General Medicine: Open Access
ISSN: 2327-5146

Kelleni, Gen Med (Los Angel) 2015, 3:4
DOI: 10.4172/2327-5146.1000204

Case Report Open Access

# Fludarabine Monotherapy Fails to Control a Case of Relapsing Non-Hodgkin's Lymphoma

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**Rec date:** June 22, 2015 **Acc date:** August 17, 2015 **Pub date:** August 24, 2015



**Abstract**

Fludarabine (Fludara), a purine nucleoside analogue, is an antineoplastic drug that has been used in the treatment of many lymphoproliferative malignancies, including various types of non-Hodgkin's lymphoma (NHL). I report a patient who has suffered from a severe deterioration in his general condition after receiving Fludara as a single agent for relapsed NHL for which he's received chemo-immunotherapy.

**Keywords:** Fludara; Non-Hodgkin's lymphoma; Pathological fractures

## Case Report

The incidence of non-Hodgkin lymphoma (NHL) has been rising in many regions and populations and it's considered as the fifth most common cancer in the US, where its incidence has been increasing over the last three decades [1,2]. Fludarabine (Fludara), a purine nucleoside analogue, has been extensively evaluated in the treatment of a number of lymphoproliferative malignancies, including various types of non-Hodgkin's lymphoma (NHL) and it's considered the most effective and most extensively studied purine analog in indolent B-cell malignancies [3,4]. Fludara has also been described as a significant single agent activity in NHL in a variety of clinical phase I/II studies. Its efficacy appears most pronounced in low grade NHL and the follicular subtype in particular as well as in Waldenstrom's macroglobulinaemia [5]. Moreover, fludara combined with other antineoplastic agents was shown to enhance the antitumor effect [6].

In the case represented in this article, Fludara was given in a regional Egyptian oncology center as a single agent to a sixty-four year old male who has relapsed CD20-positive, large B-cell NHL, the relapse was discovered as a recurrent hepatic focal lesion during routine follow up CT scan performed after less than 4 months remission after receiving 8 cycles of cyclophosphamide/doxorubicin/vincristine/prednisone (CHOP) at three week interval combined with 7 cycles of rituximab at the same interval. Soon after receiving fludara, the patient rapidly developed recurrent generalized lymphadenopathy obvious by physical examination; a brain transient ischemic attack experienced for the first time in his life as a transient hemiparesis that was spontaneously relieved in few days; and then he suffered from spontaneous pathological fractures of left humeral and right femoral necks with a widely spread bone marrow replacement of pelvic bones, proximal femori as well as the vertebrae as evident by MRI that was not that severe (Figures 1, 2a and 2b).

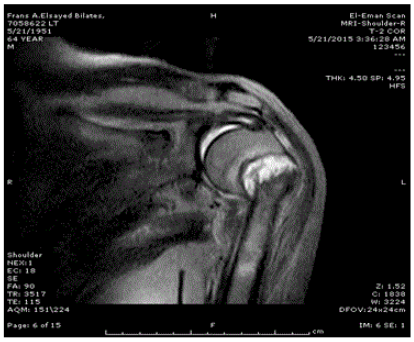

**Figure 1:** MRI image showing Pathological fracture at the humeral neck with medial displacement on the proximal bone end.

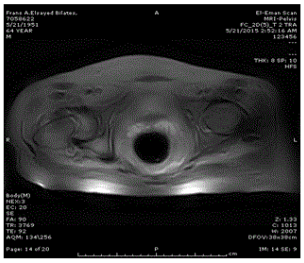

Figure 2a

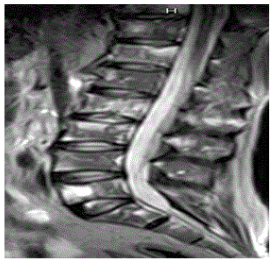

Figure 2b

**Figure 2(a and b)**: A wide spread patholociacal process of abnormal signal pattern showing marrow replacement and infiltriation as well as multiple foci and patches involving the pelvic bones, proximal femori and vertebral marrow especially at the dorsal and lumbar vertebra.

Over the last few decades, advances in immunochemotherapy have led to dramatic improvement in the prognosis of NHL. Despite these advances, relapsed and refractory disease represents a major treatment challenge [1]. There is a powerful rationale for combining rituximab with conventional chemotherapeutic agents to improve the outcome of NHL and in a study evaluating the efficacy of rituximab plus CHOP immunochemotherapy which has been conducted in 40 patients diagnosed with indolent NHL; the overall response rate was 95% (38 of 40 patients) and 22 patients (55%) experienced a complete response [7]. Unfortunately, the patient represented in this case has suffered from a relapse in a relatively short period and the unexplainable decision made to give fludara as single agent has deteriorated the case tremendously. The patient asked my advice and I've contacted the colleagues in the oncology center demanding the addition of cyclophosphamide to fludara according to the regimen described by Rao et al. [8] and they've generously accepted. Thus, the patient was given 30 mg/m$^2$/d of fludara and 300 mg/m$^2$/d of cyclophosphamide on days 1 to 3 for 2 cycles at three weeks interval, he's experienced some improvement in the physical signs e.g. disappearance of the big lymph nodes and but remission was not complete and he's now subjected to palliative sessions of cyclophosphamide/vincristine/prednisone whenever needed to oppose the deterioration of the complete blood count. The pathological fractures which have affected his arm and leg are turning his life into a ruin which he describes as a more humiliating condition than the lymphoma especially knowing that he can't withstand the joint replacement operations.

Finally, whether the deterioration represented in this case was due to disease progression or due to using the wrong choice of chemotherapeutic agents, I wish to declare my opinion against the use of fludara as a single agent in NHL in general and in the relapsed type in particular especially when we know that there're genetic abnormalities, including deletion in the short arm of chromosome 17 (del [17p]) and in the long arm of chromosome 11 (del [11q]) which are associated with poor response to fludarabine [1]. Moreover, we also know that fludara has a well-established cytotoxic activity when used as monotherapy in indolent lymphoma [9]. I would like also to recommend saving rituximab to be added to regimens dealing with the relapsing cases of NHL [10,11] especially in the developing countries where a course of this expensive drug is usually given once after spending a lot of time and effort getting official governmental permission to supply it on the expense of the health insurance.

## References

1. Chao MP (2013) Treatment challenges in the management of relapsed or refractory non-Hodgkin's lymphoma - novel and emerging therapies. Cancer Manag Res 5: 251-269.
2. Clarke CA, Glaser SL (2002) Changing incidence of non-Hodgkin lymphomas in the United States. Cancer 94: 2015-2023.
3. Anderson VR, Perry CM (2007) Fludarabine: a review of its use in non-Hodgkin's lymphoma. Drugs 67: 1633-1655.
4. Ricci F, Tedeschi A, Morra E, Montillo M (2009) Fludarabine in the treatment of chronic lymphocytic leukemia: a review. Ther Clin Risk Manag 5: 187-207.
5. Hiddemann W, Pott-Hoeck C (1994) Fludarabine in the management of malignant lymphomas. Drugs 47 Suppl 6: 50-56.
6. Lazzarino M, Orlandi E, Montillo M, Tedeschi A, Pagnucco G (1999) Fludarabine, cyclophosphamide, and dexamethasone (FluCyD) combination is effective in pretreated low-grade non-Hodgkin's lymphoma. Annals of oncology: official journal of the European Society for Medical Oncology/ESMO 10: 59-64.
7. Czuczman MS (2002) Immunochemotherapy in indolent non-Hodgkin's lymphoma. Semin Oncol 29: 11-17.
8. Rao R, Shammo JM, Enschede SH, Porter C, Adler SS (2005) The combination of fludarabine, cyclophosphamide, and granulocyte-macrophage colony-stimulating factor in the treatment of patients with relapsed chronic lymphocytic leukemia and low-grade Non-Hodgkin's lymphoma. Clinical lymphoma 6: 26-30.
9. Koenigsmann M, Knauf W, Herold M, Pasold R, Müller G, et al. (2004) Fludarabine and bendamustine in refractory and relapsed indolent lymphoma-a multicenter phase I/II Trial of the east german society of hematology and oncology (OSHO). Leuk Lymphoma 45: 1821-1827.
10. Cohen Y, Libster D, Da'as N, Amir G, Polliack A (2003) Retreatment with rituximab alone induces sustained remission in a patient with follicular lymphoma with multiple extranodal sites of involvement, relapsing soon after primary treatment with fludarabine-rituximab. The hematology journal : the official journal of the European Haematology Association/EHA 4: 151-3.
11. Fayad L, Ansell SM, Advani R, Coiffier B, Stuart R, et al. (2015) Dacetuzumab plus rituximab, ifosfamide, carboplatin and etoposide as salvage therapy for patients with diffuse large B-cell lymphoma relapsing after rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone: a randomized, double-blind, placebo-controlled phase 2b trial. Leukemia & lymphoma: 1-10.