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Hairy Cell Leukemia with Unusual Clinical Presentations: A Single Center Experience

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In this study we report 10 cases of hairy cell leukemias (HCL). Some of them were presented with atypical and rare clinical presentations: One of them was presented with ascites, another case was presented with intramuscular hematoma and four cases were presented with no splenomegaly.From 2009 to 2013, HCL diagnosed in 10 of 186 (5.3%) acute and chronic leukemias and they were included in this study. Eigth patients were treated with cladribin with 87,5% complete response and 12,5% partial response rate. One patient was treated only with palliative radiotherapy. One patient was treated in another hospital after diagnosis.

Key words: Hairy cell leukemia, lymphoproliferative disorder, ascites, atypical presentation

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ЕРЕКШЕ КЛИНИКАЛЫҚ БЕЛГІЛЕРІ БАР ШАШЖАСУШАЛЫ ЛЕЙКОЗ: БІЗДІҢ ОРТАЛЫҚТЫҢ ТӘЖІРИБЕСІ

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Мақалада біз шашжасушалы лейкоздың (ШЖЛ) 10 жағдайы туралы баяндаймыз. Бұл зерттеуде 2009-2013 жылдары ем қабылдаған созылмалы және жедел лейкозы бар 186 науқастың ішіндегі ШЖЛ анықталған 10 науқас сипатталады. ШЖЛ клиникалық ағымы жиі жағдайда атипиялық, сирек кездесетін белгілермен көрініс береді. Біздің бақылауымыздағы жағдайдың бірінде іш шемені, екіншісінде бұлшықетішілік қанқұйылу байқалды. 4 науқаста спленомегалия анықталмады. Науқастардың 8-і кладрибин қабылдады, оның 87,5%-ында емге жауап оң болса, 12,5% жағдайда – тек жартылай оң жауап байқалды. Бір науқас паллиативті сәулелік ем қабылдады. Ал енді бірі диагноз қойылғаннан соң басқа ауруханада емделген болатын.

Маңызды сөздер: шашжасушалы лейкоз, лимфопролифератиті бұзылыстар, асцит, атипиялық клиникалық ағым.

ВОЛОСАТОКЛЕТОЧНЫЙ ЛЕЙКОЗ С НЕОБЫЧНЫМИ КЛИНИЧЕСКИМИ ПРОЯВЛЕНИЯМИ: ОПЫТ ОДНОГО ЦЕНТРА

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Мы сообщаем о 10 случаях волосатоклеточного лейкоза (ВКЛ). В исследование были включены 10 пациентов с ВКЛ, диагностированных из 186 (5,3%) случаев острых и хронических лейкозов, пролеченных с 2009 по 2013 годы. Течение ВЛК очень часто характеризуется наличием атипичных и редких клинических проявлений: Один из них был представлен с асцитом, другой - внутримышечной гематомой. В 4 случаях не отмечалась спленомегалия. 8 пациентов получали кладрибин, в 87,5% ответ на лечение был положительный, а в 12,5% - отмечался только частично положительный ответ. Один пациент получал только паллиативную лучевую терапию. Другой после постановки данного диагноза лечился в другой клинике.

Ключевые слова: волосатоклеточный лейкоз, лимфопролиферативные расстройства, асцит, атипичные клинические проявления.

INTRODUCTION

Hairy cell leukemia (HCL) is a rare chronic clonal B-cell lymphoproliferative disorder [1]. The cause of HCL is not known but the morphologic findings, clinical manifestations, and pathologic features are wel described. HCL is generally characterized by splenomegaly, pancytopenia, and infiltration of the bone marrow with lymphocytes which have irregular cytoplasmic projections [2] (figure 1).

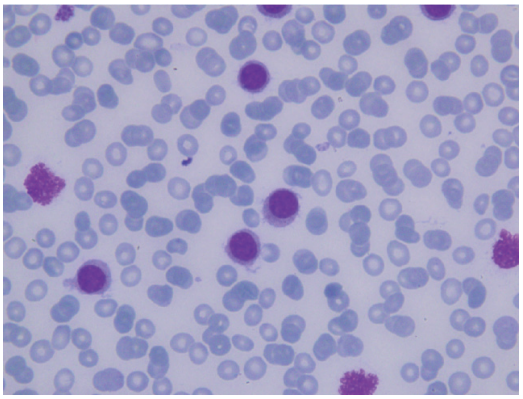

Figure1- Hairy cells

The hairy cells show expression of pan B cell surface antigens (CD19, CD20, and CD22) and also express surface antigens such as CD11c, CD25 and CD103 which are not common on B cells normally [3,4]. Most patients have few symptoms at diagnosis but some patients may have serious pancytopenia, symptomatic splenomegaly or constitutional symptoms. These serious symptoms require treatment [5]. In treatment of HCL, the purine analogs cladribine or pentostatin is the first choice of treatment [6]. In this study we report ten cases of hairy cell leukemia; some with having atypical and rare presentations.

CASE SERIES

From 2009 to 2013, HCL diagnosed in 10 of 186 (5.3%) acute and chronic leukemias and they were included in this study. HCL diagnosis was established by bone marrow biopsy, peripheral blood flowcytometry and tartrate-resistant acid phosphatase staining (TRAP, figure 2).

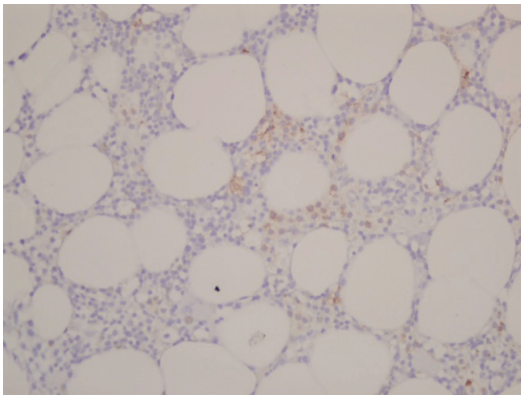

Figure 2 – H airyTRAP stain

Assessment of remission was performed with bone marrow biopsy at the end of 3 months of treatment. Mean follow up time was 14,7months. Seven of the 10 cases received cladribine (0.1 mg/kg, 7 days continue infusion) as a first line treatment. And the 8th case received cladribine as a second line treatment after rituximab. The 1st case received only palliative radiotherapy to spleen and supportive treatment because of low performance status. The 10th case was treated in another hospital after diagnosis. Demographic and laboratory findings of patients are shown in table 1 and detailed diagnostic tools are shown in table 2.

Table 1 – Laboratory and clinical findings, response situation and follow up of 10 HCL patients

	Gender	Age	Wbc(x10^9/L); neu(x10^9/L); hgb(g/dL); plt(x10^9/L)	Spleen (below the left costal margin)	Treatment	Retikulin rate	Response situation and follow up
Case 1	female	85	3,3/1,4/10,4/83	20 cm	Palliative RT	Grade I	On 4. month: exitus
Case 2	female	80	18/1,0/6,4/49	normal	Cladribin	Grade II	On 16. month: in remission
Case 3	female	72	44/3,4/11,9/151	12 cm	Cladribin	Grade II	On 11. month: in remission
Case 4	female	45	1,1/0,1/8,3/110	normal	Cladribin	Grade III	On 17. month: in remission
Case 5	male	51	3,5/0,5/6,4/43	15 cm	Cladribin	Grade III	On 19. month: in remission
Case 6	male	59	2,5/1,0/8,4/59	normal	Cladribin	Grade III	On 19. month: in remission
Case 7	male	57	3,1/0,9/4,6/76	25 cm	Cladribin	unknown	On 28. day: exitus
Case 8	male	80	1,7/0,5/4,6/37	10 cm	Rituximab + Cladribin	Grade II	On 10. Month (after cladribin): in remission
Case 9	male	42	2,8/0,75/14,4/57	normal	Cladribin	unknown	On 9. Month : in remission
Case 10	male	31	1,7/0,2/7/36	12 cm	*	unknown	*

*He received treatment in another hospital after diagnosis

Table 2 - Diagnostic findings in our HCL patients

Cases	Pancytopenia	Splenomegaly	Diagnostic bone marrow biopsy	TRAP positivity*	flow cytometry*	Dry tap
Case 1	+	+	Atypical lenfoid infiltration +	+	Not studied	+
Case 2	-	-	Atypical lenfoid infiltration +	+	CD11c: + CD25: + CD 103:+	+
Case 3	-	+	Atypical lenfoid infiltration +	+	CD11c: + CD25: + CD 103:+	-
Case 4	-	-	Atypical lenfoid infiltration +	+	CD11c: + CD25: + CD 103:+	+
Case 5	+	+	Atypical lenfoid infiltration +	Not studied	CD11c: + CD25: + CD 103:+	-
Case 6	+	-	Atypical lenfoid infiltration +	Not studied	CD11c: + CD25: + CD 103:+	-
Case 7	+	+	Atypical lenfoid infiltration +	+	CD11c: + CD25: + CD 103:-	-
Case 8	+	+	Atypical lenfoid infiltration +	Not studied	CD11c: + CD25: + CD 103:+	-
Case 9	-	-	Atypical lenfoid infiltration +	+	CD11c: + CD25: + CD 103:+	+
	+	+	Atypical lenfoid infiltration +	+	CD11c: + CD25: + CD 103:+	+
* Evaluated in bone marrow and/or pheripheral blood						

In a total of 10 cases (female: 4, male: 6) mean age was 60,2 (range 31-85). Splenomegaly was not present in four cases (40%), pancytopenia was not present in three cases (30%). One case presented with ascites (case 5) and one case presented with intramuscular hematoma (case 10). Among the 8 patients received cladribine, complete remission was achieved in 7 patients (87,5%). The seventh case, who had been given multiple chemotherapy before, died due to sepsis in the first month of the cladribin treatment. Although the symptoms were controlled and the spleen size was decreased in the patient who recieved only palliative radiotherapy, she died because of sepsis due to acute cholecystitis on the 4th month of the treatment. Response situations are shown in table-1.

Discussion

Hairy cell leukemia is known as a rare B-cell lymphoproliferative disorder. It constitutes 2% of all leukemias and occurs more frequently in men (male/female rate is 4:1) [7]. Similarly male to female ratio was 3/2 in our cases with male predominance. Rate of HCL among all leukemias was %5.3 in our patients.

Hairy cell leukemia may present with different clinical symptoms. While some of HCL patients are presenting with abdominal fullness or discomfort due to splenomegaly, others may present with systemic complaints such as fatigue, weakness, and weight loss [8]. In literature it was reported that leucocytosis is seen in 20% of HCL patients [9]. Similarly two of our patients had leucocytosis initially.Although splenomegaly is a nearly constant feature in the literature, four o four 10 patients were found not to have palpable splenomegaly. As with our patients, less marked splenomegaly at presentation is probably due to early diagnosis of HCL.

In some patients clinical presentation may be atypical and diagnosis may be difficult. Some of our HCL patients had different complaints for many years. For example seventh case has been diagnosed as CLL in 2001 and has been treated with chlorambucil and in second line with fludarabine, cyclophosphamide and rituximab. However, HCL diagnosis was made in 2011. Similarly 4th case was investigated for more than one year because of neutropenia and finally she was diagnosed as HCL. The third case who was diagnosed marginal zone lymphoma at another center was reevaluated and had the diagnosis of HCL.

Cutaneous vasculitis, leukocytoclastic angiitis, erythema nodosum, pulmonary infiltrates, polyarthritis, or Raynaud phenomenon are unusual clinical manifestations of HCL [10,11]. In addition, pleural or ascitic fluid may be seen rarely and result from hairy cell involvement of those serosal surfaces [11]. Similar to these rare findings, one of our cases (case 5) presented with

ascites in addition to splenomegaly and pancytopenia. After chemotherapy, the ascites has been resolved.

Palpable lymphadenopathy is uncommon in HCL. However, as a result of the routine use of computerized tomograph in the evaluation of patients with lymphoproliferative disorders, significant deep lymphadenopathyhas been found in up to one-third of patients with HCL [12]. One of our patients had a single superficial cervical lymphadenopathy and one had multiple deep lymphadenopathies.

Staining of the BM trephine biopsy generally shows a moderate to marked increase in reticulin fibers in HCL [2]. Similar to this data all of our cases showed grade II to III reticular fibrosis in bone marrow.

Cladribine is the first treatment choice for HCL. A single course of cladribine generally induces long-lasting complete responses in most of patients [13]. Goodman et al. reported the long-term follow up of 349 patients who had received cladribine and revealed 319 (91%) complete responses (CR) and 22 (7%) partial responses with the overall response rate of 98% [15]. Similarly in our study, 7 of 8 cases (87,5%) achieved CRwith a single course of cladribin.

Because hairy cells express the B-cell antigen CD20, a chimeric humanized mouse anti-CD20 monoclonal antibody rituximab is an other therapeutic option. Rituximab may be used in HCL patients who relapse after cladribine therapy with a response duration of less than 18 months and who demonstrate a significantly hypoplastic marrow or a prior severe opportunistic infection [7]. The 8th case of our patients received six courses of rituximab as first line treatment becuase he could not take cladribin due to health insurance problem. Partial response was achieved after rituximab.

In conclusion, keeping in mind the possibility of unusual presentations, diognosis of HCL must be considered when cytopenic patients present with ascites or other unexplained signs or symptomswith or without splenomegaly.

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