

# 48.

## BÖLÜM

Taha Ulutan KARS<sup>1</sup>

### HODGKİN LENFOMAYA GENEL BAKIŞ

Eski adı ile Hodgkin hastalığı olarak bilinen Hodgkin lenfoma (HL), malign hücrelerin heterojen neoplastik olmayan inflamatuar hücre popülasyonu ile karıştırıldığı lenfoid neoplazmlardır. HL, morfolojik ve immünofenotip temelli olarak iki ana alt gruba ayrılır: Klasik HL ve noduler lenfosit predominant HL (NLPHL). Klasik HL'nın ise 4 alt tipe ayrılır: Noduler sklerozan HL, miks sellüler HL, lenfositten zengin tip HL, lenfositten fakir tip HL<sup>1</sup>. HL'ların alt tiplerinin dağılımı coğrafik ve sosyoekonomik faktörler, yaş ve ırk ile değişmekle birlikte yaklaşık %90'ını klasik HL oluştururken, geri kalan %10'un büyük kısmını NLPHL oluşturmaktadır<sup>2</sup>. Klasik HL'nın ise yaklaşık %70'ini noduler sklerozan HL, %20-25'ini miks sellüler HL, %5'ini lenfositten zengin tip HL, %1'den azını lenfositten fakir tip HL oluşturmaktadır<sup>1</sup>.

HL insidansı yılda 100.000 kişide 2-3 olup; tüm malignitelerin %0,6'sını, tüm lenfomaların %10'unu oluşturmaktadır ve tüm ölümlerin %0,2'sinden sorumlu tutulmaktadır<sup>3-5</sup>.

### GEBELİKTE HODGKİN LENFOMA

HL, tüm lenfomaların %10'unu oluşturmmasına rağmen gebelik döneminde tanı alan lenfomaların en yaygın görülen alt tiplerinden birisidir. Bu durum, HL'nın insidansının en yüksek olduğu dönemin kadınlardaki doğurganlık dönemi ile çıkışması ile açıklanmakla birlikte gebelik ve HL arasındaki ilişki hâlâ net değildir. Her 1000 ile 6000 gebelikte bir HL tanısı konmakta ve gebelikte HL tanısı alan bu hasta grubu, tüm HL tanılı hastaların yaklaşık %3'ünü oluşturmaktadır<sup>6-8</sup>. Bu hastaların çoğunda, 40 yaşın altındaki kadınlarda görülen en yaygın alt tip olan noduler sklerozan HL görülmektedir<sup>9</sup>.

<sup>1</sup> Uzm. Dr. Necmettin Erbakan Üniversitesi Meram Tıp Fakültesi Hematoloji BD, dr.tuk@hotmail.com

## KAYNAKÇA

1. Swerdlow, S. H. WHO classification of tumours of haematopoietic and lymphoid tissues. in *WHO classification of tumours* 439 (2008).
2. Laurent, C. et al. Prevalence of Common Non-Hodgkin Lymphomas and Subtypes of Hodgkin Lymphoma by Nodal Site of Involvement. *Medicine (Baltimore)*. **94**, e987 (2015).
3. Siegel, R. L., Miller, K. D. & Jemal, A. Cancer Statistics, 2017. *CA. Cancer J. Clin.* **67**, 7–30 (2017).
4. Sant, M. et al. Incidence of hematologic malignancies in Europe by morphologic subtype: results of the HAEMACARE project. *Blood* **116**, 3724–34 (2010).
5. Smith, A., Howell, D., Patmore, R., Jack, A. & Roman, E. Incidence of haematological malignancy by sub-type: a report from the Haematological Malignancy Research Network. *Br. J. Cancer* **105**, 1684–92 (2011).
6. Woo, S. Y. et al. Radiotherapy during pregnancy for clinical stages IA-IIA Hodgkin's disease. *Int. J. Radiat. Oncol. Biol. Phys.* **23**, 407–12 (1992).
7. STEWART, H. L. & MONTO, R. W. Hodgkin's disease and pregnancy. *Am. J. Obstet. Gynecol.* **63**, 570–8 (1952).
8. Lishner, M. et al. Maternal and foetal outcome following Hodgkin's disease in pregnancy. *Br. J. Cancer* **65**, 114–7 (1992).
9. JACOBS, C. Management of the Pregnant Patient with Hodgkin's Disease. *Ann. Intern. Med.* **95**, 669 (1981).
10. Moshe, Y., Bentur, O. S., Lishner, M. & Avivi, I. The management of hodgkin lymphomas in pregnancies. *Eur. J. Haematol.* **99**, 385–391 (2017).
11. Cohen-Kerem, R., Railton, C., Oren, D., Lishner, M. & Koren, G. Pregnancy outcome following non-obstetric surgical intervention. *Am. J. Surg.* **190**, 467–473 (2005).
12. Cheson, B. D. et al. Recommendations for Initial Evaluation, Staging, and Response Assessment of Hodgkin and Non-Hodgkin Lymphoma: The Lugano Classification. *J. Clin. Oncol.* **32**, 3059–3067 (2014).
13. Takalkar, A. M., Khandelwal, A., Lokitz, S., Lilien, D. L. & Stabin, M. G. 18F-FDG PET in Pregnancy and Fetal Radiation Dose Estimates. *J. Nucl. Med.* **52**, 1035–1040 (2011).
14. Jain, C. ACOG Committee Opinion No. 723: Guidelines for Diagnostic Imaging During Pregnancy and Lactation. *Obstet. Gynecol.* **133**, 186–186 (2019).
15. Gjelsteen, A. C. et al. CT, MRI, PET, PET/CT, and Ultrasound in the Evaluation of Obstetric and Gynecologic Patients. *Surg. Clin. North Am.* **88**, 361–390 (2008).
16. Kanal, K. M. et al. ACR–AAPM–SIIM Practice Guideline for Determinants of Image Quality in Digital Mammography. *J. Digit. Imaging* **26**, 10–25 (2013).
17. RIMAWI, B. H., GREEN, V. & LINSDAY, M. Fetal Implications of Diagnostic Radiation Exposure During Pregnancy. *Clin. Obstet. Gynecol.* **59**, 412–418 (2016).
18. Hoppe, R. T. et al. NCCN Guidelines Insights: Hodgkin Lymphoma, Version 1.2018. *J. Natl. Compr. Cancer Netw.* **16**, 245–254 (2018).
19. Connors, J. M. Advanced-Stage Hodgkin Lymphoma. *Cancer J.* **24**, 230–236 (2018).
20. Hay, A. E. et al. An individual patient-data comparison of combined modality therapy and ABVD alone for patients with limited-stage Hodgkin lymphoma. *Ann. Oncol.* **24**, 3065–3069 (2013).
21. Pereg, D., Koren, G. & Lishner, M. The treatment of Hodgkin's and non-Hodgkin's lymphoma in pregnancy. *Haematologica* **92**, 1230–1237 (2007).
22. Ryu, R. J. et al. Pharmacokinetics of doxorubicin in pregnant women. *Cancer Chemother. Pharmacol.* **73**, 789–797 (2014).
23. Tasrif, Y., Morado, J. & Hebert, M. Pregnancy-related pharmacokinetic changes. *Clin. Pharmacol. Ther.* **100**, 53–62 (2016).
24. Van Calsteren, K. et al. Pharmacokinetics of chemotherapeutic agents in pregnancy: a pre-clinical and clinical study. *Acta Obstet. Gynecol. Scand.* **89**, 1338–1345 (2010).

25. van Hasselt, J. G. C. *et al.* Optimizing anticancer drug treatment in pregnant cancer patients: pharmacokinetic analysis of gestation-induced changes for doxorubicin, epirubicin, docetaxel and paclitaxel. *Ann. Oncol.* **25**, 2059–2065 (2014).
26. Leslie, K. K., Koil, C. & Rayburn, W. F. Chemotherapeutic Drugs in Pregnancy. *Obstet. Gynecol. Clin. North Am.* **32**, 627–640 (2005).
27. Rizack, T., Mega, A., Legare, R. & Castillo, J. Management of hematological malignancies during pregnancy. *Am. J. Hematol.* **84**, 830–841 (2009).
28. Evens, A. M. *et al.* Lymphoma Occurring During Pregnancy: Antenatal Therapy, Complications, and Maternal Survival in a Multicenter Analysis. *J. Clin. Oncol.* **31**, 4132–4139 (2013).
29. Odelia, A. *et al.* Continuing dilemmas in the management of lymphoma during pregnancy: review of a 10-point case-based questionnaire. *Int. J. Clin. Oncol.* **22**, 190–199 (2017).
30. Bachanova, V. & Connors, J. M. Hodgkin Lymphoma in Pregnancy. *Curr. Hematol. Malig. Rep.* **8**, 211–217 (2013).
31. ROSENZWEIG, A. I. Vinblastine Sulfate in Hodgkin's Disease in Pregnancy. *Ann. Intern. Med.* **61**, 108 (1964).
32. Armstrong, J. G., Dyke, R. W. & Fouts, P. J. Vinblastine Sulfate Treatment of Hodgkin's Disease during a Pregnancy. *Science (80-.)* **143**, 703–703 (1964).
33. Wapner, R. J. *et al.* Long-Term Outcomes after Repeat Doses of Antenatal Corticosteroids. *N. Engl. J. Med.* **357**, 1190–1198 (2007).
34. Rodríguez-Pinilla, E. & Luisa Martínez-Frías, M. Corticosteroids during pregnancy and oral clefts: A case-control study. *Teratology* **58**, 2–5 (1998).
35. Palmsten, K. *et al.* Patterns of prednisone use during pregnancy in women with rheumatoid arthritis: Daily and cumulative dose. *Pharmacoepidemiol. Drug Saf.* **27**, 430–438 (2018).
36. Bandoli, G., Palmsten, K., Forbess Smith, C. J. & Chambers, C. D. A Review of Systemic Corticosteroid Use in Pregnancy and the Risk of Select Pregnancy and Birth Outcomes. *Rheum. Dis. Clin. North Am.* **43**, 489–502 (2017).
37. Pinnix, C. C. *et al.* Maternal and Fetal Outcomes After Therapy for Hodgkin or Non-Hodgkin Lymphoma Diagnosed During Pregnancy. *JAMA Oncol.* **2**, 1065 (2016).
38. Avilés, A., Díaz-Maqueo, J. C., Talavera, A., Guzmán, R. & García, E. L. Growth and development of children of mothers treated with chemotherapy during pregnancy: Current status of 43 children. *Am. J. Hematol.* **36**, 243–248 (1991).
39. Avilés, A. & Neri, N. Hematological Malignancies and Pregnancy: A Final Report of 84 Children Who Received Chemotherapy In Utero. *Clin. Lymphoma* **2**, 173–177 (2001).
40. Cardonick, E. & Iacobucci, A. Use of chemotherapy during human pregnancy. *Lancet Oncol.* **5**, 283–291 (2004).
41. Hurley, T. J., McKinnell, J. V. & Irani, M. S. Hematologic Malignancies in Pregnancy. *Obstet. Gynecol. Clin. North Am.* **32**, 595–614 (2005).
42. Mazonakis, M., Varveris, H., Fasoulaki, M. & Damilakis, J. Radiotherapy of Hodgkin's disease in early pregnancy: embryo dose measurements. *Radiother. Oncol.* **66**, 333–339 (2003).
43. MARTIN, D. D. Review of Radiation Therapy in the Pregnant Cancer Patient. *Clin. Obstet. Gynecol.* **54**, 591–601 (2011).
44. Mazonakis, M. & Damilakis, J. Estimation and reduction of the radiation dose to the fetus from external-beam radiotherapy. *Phys. Medica* **43**, 148–152 (2017).
45. Lishner, M. *et al.* Hematologic Malignancies in Pregnancy: Management Guidelines From an International Consensus Meeting. *J. Clin. Oncol.* **34**, 501–508 (2016).
46. Beksac, K. *et al.* Chemotherapy during Pregnancy: Cases of Hodgkin's and Non-Hodgkin's Lymphoma, Chronic Myeloid Leukemia, Breast Cancer, Nasopharyngeal Cancer, and Choriocarcinoma. *Oncol. Res. Treat.* **40**, 441–445 (2017).
47. Avilés, A., Neri, N. & Nambo, M. J. Long-term evaluation of cardiac function in children who received anthracyclines during pregnancy. *Ann. Oncol.* **17**, 286–288 (2006).
48. GZIRI, M. M. *et al.* Chemotherapy during pregnancy: effect of anthracyclines on fetal and maternal cardiac function. *Acta Obstet. Gynecol. Scand.* **91**, 1465–1468 (2012).

49. Mennuti, M. T., Shepard, T. H. & Mellman, W. J. Fetal renal malformation following treatment of Hodgkin's disease during pregnancy. *Obstet. Gynecol.* **46**, 194–196 (1975).
50. GLANCE, C. A. T. A. & NP, A. Specialty Drug Criteria and Utilization Recommendations. (2017).
51. Gurevich - Shapiro, A. & Avivi, I. Current treatment of lymphoma in pregnancy. *Expert Rev. Hematol.* **12**, 449–459 (2019).
52. Amit, O., Barzilai, M. & Avivi, I. Management of Hematologic Malignancies: Special Considerations in Pregnant Women. *Drugs* **75**, 1725–1738 (2015).
53. Connors, J. M. Challenging Problems: Coincident Pregnancy, HIV Infection, and Older Age. *Hematology* **2008**, 334–339 (2008).
54. Weibull, C. E. *et al.* Pregnancy and the Risk of Relapse in Patients Diagnosed With Hodgkin Lymphoma. *J. Clin. Oncol.* **34**, 337–344 (2016).
55. Mendler, J. H. & Friedberg, J. W. Salvage Therapy in Hodgkin's Lymphoma. *Oncologist* **14**, 425–432 (2009).
56. Siepermann, M. *et al.* Oral low-dose chemotherapy: Successful treatment of an alveolar rhabdomyosarcoma during pregnancy. *Pediatr. Blood Cancer* **58**, 104–106 (2012).
57. Ansell, S. M. *et al.* PD-1 Blockade with Nivolumab in Relapsed or Refractory Hodgkin's Lymphoma. *N. Engl. J. Med.* **372**, 311–319 (2015).