International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

Classical Hodgkins Lymphoma Involving Supra and Infra - Diaphragmatic Lymph Nodes in a 2.5 - Year Female Child Dilemma in Treating both the Site: Case Report

Prarabdh Singh[1], Sambit S Nanda[2], Ashutosh Mukherji[3], Aditi Singh[4]

[1, 2, 3, 4]Department of Radiation Oncology, MPMMCC& HBCH Varanasi

Abstract: ***Pediatric HL involving both supra and infra - diaphragmatic adenopathy is not a common entity. Initial evaluation and assessment is very crucial for appropriate staging and treatment of patients. Before starting treatment proper staging and risk stratification is important prior to starting of treatment. Owing to sensitivity of HL, chemotherapy and radiotherapy forms important cornerstone of treatment. With recent advances survival outcomes have improved over the period of time. In our case report we present a young 2.5 year female child with advanced HL and her management. Patient presented with complaints of loss of appetite, weight loss and left cervical lymph nodes enlargement. This case report offers a generalized overview in pediatric HL.***

Keywords: Pediatric HL and infra - diaphragmatic adenopathy,

1. Introduction

Classical comprises main is most commonly seen in young age group comprising of age between 15 & 19 years of age group & comprises of around 18% of diagnosed cancer annually in the united states [1]. With the advances in multimodality treatment comprising of radiation therapy & chemotherapy survival outcomes have improved up to 90%. HL are restricted to supra - diaphragmatic lymph node in 70% of case which involves from one nodal station to other [2]. Here we present a case report of very young 2.5 year female child with diagnosed supra & infra - diaphragmatic adenopathy.

2. Case Presentation:

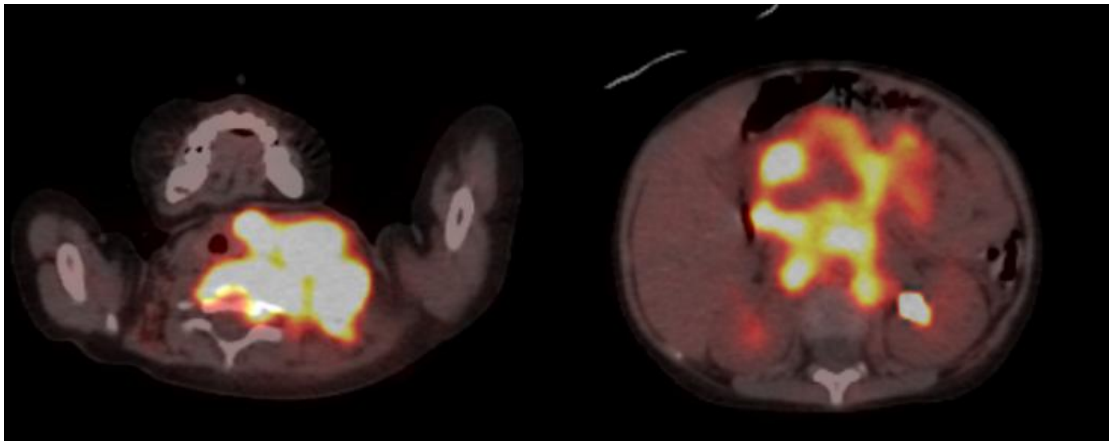
2.5 - year female child was referred to our outpatient department of pediatric hematology & oncology with complaints of loss of appetite, gradually decreasing weight loss and left sided cervical nodes enlargement over a span of 3month. Initially patient was started with symptomatic management of cervical lymphadenitis secondary to upper respiratory tract infection by native doctor. Upon retrospective questioning while acquiring treatment history we discovered that patient caretaker had taken brief visit to local quacks also. When condition did not improve, they came to our center. On examination there was enlargement of left sided cervical lymph nodes which were firm, non - tender on touch with on and off. There was no history of tuberculosis or contacts in family. Biopsy from supraclavicular lymph node showed partially effaced lymphoid architecture by a polymorphous population consisting of small lymphocytes, plasmacells, histiocytes, & occasional eosinophils admixed with large mononuclear cells. These cells have lobated nuclei, prominent nucleoli and moderate amount of cytoplasm. On immunohistochemistry, the large atypical cells were positive for CD30 while negative for LCA, CD20, CD3, PAX5, CD15, EBV - LMP1 and EBER - ISH, overall suggestive of Classical Hodgkin lymphoma. Staging PET - CECT showed FDG avid conglomerated left cervical nodal mass involving cervical level III - V measuring 7.7X2.8X7.3 cm with SUV value of 19.60, FDG avid left paravertebral soft tissue mass in cervical region (C3 - C7) with intraspinal soft - tissue component measuring 4.8X3.1cm with SUV value 22.89, FDG avid conglomerated mesenteric & retroperitoneal mass measuring 9.8X5.9X8cm with SUV max,: 16.32, focal FDG uptake in right renal cortex SUV max: 6.26, Focal FDG uptake in left distal femur with SUV max: 2.33. It was staged as stage IV BX (Bulky site being cervical nodes & infra - diaphragmatic nodes).

As per institutional in line to standard treatment protocol patient was started with ABVD chemotherapy comprising of adriamycin, bleomycin, vinblastin and DTIC, immediately after staging and confirmation of diagnosis. Patient had received 4 cycles of chemotherapy well without undue gap and anticipated toxicity well. Post completion of second cycle of chemotherapy response PET - CECT was done which revealed complete metabolic and morphological response in all site with Deauville score 1. After receiving 4 cycles of chemotherapy they defaulted for treatment, due to personal reasons and reviewed in our OPD after 4 months for follow - up. A PET - CECT was done to see disease status which revealed complete metabolic& morphological response in both supra and infra - diaphragmatic adenopathy. Patient was then referred to our OPD for radiation. The dilemma was irradiating of both sites keeping in mind the young age, anticipated toxicity and respective outcome of the same. Thereafter after extensive discussion curtailing benefit versus risk ratio, young age of 2.5 years radiotherapy was involved field radiotherapy was offered using 19.8Gray in 11 fractions at the rate of 1.8Gy per fraction in 2 phases. In first phase the left cervical chain was irradiated while in second phase retroperitoneal mass was irradiated using appropriate energy, fractions& techniques respecting normal tissue tolerance. Child tolerated radiation well without undue gap in between with no anticipated toxicity. Patient was

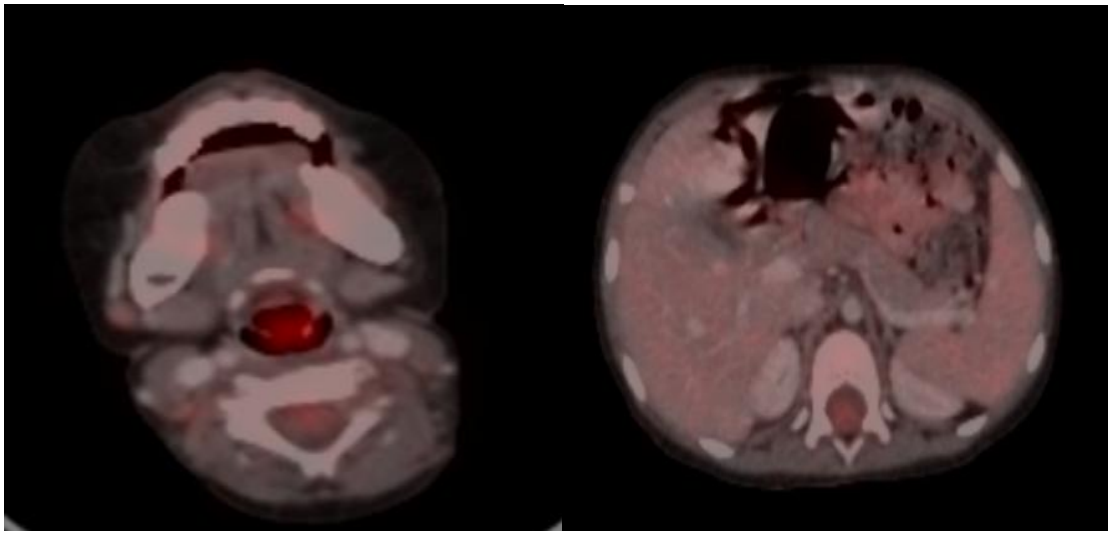
recently visited in OPD for assessment, child is active, cheerful and playful and response PET - CECT scan showed complete metabolic and morphological response.

3. Discussion

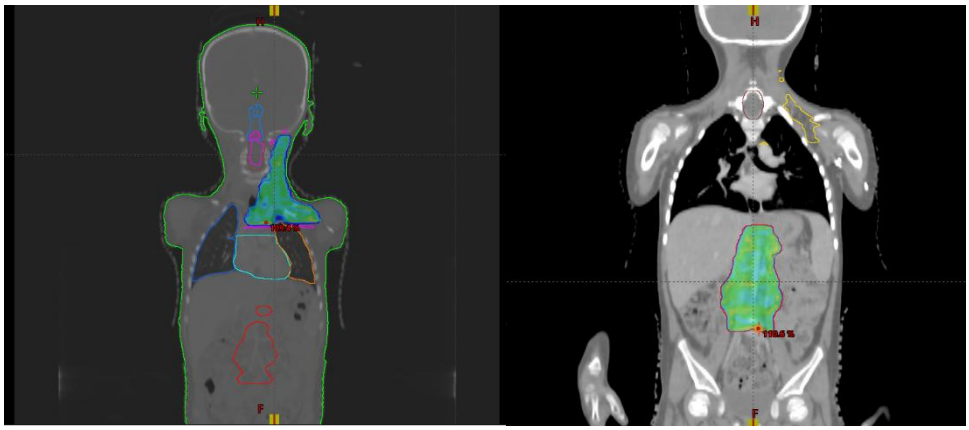
Historically pediatric patients diagnosed with HL have been classified to low, intermediate and high - risk groups based on stage, bulk of disease and presence or absence of B - symptoms. In all risk group treatment paradigm have utilized combination of conventional chemotherapeutic agents consisting of alkylating and anthracyclines with or without radiation therapy. Treatment depends on specific risk stratification. Forlow - risk multiple treatment approaches have been used successfully.5 - year event free survival ranges from 85 - 92% [3 - 6]. Various chemotherapy regimens comprise of OEPA (Vincristine, etoposide, prednisone, and Doxorubicin) for boys, OPPA (Vincristine, procarbazine, prednisone and doxorubicin) for girls, VAMP (Vinblastine, doxorubicin, methotrexate, and prednisone), AV - PC (Doxorubicin, Vincristine, prednisone, cyclophosphamide) and ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine) [7 - 8]. Several trails have focused on optimizing chemotherapy and omitting radiation therapy in patients having complete response. As in prospective GPOH95 trial RT was omitted in CR after 2 cycles of OEPA or OPPA chemotherapy, but patient achieving who had residual disease received RT to a dose of 20Gy with 10 - 15 Gray boost to larger residual disease. Patient with low risk disease treated with this approach had 10 year EFS rates of 96% [9]. Likewise in aphase II trial patient treated with VAMP chemotherapy and RT was omitted in those who achieved a CR after cycle 2. The 2 year EFS was around 91% [4]. In Intermediate risk HL the prime focus is on reduction in therapy in good responding patients while boosting in poor responders. Study by COG clinical trial AHOD0031 have shown that early response assessment supported therapeutic modulation (omission of radiotherapy in rapid early responders with CR & escalating chemotherapy in slow early responders with PET positive disease) [6] likewise study by EURONET - PHL - C1 have shown outcomes little better in those treated with COPP vs COPDAC with 5 - year EFS of 89.9%and 86.1% respectively, but it was seen that gonadotoxicity was greater among those treated with COPP [10]. Children with high - risk HL requires augmentation of further treatment, Recent studies have investigated role of Brentuximab vedotin (BV) in initial therapy, which is an antibody - drug conjugate composed of anti - CD30 monoclonal antibody conjugated by a protease - cleavable linker to monomethyl auristatin E, a microtubule - disrupting agent [11, 12]. ECHELON - 1 trial have shown addition of BV to AVD backbone has resulted in superior PFS compared to ABVD (82.1% vs 77.2% respectively, p=0.04). Study by Metzger etal and Hochberg et al have established role of Brentuximab as cornerstone in treatment of high risk HL. BV has been recently FDA approved in combination with AVE - PC in patients age 2 years and older with previously untreated high - risk HL. Due to radiosensitive nature of HL, radiation therapy forms essential component of treatment. In our study due to baseline bulky disease in both supra and infra - diaphragmatic radiation was offered adhering to institutional protocol and standard guidelines. In our case study the young age and dual location radiation was delivered with utmost precision and conformity to get good survival outcomes, initial there were thought clustering regarding radiation should be offered or not considering the age and disease bulk but meticulous discussion and careful planning resulted in successful delivery of treatment. Patient has followed recently in our OPD with good clinical and radiological response. There have been small number of case report of pediatric patients with HL but this is the one of few cases with both supra and infra - diaphragmatic adenopathy.



A) PET - CECT showing supra and infra - diaphragmatic adenopathy



B) Response PET - CECT post chemotherapy reveals complete metabolic and morphological response



C) 95 % color wash of the target volume on both sites.

References

[1] http: //refhub. elsevier. com/S1521 - 6926 (23) 00006 - 3/sref1

[2] A. Guermazi, P. Brice, E. E. de Kerviler, C. Ferme, C. Hennequin, V. Meignin, *et al.*

[3] Mauz - Korholz ¨ C, Hasenclever D, Dorffel ¨ W, Ruschke K, Pelz T, Voigt A, et al. Procarbazine - free OEPA - COPDAC chemotherapy in boys and standard OPPA - COPP in girls have comparable effectiveness in pediatric Hodgkin's lymphoma: the GPOH - HD - 2002 study. Epub 20100712 J Clin Oncol 2010; 28 (23): 3680–6. https: // doi. org/10.1200/jco.2009.26.9381. PubMed PMID: 20625128.

[4] Metzger ML, Weinstein HJ, Hudson MM, Billett AL, Larsen EC, Friedmann A, et al. Association between radiotherapy vs no radiotherapy based on early response to VAMP chemotherapy and survival among children with favorable - risk Hodgkin lymphoma. JAMA 2012; 307 (24): 2609–16. https: //doi. org/10.1001/ jama.2012.5847. PubMed PMID: 22735430; PubMed Central PMCID: PMC3526806.

[5] Keller FG, Castellino SM, Chen L, Pei Q, Voss SD, McCarten KM, et al. Results of the AHOD0431 trial of response adapted therapy and a salvage strategy for limited stage, classical Hodgkin lymphoma: a report from the Children's Oncology Group. Epub 2018/05/09 Cancer 2018; 124 (15): 3210–9. https: //doi. org/ 10.1002/cncr.31519. PubMed PMID: 29738613; PubMed Central PMCID: PMC6097921

[6] Friedman DL, Chen L, Wolden S, Buxton A, McCarten K, FitzGerald TJ, et al. Dose - intensive response - based chemotherapy and radiation therapy for children and adolescents with newly diagnosed intermediate - risk hodgkin lymphoma: a report from the Children's Oncology Group Study AHOD0031. Epub 2014/10/15 J Clin Oncol 2014; 32 (32): 3651–8. https: //doi. org/10.1200/jco.2013.52.5410. PubMed PMID: 25311218; PubMed Central PMCID: PMC4220044 are found at the end of this article.

[7] Nagpal P, Akl MR, Ayoub NM, Tomiyama T, Cousins T, Tai B, et al. Pediatric Hodgkin lymphoma: biomarkers, drugs, and clinical trials for translational science and medicine. Oncotarget 2016; 7 (41): 67551–73. https: //doi. org/10.18632/oncotarget.11509. PubMed PMID: 27563824; PubMed Central PMCID: PMC5341896

[8] Giulino - Roth L, Keller FG, Hodgson DC, Kelly KM. Current approaches in the management of low risk Hodgkin lymphoma in children and adolescents. Epub 20150330 Br J Haematol 2015; 169 (5): 647–60. https: //doi. org/10.1111/bjh.13372. PubMed PMID: 25824371

[9] Dorffel ¨ W, Rühl U, Lüders H, Claviez A, Albrecht M, Bokkerink ¨ J, et al. Treatment of children and

adolescents with Hodgkin lymphoma without radiotherapy for patients in complete remission after chemotherapy: final results of the multinational trial GPOH - HD95. J Clin Oncol: official journal of the American Society of Clinical Oncology 2013; 31 (12): 1562–8. https: //doi. org/10.1200/jco.2012.45.3266. PubMed PMID: 23509321.

[10] Mauz - Korholz ¨ C, Landman - Parker J, Balwierz W, Ammann RA, Anderson RA, Attarbaschi A, et al. Response - adapted omission of radiotherapy and comparison of consolidation chemotherapy in children and adolescents with intermediate - stage and advanced - stage classical Hodgkin lymphoma (EuroNet - PHL - C1): a titration study with an open - label, embedded, multinational, non - inferiority, randomised controlled trial. Epub 20211209 Lancet Oncol 2022; 23 (1): 125–37. https: //doi. org/10.1016/s1470 - 2045 (21) 00470 - 8. PubMed PMID: 34895479; PubMed Central PMCID: PMC8716340

[11] Connors JM, Jurczak W, Straus DJ, Ansell SM, Kim WS, Gallamini A, et al. Brentuximab vedotin with chemotherapy for stage III or IV hodgkin's lymphoma. N Engl J Med 2017; 378 (4): 331–44. https: //doi. org/10.1056/NEJMoa1708984. PubMed PMID: 29224502.

[12] Brentuximab Adcetris. Vedotin 2022. Available from: https: //www.adcetrispro. com/?&utm_source=GOOGLE&utm_medium=cpc& utm_campaign=GS_ Branded_PTCL_Subtype_2.0&utm_content=Branded + - +PTCL_Subtype_PH&utm_term=adcetris+chp&gclsr c=ds&gclid=Cj0KCQiA_ bieBhDSARIsADU4zLcU4skQ7KE0grCA1ywVB1b ELwMfdOmYS8IQHX3Nkdivlr54TVjd1q0aAjwME ALw_wcB&gclsrc=aw. ds.

[13] Metzger ML, Link MP, Billett AL, Flerlage J, Jr JTL, Mandrell BN, et al. Excellent outcome for pediatric patients with high - risk hodgkin lymphoma treated with brentuximab vedotin and risk - adapted residual node radiation. J Clin Oncol 2021; 39 (20): 2276–83. https: //doi. org/10.1200/jco.20.03286. PubMed PMID: 33826362

[14] Hochberg J, Basso J, Shi Q, Klejmont L, Flower A, Bortfeld K, et al. Risk - adapted chemoimmunotherapy using brentuximab vedotin and rituximab in children, adolescents, and young adults with newly diagnosed Hodgkin's lymphoma: a phase II, non - randomized controlled trial. J Immunother Cancer 2022; 10 (5). https: //doi. org/10.1136/jitc - 2021 - 004445. PubMed PMID: 35584865; PubMed Central PMCID: PMC9119160.

[15] FDA approves brentuximab vedotin in combination with chemotherapy for pediatric patients with classical Hodgkin lymphoma [Internet]. November2022; 10: 2022

[16] Hall MD, Terezakis SA, Lucas JT, Gallop - Evans E, Dieckmann K, Constine LS, et al. Radiation therapy across pediatrichodgkin lymphoma research group protocols: a report from the staging, evaluation, and response criteria harmonization (SEARCH) for childhood, adolescent, and young adult hodgkin lymphoma (CAYAHL) group. Epub 20210812 Int J Radiat Oncol Biol Phys 2022; 112 (2): 317–34. https: //doi. org/10.1016/j. ijrobp.2021.07.1716. PubMed PMID: 34390770; PubMed Central PMCID: PMC8802654.