; cytarabine has overall lower fetotoxic potential.

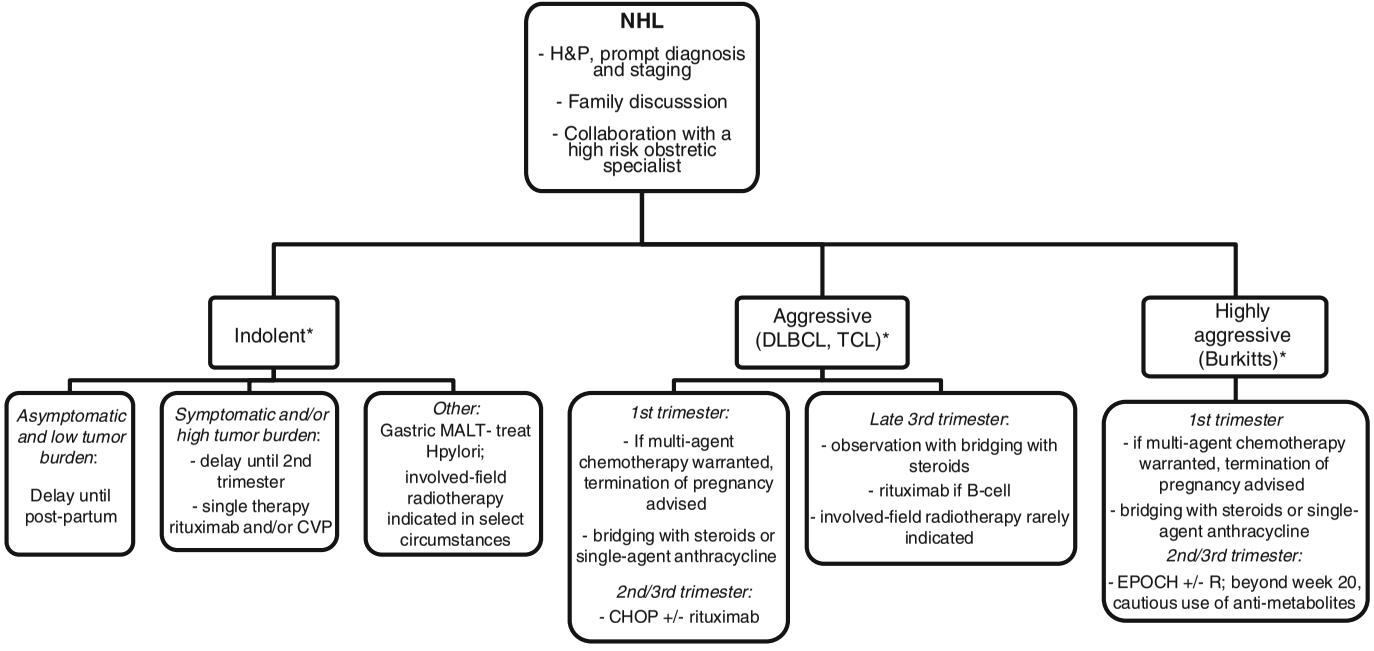

Fig. 14.1 Algorithm for treatment of NHL in pregnancy. *Recommendations given are listed vertically in order of overall preference. Abbreviations: *NHL* non-Hodgkin lymphoma; *DLBCL* diffuse large B-cell lymphoma; *TCL* T-cell lymphoma; *CVP* cyclophosphamide, vincristine, prednisone; *CHOP* cyclophosphamide, Adriamycin, Oncovin, prednisone; *EPOCH* etoposide, prednisone, Oncovin, cyclophosphamide, Adriamycin

Highly aggressive NHLs (e.g., Burkitt's lymphoma) and/or ones that warrant antimetabolite therapy (e.g., primary CNS lymphoma) are challenging to treat. There are reports in the literature utilizing antimetabolites during pregnancy [16, 17]; however, caution is advised regarding fetal teratogenicity (e.g., methotrexate syndrome and myelosuppression). Thus, as noted before, antimetabolites are not recommended before 20 weeks gestation and should also be used thereafter with caution. Additionally, use of etoposide, prednisone, Oncovin, cyclophosphamide, and doxorubicin (EPOCH) infusional therapy may be considered beyond the 1st trimester similar as to recommendations for CHOP. There are no published data of EPOCH during pregnancy, however, lymphoma experts have advocated this approach in select cases (personal communication, Dr. Wyndham Wilson, NCI) interestingly.

Treatment of HL

Treatment decisions in the pregnant patient with HL should be guided by both the stage of the disease and the gestation of pregnancy. Almost all chemotherapeutic agents have documented teratogenic effects either in animal models or in humans [3, 9]. The use of combination chemotherapy is associated with a higher risk of major malformations in the first trimester compared with the risk of single-agent chemotherapy [3, 18, 19]. Although this data is based largely on older chemotherapy regimens that are not commonly in use today, combination chemotherapy should be avoided during the first trimester when the risk of teratogenicity and miscarriage is highest [3].

For early-stage disease diagnosed in the first trimester, the patient may be followed closely, and treatment can be delayed until the second trimester when the risk of congenital malformation is significantly reduced. Another option is to initiate single-agent chemotherapy with a vinca alkaloid or anthracycline [3, 9, 20] during the first trimester. Although this is considered safe for the fetus, the efficacy of single-agent chemotherapy in early-stage HL is reduced compared with combination chemotherapy, and the patient may require combination chemotherapy during the second trimester. In select cases, radiotherapy can be considered for the treatment of early-stage HL. This should be considered primarily for patients with isolated and symptomatic supradiaphragmatic disease involvement [3]. Anthropomorphic phantoms can safely achieve 25 Gy tumor dose while keeping the fetal exposure below 0.1 Gy during first trimester [21].

For patients with advanced HL in the first trimester, the risk to the mother must be weighed against the risk to the fetus. As delaying therapy may adversely affect patient survival, combination chemotherapy with ABVD is recommended. The risk of major malformation with chemotherapy during the first trimester is 10–20 % [22]. Due to the high risk of congenital abnormalities associated with combination chemotherapy, it is appropriate to discuss termination of the pregnancy. There may also be consideration for use of vinblastine and/or steroid therapy in order to bridge patients to the 2nd trimester. During the second and third trimesters, the risk of teratogenicity associated with chemotherapy is significantly reduced, and there is data supporting the safety for both the mother and the fetus of combination chemotherapy [3, 9, 22–29]. Patients with symptomatic HL in the second and third trimesters may be treated with combination chemotherapy as they would if they were not

pregnant (e.g., ABVD). More intensive combination chemotherapy regimens are not recommended (e.g., BEACOPP) due in part to higher doses of anthracycline and the inclusion of alkylating agents in this regimen. For patients with nonaggressive clinical disease, the use of antenatal single-agent vinblastine, reserving combination chemotherapy until after delivery, is an alternative option [20]. During the third trimester, delivery should be planned during a non-cytopenic period of the treatment cycle to minimize the risks of maternal infection and bleeding and the risks of drug accumulation and hematologic suppression in the neonate [30]. As noted before, a critical overarching goal of all therapy should be for full-term delivery (i.e., 37 weeks and beyond). Additionally, chemotherapy should not be administered after weeks 35–36 of pregnancy as the spontaneous delivery becomes more likely.

For highly select cases, radiotherapy may be considered in the second and third trimesters, although the risk of fetal exposure is increased compared to the first trimester. During the second and third trimesters, the progression of the pregnancy results in an increased total fetal dose of 0.12–0.19 Gy even with abdominal shielding due to increased fetal size and close proximity of the fetus to the treatment volume [21]. However, these simulations were done using mantle field radiation, which is no longer recommended for the treatment of HL. Radiotherapy at distant sites from the abdominopelvic region such as for the nasopharynx was shown to result in exposures of less than 0.1 Gy no matter what is the stage of pregnancy [21]. If risks of chemotherapy are deemed prohibitive and treatment is warranted, patients can be considered for treatment with involved field radiotherapy of isolated cervical or axillary disease (primarily for control of local symptoms) with appropriate abdominal shielding during the second and third trimesters [3, 31].

Overall, data on outcomes of pregnant women with HL have shown 3-year progression-free survival of 82 % and overall survival of 97 % at a median follow-up of 41 months among pregnant women with HL [24]. These data also showed acceptable fetal outcomes with no cases of fetal demise, NICU admission, or malformation [24]. For further information on complications related to treatment, please see the section on "Complications" (Fig. 14.2).

Targeted Therapy

There are limited data on the use of biologic agents in pregnancy. Of available data in the literature, rituximab has been the best studied in the treatment of both indolent and aggressive lymphoma pregnancy. An obstetric complication seen in rituximab-treated patients is preterm birth; of 153 reported pregnancies exposed to rituximab globally, there were a total of 90 live births; 27 % were mothers with NHL; 76 % resulted in full-term deliveries and 19 % in preterm deliveries. This rate of preterm delivery is above that seen in the general population (10–12 %) [32]. However, it is unclear if this is rituximab related or an independent risk from malignant disease.

As rituximab may deplete CD20+ B cells for up to 6 months, there is also a potential risk of B-cell suppression in the neonate regardless of rituximab dose. This

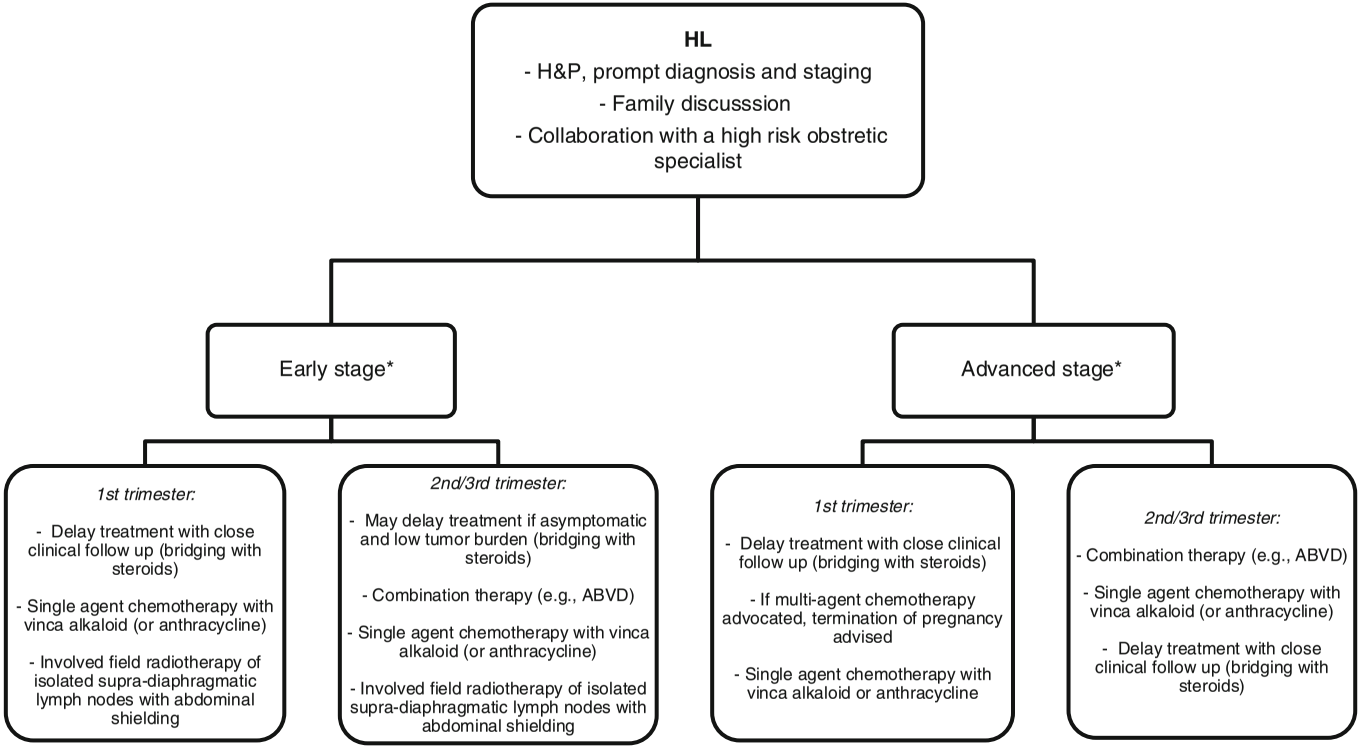

Fig. 14.2 Algorithm for treatment of HL in pregnancy. *Recommendations given are listed vertically in the order of overall preference. Abbreviations: *HL* Hodgkin lymphoma, *H&P* history and physical, *ABVD* Adriamycin, bleomycin, vinblastine, and dacarbazine

was seen in a pregnant 32-year-old female treated with R-CHOP for DLBCL in which cord blood had no CD20+ B cells, IgM, IgA, and low IgG levels [33]. In spite of this, the child had no serious infectious complications and B-cell counts normalized following birth; this was also noted by Klink et al. likely owing to the neonate's dependence on maternal IgG while B cells developed [34]. Overall, with caution given toward B-cell depletion, which is typically reversible, rituximab appears to be generally safe in pregnancy [35]. Other than generic manufacturer drug warnings, there are no additional data regarding the use of other cellularly targeted therapeutic agents such as obinutuzumab, ibrutinib, or brentuximab vedotin during pregnancy. As recently reviewed [35], small molecules like tyrosine kinase inhibitors (TKIs), like chemotherapy, are known to cross the placenta during pregnancy; due in part to this as well as the potential effect of TKIs on physiologic function, their use are currently not advocated.

Supportive Therapy

Supportive care recommendations for the treatment of cancer during pregnancy can be found in a separate chapter dedicated to this topic.

Maternal and Fetal Complications

Data on maternal and obstetric complications of lymphoma in pregnant women are somewhat limited, and the vast majority of available information stems from retrospective analyses. Consideration must be given to physiologic changes in pregnancy as they may relate to chemotherapy including increased plasma volume, increased renal clearance of drugs, and the third space created by amniotic fluid [3].

In a retrospective study by Evens et al., patients diagnosed with NHL and HL during pregnancy were reported to have a slightly higher incidence of postpartum hemorrhage (defined as >500 mL for vaginal delivery or greater than 1,000 mL for cesarean) with 10 % in the group receiving antenatal therapy vs. 0 patients in the groups who received no antenatal therapy. An equal number of patients with NHL in the treatment and nontreatment groups had postpartum hemorrhage (4 % patients in treatment group vs. 8 % patients in nontreatment group) [24]. These same data showed that 44 % of all patients had preterm labor. In the HL group, 39 % of patients who received antenatal treatment had preterm labor as compared with 38 % of patients who had no antenatal therapy. In the NHL group, 32 % of the antenatal treatment group compared with 40 % of the nontreatment group had preterm deliveries [24]. There was a nonsignificant trend toward increased spontaneous preterm delivery (premature rupture of membranes or preterm labor).

In the NHL group, 18 % of the antenatal therapy group versus 23 % of the nontreatment group had premature rupture of membranes. Of the HL group, only one patient experienced premature rupture of membranes, and she was in the no therapy arm [24]. There was also a trend toward increased incidence of preeclampsia that

did not reach statistical significance. These data suggest similar or slightly higher rates of cesarean section compared to the general population. Notably, there was no significant increase of endometritis or gestational diabetes seen.

For fetal outcomes, the effect of chemotherapy and radiation has been studied in lymphoma as well as other malignancies. As elucidated before, the teratogenicity of a drug depends on the timing of exposure, drug dose, and drug characteristics affecting placental transfer. High lipid solubility, low molecular weight, and loose binding to plasma proteins increase transfer of drugs from the mother to fetus [9]. There is an increased risk of spontaneous abortion in the first trimester. Prior to the second week of pregnancy, spontaneous abortion is the most likely result of an insult. As discussed, the highest risk for malformation occurs during organogenesis in the 2nd to 8th weeks of gestation. After organogenesis, the eyes, genitals, hematopoietic systemic, and CNS remain susceptible to chemotherapy. The risk of severe malformation and mental retardation is significantly reduced after the 13–15th week of gestation [3, 9]. These risks are reduced with single-agent chemotherapeutic regimens versus combination regimens [18, 19]. They are also reduced when antimetabolites are excluded [3, 18, 19]. Second and third trimester exposure is not associated with malformations [3, 9, 23].

In data specific to lymphoma, Evens et al. showed a nonstatistically significant trend for neonates to be small for gestation age if the mother received antenatal versus deferred therapy, but no increase in ICU admissions [24]. There has been controversy in the past regarding the effect of anthracyclines on fetal cardiac outcomes; however, more contemporary data support the general safety during pregnancy. This includes an analysis of 81 children with fetal exposure to anthracyclines without evidence of myocardial damage on echocardiogram or functional assessment [3, 15, 36]. In addition, a recent prospective study among 47 children exposed to antenatal therapy (including sub-analysis of 26 children exposed to anthracyclines during pregnancy) showed normal cardiac structure and function by electrocardiography and echocardiography at 36 months [37]. In terms of the effect of radiation on fetal outcomes, this may be found in a separate chapter dedicated to this topic.

More data regarding long-term neurodevelopment of children exposed to chemotherapy is needed, but existing data are reassuring. Aviles et al. found no cognitive, neurological, or psychological abnormalities in 84 children exposed prenatally to chemotherapy, including 18.7 years of follow-up [25]. Formal fertility and cognitive abilities were documented in 12 second-generation children. A combined retrospective and prospective multicenter study involving children who had prenatal exposure to chemotherapy identified a 2.5-point decrease in IQ associated with each week of prematurity in children exposed to chemotherapy [38]. The prospective component of this study was enlarged and prolonged; among 115 children exposed to varied antenatal treatments who had prospective assessment of neurologic function through 36 months, there was no impairment in cognitive or general development [37]. Furthermore, similar to the prior analysis, the cognitive score of children exposed to antenatal therapy was closely linked to gestational age. The average cognitive score increased by 2.9 points for each additional week in gestational age at birth. These data underscore the critical importance of avoiding iatrogenic

prematurity so that impairment in neurodevelopment may be prevented. The safety of breastfeeding during chemotherapy should be evaluated based on maternal health and medications used, although breastfeeding generally is not advised [39].

Special Considerations

Data regarding diabetic pregnant patients with lymphoma are limited. These patients should be treated as per best consensus recommendations on diabetic control with pregnancy. HIV increases the risk of lymphoma, although there is no data on change in incidence during pregnancy. NHL is an AIDS-defining illness, while HL is not [40, 41]. Outcomes of AIDS-related lymphoma have been greatly improved with the use of antiretroviral medications. Data on this population are limited mainly to case reports suggesting that HIV-positive pregnant women with lymphoma should be treated as other women with the addition of double or triple antiretroviral therapy throughout pregnancy [41–43]. Additional prophylaxis for pneumocystis and mycobacterium avium complex should also be considered [41].

Venous thromboembolism during pregnancy is a concern with pulmonary embolism (PE) being a leading cause of maternal death. This is compounded by the fact that cancer is considered to be the second leading cause of maternal mortality behind pregnancy-associated vascular complications. Pregnancy itself is a risk factor for deep vein thrombosis (DVT) (i.e., 4–50 times higher than nonpregnant individual) and can present as DVT in the leg and unusual sites (i.e., cerebral and splanchnic veins) and pulmonary embolism [44]. Preferred treatment includes low molecular weight heparin (LMWH) for short- and long-term anticoagulation [45] as it does not freely cross the placenta and is relatively safe for the woman and fetus. There is also improved efficacy of LMWH compared with coumadin in patients with cancer [46]; aspirin is not indicated. The optimal duration is unknown, but one should keep in mind the increased risk of DVT in the postpartum period. Anticoagulant therapy should be continued for at least the initial 6 weeks following birth. Fondaparinux and the novel anticoagulants including oral factor XA and direct thrombin inhibitors have not been evaluated in pregnant patients and should be avoided.

Conclusions

Lymphoma is one of the most common cancers diagnosed during pregnancy. HL is slightly more common than NHL with NHL patients often presenting with aggressive histology and extranodal disease. Staging studies should include judicious use of radiation with US ± MRI being the recommended imaging modalities. The decision to administer chemotherapy and/or other therapeutic agents during gestation is individualized with the risks of antenatal therapy weighed against the potential adverse effect of delaying curative therapy. Collectively, there should be a strong consideration to have all (nonsteroid) treatment delayed until after the first trimester, and in select scenarios (e.g., indolent lymphomas, diagnoses in late third trimester, etc.), until after delivery.

A therapeutic abortion should be considered if combination chemotherapy is warranted during the first trimester (especially before week 8), owing to the heightened risk of teratogenicity. Intermediate-to-high-dose corticosteroids may be used as "bridging" therapy, providing symptom management for lymphoma, especially in the first trimester. Recent data have shown that standard chemotherapy regimens for NHL and HL (without antimetabolites) administered during the second and third trimester, including as early as 13 weeks gestation, are associated with minimal maternal complications or fetal detriment. The most commonly identified perinatal events that occur in pregnant patients with lymphoma include induction of labor, PROM, and cesarean delivery, with no obvious differences seen among patients who receive antenatal versus deferred therapy. It is also important to highlight that labor should not be induced to expedite therapy. An overarching goal in the care of all pregnant patients with NHL or HL is to have delivery at full term (i.e., beyond 37 weeks). In addition, all patients should be managed concurrently with high-risk maternal–fetal medical expertise and in centers with experience in managing cancer during pregnancy.

Altogether, recent data have helped define optimal timing of therapy, maternal complications, perinatal events, and fetal and maternal outcomes. However, the assessment and management of patients diagnosed with lymphoma during pregnancy remains complex and highly individualized. Continued studies and additional prospective data are needed to continue to help guide clinicians in order to optimize maternal survival and fetal and childhood outcomes.

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Survivorship: Support Group Resources

http://www.cancercare.org/diagnosis/lymphoma.
http://www.cancer.org/treatment/supportprogramsservices/index
http://www.lymphoma.org/site/pp.asp?c=bkLTKaOQLmK8E&b=6298225