
Document heading: Case report

Metachronous carcinoma cervix in a treated case of Non-Hodgkins Lymphoma - A rare case report

Dr. P.MasthanBasha¹, Dr. Pranabandhu Das², Dr. B.V.Subramanian³, Dr. Ranadheer Gupta⁴, Dr.Amit Kumar Chowhan⁵, Dr.SilpaKadiyala⁶, Dr.N. Rukmangadha⁶, Mr. M. Nagaraja⁷

¹Junior resident, Department of Radiation Oncology, Sri Venkateswara Institute of Medical Sciences(SVIMS),Tirupati, Andhra Pradesh, India

²Assistant Professor, Department of Radiation Oncology,Sri Venkateswara Institute of Medical Sciences(SVIMS),Tirupati, Andhra Pradesh, India

³Associate Professor, Department of Radiation Oncology,Sri Venkateswara Institute of Medical Sciences(SVIMS),Tirupati, Andhra Pradesh, India

⁴Associate Professor, Department of Nuclear Medicine, Sri Venkateswara Institute of Medical Sciences(SVIMS), Tirupati, Andhra Pradesh, India

⁵Associate Professor, Department of Pathology, Sri Venkateswara Institute of Medical Sciences(SVIMS),Tirupati, Andhra Pradesh, India

⁶Associate Professor, Department of Radiology, Sri Venkateswara Institute of Medical Sciences(SVIMS), Tirupati, Andhra Pradesh, India

⁷Research Scientist, ICMR-DHR-VDL, Sri Venkateswara Institute of Medical Sciences(SVIMS),Tirupati, Andhra Pradesh, India

Received: 18-10-2018 / Revised: 28-11-2018 / Accepted: 10-01-2019

Abstract

The prevalence of Non-Hodgkin lymphomas (NHL) survivors is increasing because of the advances in multimodality treatment approaches which later has become the reason for various late side-effects especially secondary malignant neoplasms. Among these secondary malignancies gynaecological cancers are rarely found in literature. Here we report one previously treated case of NHL in a middle aged female who later developed carcinoma cervix as a metachronous second primary malignancy.

Keywords: NHL, Metachronous, Carcinoma cervix.

Introduction

Non-Hodgkin lymphomas (NHL) are a heterogeneous group of malignancies of the lymphoid system characterized by an abnormal clonal proliferation of B cells, T cells, or both. According to GLOBOCAN 2018 data NHLs are 11th most common cancers in India with incidence of 28110 cases (2.68% of total). In India, carcinoma of cervix is the second most common cancer in females after breast cancer and is the most common gynaecological malignancy.

According to GLOBOCAN 2018 data incidence is 96922 cases (9.23% of total and 16.5% of female cancers)[1]. Survivors of NHL patients may rarely have a chance of developing second malignancies especially in gynaecological region.

Case report

A 54 year old female with no comorbidities presented on 11/11/2010 with complaint of swelling in both sides of neck since 2 months. No other complaints like difficulty in swallowing, pain, fever. Biopsy done outside suggested that secondary carcinomatous deposit. After that, patient presented to Medical Oncology outpatient department in Sri Venkateswara Institute Of Medical Sciences (SVIMS). Endoscopy was normal, Indirect laryngoscopy was normal and direct nasal examination also normal.

*Correspondence

Dr. Pranabandhu Das

Asst. Professor, Department of Radiation Oncology
S.V. Institute of Medical Sciences
(SVIMS) University Cancer Center,
Tirupati, Andhrapradesh, 517507

E-Mail: daspranabandhu@gmail.com

Review biopsy(RB196/10) suggestive of Non hodgkins lymphoma- diffuse small and large cleared cell type-intermediate grade. On Immunohistochemical examination (IRB 196/10): neoplastic cells were CD20: positive, UCHL- I : T cells shows moderate to intense positivity, Kp-I: moderate to intense positivity, BCL2: moderate to intense positivity ,CD10: Negative . Suggested the Impression of Diffuse large B cell NHL -High grade.Trephine biopsy: B5417/10(17.12.10): Hypercellular micro normoblastic bonemarrow with neoplastic infiltration.BM Examination BM1184/10(21.12.10): Hypercellular micro normoblastic bonemarrow with neoplastic infiltration. Chest X ray : normal study.Haemogram was within normal limits.EHCO: LVEF 59%, no RWMA, Normal LV systolic function. Patient treated with 6 cycles of CHOP(Cyclophosphamide, Doxorubicin, Vincristine, Prednisolone) regimen, last

cycle on 11/5/2011. After that patient defaulted for 4 years due to her personal reasons. Again patient was presented after 6 years on 25/5/2017 to Radiation Oncology outpatient department with complaints of lower abdominal pain and bleeding per vagina . Physical examination revealed her blood pressure 110/82 mm of Hg , pulse rate 90/min , respiratory rate 14/min. Gynaecological examination suggestive of ulceroproliferative growth of size 4×3 cm arising from cervix. All fornices and upper half of anterior vaginal wall involved and left parametrium medially involved. No involvement of inguinal and supraclavicular lymphnodes. Biopsy done from the growth and diagnosed as infiltrating moderately differentiated squamous cell carcinoma (Fig.1 & Fig.2). Patient diagnosed as carcinoma cervix stage IIB and metastatic workup done.

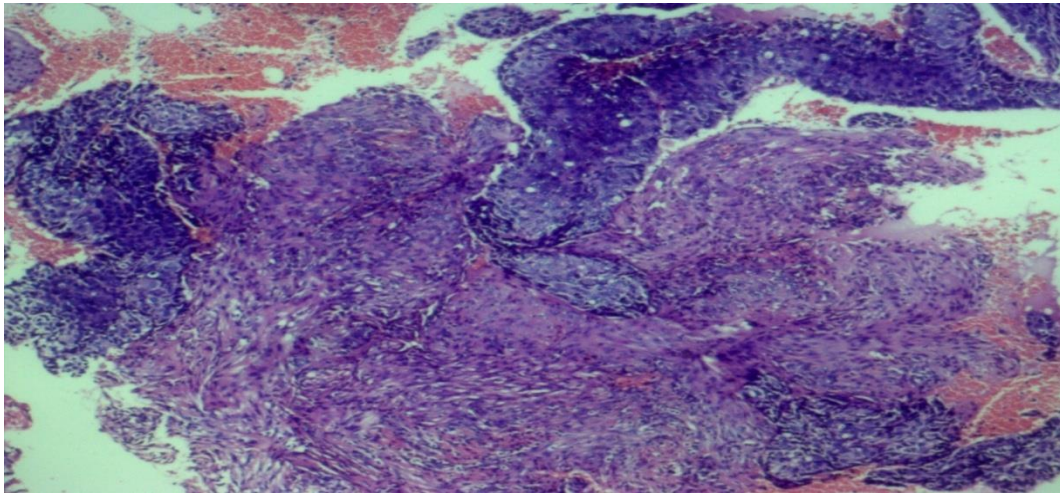


Fig.1: Photomicrograph showing moderately differentiated malignancy (Haematoxylin and eosin ×40)

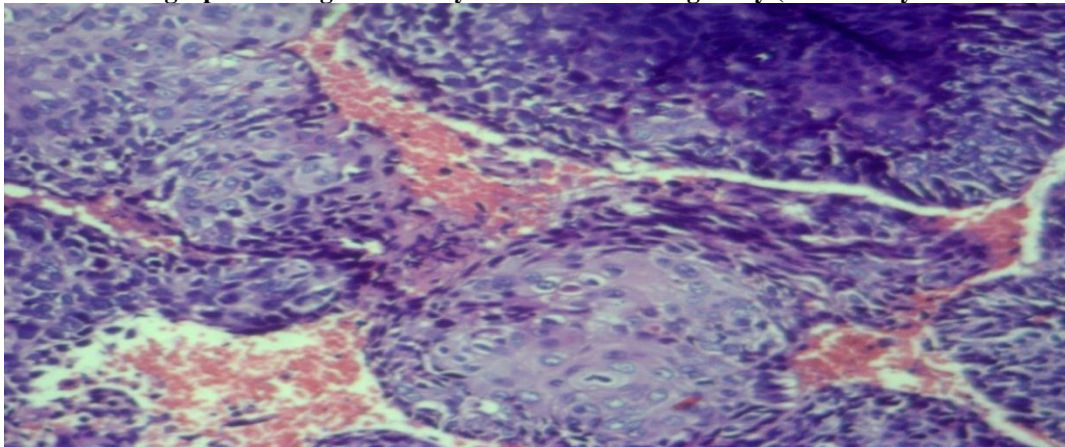


Fig.2: Photomicrograph showing infiltrating moderately differentiated squamous cell malignancy (Haematoxylin and eosin ×100)

Routine blood investigations such as haemogram, renal function test, liver function test are normal.

patient is diagnosed positive for Hepatitis B antigen HBsAg by ELISA test and human papilloma virus DNA detected from cervical growth by nested multiplex polymerase chain reaction (NM-PCR).

FDG PET CT done in view of previous history of non hodgkins lymphoma suggestive of metabolically active soft tissue density lesion in cervix with bilateral parametrial fat stranding noted with pyometra.

Metabolically active left external iliac (1.6×1.2 cm) and aortocaval (1×0.7 cm) lymphnodes present.No evidence of distant metastasis (Fig.3).

Patient was admitted for radiotherapy and treated with external beam radiotherapy of dose 50.4 Gy (grey) in 28 # (fractions) @ 1.8 Gy per fraction and with three fractions of intracavitary brachytherapy @ 7 Gy per fraction, completed treatment on 01.10.2017. Now she is on followup, feeling well without any recurrence or progression, last followup was on 22.09.2018.

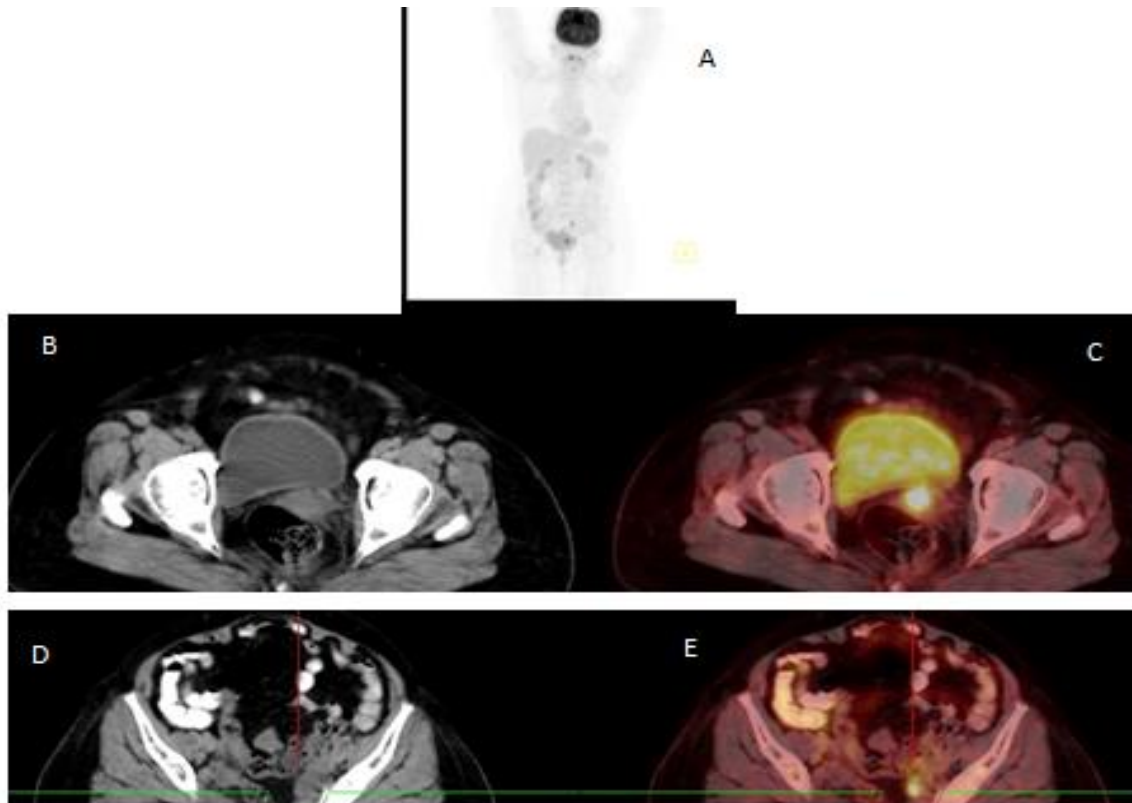


Fig.3: Maximum intensity projection image(A). CT axial image(B) and fused PET-CT image(C) Showing intense FDG uptake in cervix. CT axial image(D) and fused PET-CT image(E) showing intense FDG uptake in left external iliac lymphnode.

Discussion

NHL is a heterogeneous group of malignancies characterized by an abnormal clonal proliferation of T-cells, B-cells or both. The majority of the adult NHLs are of B-cell origin[2]. NHLs range from indolent malignancies (low-grade histologies) to rapidly growing and highly aggressive tumors (high-grade histologies). The overall median age at presentation is 42 years and the incidence increases with advancing age. NHL usually involves the lymph nodes but can

involve extranodal sites and can occur in the stomach, skin, lung, salivary glands and rarely in the mouth[3].

The main symptom of NHL is swelling of lymph nodes in the neck, under the arms or in the groin. Other symptoms can include fever, night sweats, fatigue, abdominal pain and unexplained weight loss. Lymphomas usually are painless; lymph nodes may get larger slowly over a long time before the patient notices. Fever commonly associated with lymphoma may appear and disappear for several weeks[4].

Chemotherapy with or without radiation therapy has been the mainstay of non-Hodgkin's lymphoma (NHL) treatment. In the past few years, evolving therapies have led to improved long-term survival for some histological subtypes, and the introduction of monoclonal antibody treatments has further improved the prognosis of indolent [5-7] and aggressive [8-12] B-cell NHL. High-dose chemotherapy followed by autologous stem-cell transplantation (ASCT) and allogeneic bone marrow transplantation has emerged as another promising approach for the treatment of relapsed lymphoma or as part of planned treatment of neoplasm with a poor prognosis [13-16]. As a result of these advances, the prevalence of NHL survivors is increased and late side-effects of treatment such as secondary malignant neoplasms (SMNs), ischemic heart disease, anthracycline-related cardiotoxicity, and radiation or bleomycin-induced pulmonary toxicity [17].

Results from a metaanalysis including 23 studies of NHL patients showed that there is a higher risk of developing secondary malignancies in NHL survivors compared to general population, the Pooled relative risk for overall and for solid tumors were 1.88 and 1.32, respectively [18]. Among solid tumors lung cancers are most common followed by skin, head and neck cancers [19], hence the development of carcinoma cervix is relatively rare compared to other malignancies. To the best of our knowledge this is a one of the rare case reports of metachronous carcinoma cervix in treated case of Non Hodgkins Lymphoma.

Conclusion

As gynaecological malignancies such as carcinoma cervix is rarely reported as metachronous second primary malignancy in a previously treated case of NHL which can be attributed to previous treatment or a sporadic event, the possibility of its occurrence should not be underestimated, there by the timely screening and early diagnosis of carcinoma cervix as second neoplasms can improve the survival and quality of life in NHL survivors.

References

1. Freddie Bray, Jacques Ferlay, Isabelle Soerjomataram, Rebecca L.Siegel, Lindsey A. Torre, Ahmedinjemal. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *A Cancer Journal for Clinicians* 2018;0:1-31.
2. Jayakrishnan R, Thomas G, Kumar A, Nair R. Non-Hodgkin's lymphoma of the hard palate. *J Oral Maxillofac Pathol.* 2008;12:85-7.
3. Wolvius EB, van der Valk P, van der Wal JE, van Diest PJ, Huijgens PC, van der Waal I, et al. Primary extranodal non-Hodgkin lymphoma of the oral cavity. An analysis of 34 cases. *Eur J Cancer B Oral Oncol.* 1994;30B:121-5.
4. Sathiya M, Muthuchelian K. Significance of immunologic markers in the diagnosis of lymphoma. *Acad J Cancer Res.* 2009;2:40-50.
5. Fisher RI, LeBlanc M, Press OW et al. New treatment options have changed the survival of patients with follicular lymphoma. *J Clin Oncol* 2005; 23: 8447-8452.
6. Marcus R, Imrie K, Solal-Celigny P et al. Phase III study of R-CVP compared with cyclophosphamide, vincristine, and prednisone alone in patients with previously untreated advanced follicular lymphoma. *J Clin Oncol* 2008; 26: 4579-4586.
7. Sacchi S, Pozzi S, Marcheselli L et al. Introduction of rituximab in front-line and salvage therapies has improved outcome of advanced-stage follicular lymphoma patients. *Cancer* 2007; 109: 2077-2082.
8. Coiffier B, Lepage E, Briere J et al. CHOP chemotherapy plus rituximab compared with CHOP alone in elderly patients with diffuse large-B-cell lymphoma. *N Engl J Med* 2002; 346: 235-242.
9. Habermann TM, Weller EA, Morrison VA et al. Rituximab-CHOP versus CHOP alone or with maintenance rituximab in older patients with diffuse large B-cell lymphoma. *J Clin Oncol* 2006; 24: 3121-3127.
10. Pfreundschuh M, Trumper L, Osterborg A et al. CHOP-like chemotherapy plus rituximab versus CHOP-like chemotherapy alone in young patients with good-prognosis diffuse large-B-cell lymphoma: a randomised controlled trial by the MabThera International Trial (MInT) Group. *Lancet Oncol* 2006; 7: 379-391.
11. Sehn LH, Donaldson J, Chhanabhai M et al. Introduction of combined CHOP plus rituximab therapy dramatically improved outcome of diffuse large B-cell lymphoma in British Columbia. *J Clin Oncol* 2005; 23: 5027-5033.
12. Fu K, Weisenburger DD, Choi WW et al. Addition of rituximab to standard chemotherapy improves the survival of both the germinal center B-cell-like and non-germinal center B-cell-like subtypes of diffuse large B-cell lymphoma. *J Clin Oncol* 2008; 26: 4587-4594.
13. Philip T, Guglielmi C, Hagenbeek A et al. Autologous bone marrow transplantation as compared to salvage chemotherapy in relapses of chemotherapy sensitive non-Hodgkin's lymphoma. *N Engl J Med* 1995; 333: 1540-1545.
14. Bierman PJ, Vose JM, Anderson JR et al. High-dose therapy with autologous hematopoietic rescue for

- follicular low-grade non-Hodgkin's lymphoma. *J Clin Oncol* 1997; 15: 445–450.
15. Apostolidis J, Gupta RK, Grenzeliias D et al. High-dose therapy with autologous bone marrow support as consolidation of remission in follicular lymphoma: longterm clinical and molecular follow up. *J Clin Oncol* 2000; 18: 527–536.
 16. Haioun C, Lepage E, Gisselbrecht C et al. Benefit of autologous bone marrow transplantation over sequential chemotherapy in poor-risk aggressive non-Hodgkin's lymphoma: updated results of the prospective study LNH87–2. Grouped'Etude des Lymphomes de l'Adulte. *J Clin Oncol* 1997; 15: 1131–1137.
 17. Chow LM, Nathan PC, Hodgson DC, et al: Survival and late effects in children with Hodgkin's lymphoma treated with MOPP/ABV and low-dose, extended-field irradiation. *J Clin Oncol* 2006; 24:5735-5741.
 18. M. Pirani, R. Marcheselli, L. Marcheselli, A. Bari, M. Federico & S. Sacchi: Risk for second malignancies in non-Hodgkin's lymphoma survivors: a meta-analysis. *Annals of Oncology* 2011; 22: 1845–1858.
 19. Marc André , Nicolas Mounier, Xavier Leleu, Anne Sonet, Pauline Brice, Michel Henry-Amar, Hervé Tilly, Bertrand Coiffier, André Bosly, Pierre Morel, Corinne Haioun, Philippe Gaulard, Felix Reyes, and Christian Gisselbrecht for the Grouped'Etude des Lymphomes de l'Adulte (GELA) : Second cancers and late toxicities after treatment of aggressive non-Hodgkin lymphoma with the ACVBP regimen: a GELA cohort study on 2837 patients. *Blood journal* 2004; 103: 1222-1228.

Source of Support: Nil

Conflict of Interest: Nil