

## CASE REPORT

### RITUXIMAB IN THE TREATMENT OF THE VARIANT OF HAIRY CELL LEUKAEMIA: A CASE REPORT

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**A b s t r a c t:** Hairy cell leukaemia (HCL) is an uncommon, low-grade B-cell lymphoproliferative disorder. HCL-variant describes an entity of HCL that is important from the point of view of requiring differential diagnosis from HCL, and for requiring careful consideration of the treatment approach. HCL-variant differs from the classic form with respect to the lack of monocytopenia, its elevated WBC and unique morphology and immunophenotype. Indeed, there is currently no adequate standard treatment for this condition – HCL-variant is generally resistant to interferon- $\alpha$ , and complete remission is rarely achieved with either pentostatin or cladribine.

We report a 57-year-old female patient who presented at our institution in November 2004 with high white blood counts and splenomegaly. Based on her blood morphology, bone marrow and spleen histology, immunophenotype and clinical characteristics, the patient was diagnosed as having HCL-variant, with blastoid variant transformation. The patient had advanced-stage disease. She was initially treated with splenectomy, which resulted in short-term normalization of blood counts. One month later the blood counts deteriorated, she developed peripheral and abdominal lymphadenopathy and had poor performance status. One cycle of cladribine combined with rituximab was immediately administered. We started with rituximab 375 mg/m<sup>2</sup>, which resulted in a remarkable recovery of blood counts, followed by cladribine 0.1 mg/kg for 7 days. However, the patient's general condition worsened, and she subsequently died from heart failure.

Our experience from this case suggests that rituximab is a promising therapy for patients with HCL-variant, particularly when combined with cladribine. However, further clinical study is required before rituximab can be considered as a front-line therapy for this form of malignancy.

**Key words:** Hairy cell leukaemia, variant, blastoid transformation, cladribine, rituximab.

### Introduction

Hairy cell leukaemia (HCL) is an uncommon, low-grade B-cell lymphoproliferative disorder.

Hairy cell leukaemia-variant (HCL-V) is a distinct clinicopathological entity. It differs from classic HCL in its morphological, immunological and clinical features.

In HCL-V, bone marrow and spleen histology resemble typical HCL, but the circulating cells have a round or oval nucleus and a prominent nucleolus (resembling prolymphocytes) and moderately basophilic villous cytoplasm [3, 4]. The cells have a B-cell phenotype and often express IgG on the cell membrane, but lack typical hairy cell antigens, and always express CD25 and sometimes also CD103 and HCL2 [3, 4, 5, 10] (Table 1).

Tabele 1 – Табела 1

*Differences between the expression of cell markers in HCL and HCL-V*  
*Разлики међу експресијата на келијните маркери кај HCL и HCL-V*

Antigen	slg.	HLA-DR	CD5	CD10	CD20	CD23	FMC7	CD11c	CD25	HCL2	CD103
HCL	+	+	-	-	+	-	+	+	+	+	+
HCL-V	+	+	-	-	+	-	+	+	-	±	±

Patients typically present with a high white blood cell count (WBC:  $50 \times 10^9/L$ ) and lack of monocytopenia. The clinical course of HCL-V is variable, but usually aggressive and associated with a short survival [3, 4, 9].

There is no adequate treatment for this condition. Recently, in view of the efficacy demonstrated by cladribine in HCL, this drug has been used in HCL-V, but with a lower response rate than in classic HCL. Very rarely, patients may achieve complete remission (CR) after three or four courses of cladribine. There are no reported CRs with any other agent [1, 3, 4, 8].

Monoclonal antibodies which target CD20 expressing cells, such as rituximab, have been tested successfully in the treatment of HCL [2, 3, 6, 7].

Here we report a patient who was diagnosed as HCL-V and treated with chemotherapy combined with rituximab.

### Case report

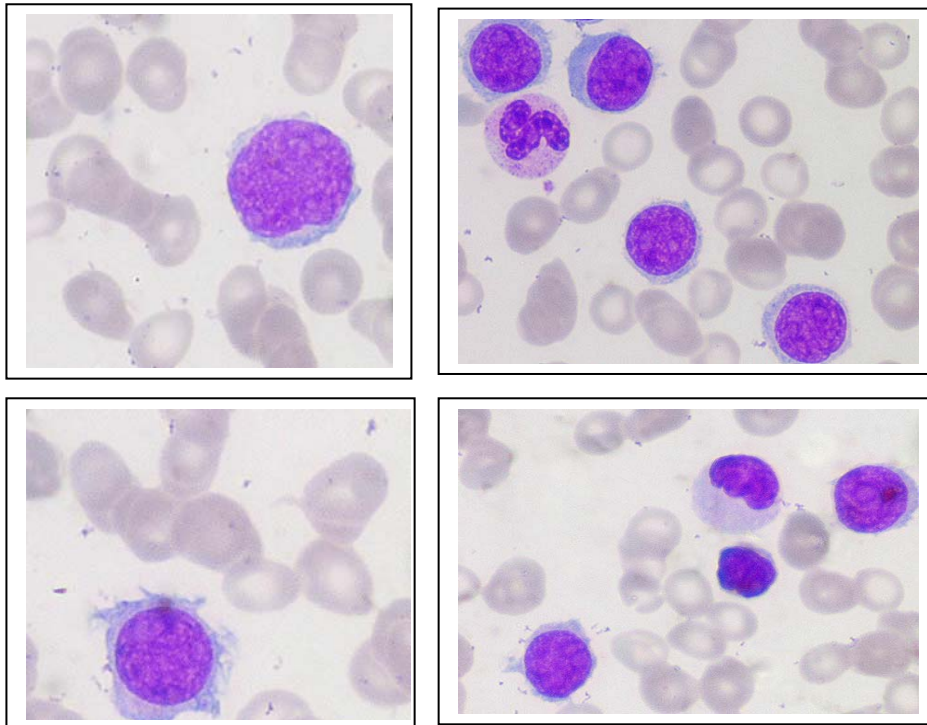
A 57-year-old female patient presented at our department in November 2004 with high WBC ( $47-65 \times 10^9/L$ ), low Hb (86 g/L), low platelet count

( $80 \times 10^9/L$ ), night sweats, weakness and fatigue. On examination the spleen was palpable 20 cm, accompanied with painful abdominal discomfort. There was no hepatomegaly or lymphadenopathy. RFT/LFT/electrolyte/urate were in the normal range except LDH (1292 U/L).

Based on blood morphology, bone marrow and spleen histology, cytochemistry and immunophenotype, the patient was diagnosed as having HCL-V. The diagnosis was confirmed in two different laboratories.

The immunophenotype of the HCL-V cells was IgD+, IgM+, CD20+, CD5-, CD23-, CD10-, cyclinD1-, DBA44+, CD103+ and with no nuclear expression of BCL6.

Blood smears showed infiltration with hairy-cells of 56% and blastoid forms of 10% (Fig. 1).



*Figure 1 – Blood smears showing hairy cell variant in blastoid transformation*  
*Слика 1 –Крвните размаски покажуваат варијанта на влакнеста ќелија во бластоидна трансформација*

The patient had advanced-stage disease, with blastoid-variant transformation.

She had already had the disease for at least 2 years. She was initially treated with splenectomy, which resulted in short-term normalization of blood counts.

One month later the blood counts deteriorated, she developed peripheral and abdominal lymphadenopathy and had poor performance status.

One cycle of cladribine combined with rituximab was immediately administered.

We started with rituximab 375 mg/m<sup>2</sup>, which resulted in a remarkable recovery of blood counts (WBC decreased from 104 × 10<sup>9</sup>/L to 5.6 × 10<sup>9</sup>/L within 24 hours), followed by cladribine 0.1 mg/kg as a continuous iv infusion for 7 days.

However, the patient's general condition worsened and she subsequently died from heart failure.

### Conclusions

The application of rituximab combined with cladribine resulted in a remarkable recovery of blood counts in our patient with HCL-V in blastoid transformation.

Our experience from this case suggests that rituximab is a promising therapy for patients with HCL-V, particularly when combined with cladribine.

However, further clinical study is required before rituximab can be considered as a front-line therapy for this form of malignancy.

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### Резиме

## РITUXИМАВ ВО ТРЕТМАНОТ НА ВАРИЈАНТА НА HAIRY CELL ЛЕУКЕМИЈА (ПРЕГЛЕД НА СЛУЧАЈ)

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Леукемија на влакнести ќелии (Hairy cell Leukemia) е ретко хронично лимфопрлиферативно заболување. Една од варијантите на оваа леукемија (Hairy-cell Leukemia-variant) е значајно да се разграничи од класичната форма заради потребата од посебен тераписки пристап. Варијантата се карактеризира со зголемен број на леукоцити, отсуство на моноцитопенија, единствена морфологија и имунофенотип. Таа е резистентна на интерферон- $\alpha$ , а комплетна ремисија ретко се постигнува со 3–4 циклуси на пентостатин или кладрибин.

На нашата клиника (ноември 2004 год.) беше примена 57-годишна пациентка со висока леукоцитоза и изразена спленомегалија. Врз основа на клиничките карактеристики, морфологијата на ќелиите во крвта, хистопатолошките карактеристики на коскениот мозок и слезината и имунофенотипот, пациентката беше дијагностицирана како леукемија на влакнести ќелии – варијанта во бластоидна трансформација. Таа беше пациент во напреднат стадиум на болеста.

Иницијално, кај пациентката беше направена спленектомија со краткотрајно нормализирање на крвната слика. По еден месец од спленектомијата дојде до прогресија на болеста со брз пораст на леукоцитите и појава на периферна и абдоминална лимфаденопатија. Пациентката веднаш беше поставена на терапија со кладрибин и ритуксимаб. Лекувањето започна со

ритуксимаб 375 мг/м<sup>2</sup> што доведе до значително намалување на леукоцитите, проследено со континуирана инфузија на кладрибин 0,1 мг/кг во текот на седум дена. Набрзо по завршувањето на терапијата состојбата на пациентката прогресивно се влошуваше и таа почина од срцева слабост.

Ова наше искуство покажа дека ритуксимаб во комбинација со кладрибин може да биде надежна терапија во лекувањето на ова многу ретко заболување. Меѓутоа, потребни се понатамошни клинички студии за употребата на ритуксимаб како првостепенa терапија кај ова заболување.

**Клучни зборови:** леукемија на влакнести ќелии, варијанта, бластна трансформација, кладрибин, ритуксимаб.

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