

# Good clinical response following Ibrutinib treatment of a rare case of lymphoplasmacytic lymphoma secreting IgA kappa paraprotein: A case report

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**Abstract.** Lymphoplasmacytic lymphoma (LPL) is a malignant proliferation of small lymphocytes, lymphoplasmacytoid cells and plasmocytes affecting the bone marrow, lymph nodes and spleen. Its incidence is 1/100,000 and represents 8% of all lymphomas. A total of ~5% of patients with LPL may secrete non-IgM of IgG, IgA, kappa or lambda type or be non-secretory. In the present study, a case of a 62-year-old female patient who was diagnosed with non-IgM LPL with kappa light chain monoclonal paraprotein production and normal serum immunoglobulin levels was reported. The *MYD88* L265P mutation was detected by molecular genetic analysis using a sample of the bone marrow. The patient underwent initial treatment with a combination of Bendamustine-Rituximab, and later on, Ibrutinib (a Bruton kinase inhibitor) was added to the treatment protocol. The authors' aim was to describe a case of a rare type of LPL studied and cured at the University Hospital 'St. Ivan Rilski', as well as to show the methods used for its diagnosis and their applicability. The difficulty in diagnosing such rare cases of LPL which are associated with marked plasmacytic differentiation and IgA paraprotein secretion resembling plasma cell neoplasia was addressed. From the other side, the characteristic features in favor of LPL diagnosis are the immunophenotype profile of plasmocytes, as well as the presence of *MYD88* L265P mutation. Finally, the methods

of management and treatment of this type of lymphoma were reported, highlighting the favorable effect of the treatment with Bruton TK inhibitor (Ibrutinib).

## Introduction

Lymphoplasmacytic lymphoma (LPL) is a rare low-grade non-Hodgkin lymphoma which affects the B-lymphocytes and causes their abnormal growth and dysregulation (1). The abnormal B-cells show features of both lymphocytes and plasma cells, hence originates the name of the disease. Most patients have the clinical syndrome of Waldenström macroglobulinemia (WM), which is defined as LPL with an associated immunoglobulin M (IgM) serum monoclonal protein. Roughly 5% of LPL patients secrete non-IgM paraproteins (e.g., IgG, IgA, kappa, lambda) or are non-secretory (2).

Due to its extreme rarity (only 5% of all LPL cases), non-IgM LPL is challenging to diagnose and, also, to treat and cure. Moreover, those rare cases usually present with a heterogeneous clinical phenotype and there is generally a lack of reported cases. To the best of our knowledge, this is the second non-IgM LPL case reported in scientific literature with kappa chain production (3). Before that, Cautha *et al* (2) reported a case of a non-IgM LPL with lambda light chain monoclonal paraprotein expression. In addition, it was presented how the management strategy was modified from the time of diagnosis until the patient finally benefitted from a treatment using a Bruton TK inhibitor (Ibrutinib). This case will be useful in hematological practice to shorten the time of diagnosis of such complicated and rare cases and to suggest the most beneficial treatment protocol.

## Case report

A 62-year-old female patient was accepted initially in a regional hospital (September 2022; Hospital 'St. George', Plovdiv, Bulgaria) suspected with a plasma cell neoplasia (PCN). At that time, flow cytometry of the bone marrow revealed that 75% of the lymphocytes had phenotype as CD19<sup>+</sup>/CD20<sup>+</sup>/CD79b<sup>+</sup>/CD5<sup>-</sup>/CD200<sup>-</sup>/CD23<sup>-</sup>/CD10<sup>-</sup>/CD43<sup>-</sup>. In total, 16% of the lymphocytes belonged to T-subtype (CD3<sup>+</sup>),

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**Abbreviations:** LPL, lymphoplasmacytic lymphoma; WM, Waldenström macroglobulinemia; WBC, whole blood count; PR, partial response; PCN, plasma cell neoplasia

**Key words:** LPL, rare, IgA kappa, treatment, Ibrutinib

11% were Th cells (CD3<sup>+</sup>CD46) and 4.55% were Tc (CD3<sup>+</sup>CD8<sup>+</sup>). The ratio Th/Tc was 2.2; 2.31% were NK cells (CD3<sup>+</sup>CD56<sup>+</sup>CD16<sup>+</sup>) and 2% of the cells in the aspirate were plasma cells with a phenotype CD38<sup>+</sup>/CD138<sup>+</sup>/CD19<sup>±</sup>/CD45<sup>+</sup>/CD56 kappa<sup>+</sup>. As those results were suspected for B-cell lymphoma kappa (+), a molecular genetic analysis was recommended. PCR analysis followed by 2% agarose gel electrophoresis with ethidium bromide revealed a carriership of a somatic mutation L265P in *MYD88* gene. The flow cytometric and molecular-genetic analyses were performed before the admission of the patient to our clinic, and thus, the presented results were retrieved from the official medical records, which is one of the limitations of the present study.

Trepanobiopsy showed cells typical for LPL, bearing marks both of lymphocytes and plasma cells (Fig. 1A and B). Staining of the bone marrow sample revealed a massive infiltration by lymphoplasmacytic cell populations (Fig. 1C). The subsequent staining for markers CD138 (Fig. 2A) and CD20 (Fig. 3A) was positive. A substantial part of the analyzed cells were Pax5-positive (a nuclear marker of mature B cells), CD5 staining was positive only in a small amount of dispersed lymphoids, and CD56 staining was positive in osteoclasts and osteoblasts. MUM1 (a marker of a transition of mature B cells towards plasma cells) was also expressed in a part of the cell content; moderate fibrosis was detected (stage MF-2). The subsequent agarose gel electrophoresis demonstrated a presence of M gradient. The staining data were taken directly from the medical records of the patient. An initial therapy was initiated by one course of Bendamustine/Rituximab. The treatment provoked a reaction of general kidney failure and anuria and the patient was accepted at the Nephrology department for treatment.

Later on, upon a reason of her kidney problems, the patient decided to seek a second opinion and referred to the Hematology ward of the University Hospital 'St. Ivan Rilski' where she had been admitted. She was assigned additional testing, including serum isoelectric focusing (IEF), which demonstrated a distinct amount of paraprotein in the serum type IgA/kappa (Gamma M-spike 63.97 g/l, KF 119.94 mg/l) (Fig. 4A) and myelogram that reported cytological data for LPL with moderate and expressed hypoplasia of the bone marrow (54% lymphoplasmacytes). Computed tomography (CT) demonstrated rounded cervical lymph nodes with maximum axial dimensions 8.8/8.5 mm; axial lymph nodes bilaterally [dimensions: 13.5/11 mm from the left side and 15/11 mm from the right (Fig. 5)]. No pleural effusion was visualized. The trachea had lumen of normal width and wall thickness. The bronchi bilaterally were freely passable up to the segmental level. No infiltrative changes or nodular lesions were visualized in the lung parenchyma. CT data of enlarged mediastinal lymph nodes with axial size 27/13 mm (Fig. 6). There were no focal lesions in the structure of the liver and the spleen; adrenal glands and both kidneys were intact. CT data for axillar, mediastinal, abdominal (Fig. 7C), pelvic and inguinal lymphadenopathy (Fig. 7A and B). The diagnosis of LPL IV B clinical stage, stage D LPL was confirmed. The treatment was based on NCCN clinical practice guidelines in oncology (4) and the patient was assigned three more courses of Bendamustine/Rituximab (from November of 2022 to January of 2023). At that stage, the patient decided to continue her treatment and follow up at the University Hospital.

In February 2023, the patient was accepted again for control examinations and re-assessment of the treatment. Trepanobiopsy provided evidence of partial response (PR) to the treatment. IEF confirmed the decrease in the paraprotein type IgA/K-Gamma M-spike in the serum 44.57 g/l (Fig. 4B). Even if there was a partial reduction, the plasma cell populations were again stained positive (Fig. 1D). The lymphoplasmacytes still accounted for >50% of the cell contents (Fig. 2B), indicating that the level of plasma cell populations in the bone marrow was still high. There was a complete lack of cells expressing CD20 (Fig. 3B). The results from the WBC are included in Table I.

Following the PR to the treatment, it was decided to continue on the same regimen for another 2 courses of immuno-chemotherapy. The patient's treatment course included Rituximab 600 mg at day 1, Bendamustine 100 mg at days 2 and 3, dexamethasone 20 mg/day for 4 days, Fraxiparine 0.4 mg/day and additional drugs for her high blood pressure and kidney failure.

After 6 courses in total with Bendamustine/Rituximab, the patient was evaluated again with serum IEF exhibiting a persistence of paraprotein type IgA/kappa in the serum (Gamma M-spike 44.57 g/l, KF 39.74 mg/l) (Fig. 4C). From April 2023 she started therapy with Bruton kinase inhibitor [Ibrutinib (brand name, Imbruvica)]-3 tablets/day (total 420 mg/day).

The last control examinations of the patient dated from August 2023. After four months of treatment with Imbruvica, she had substantially improved her health condition (Table II) and had lowered the level of IgA with ~30 g (from October 2022 until July 2023). The serum electrophoresis reported Gamma M-spike concentration of 29.27 mg/l (Fig. 4D). Currently the patient is feeling well; her ECOG PS performance status is 1, as of December 2023. The patient's blood examinations revealed mild anemia (HGB, 109 g/l), neutropenia (Neu, 1.01 g/l) and the biochemical results revealed slightly elevated levels of total protein 87.8 g/l (normal range 64-83 g/l). Her condition is continued to be monitored by regular IEF of blood and urine samples.

## Discussion

WM is a term indicating LPL with an associated immunoglobulin M (IgM) serum monoclonal protein (5). LPL, associated with IgA paraprotein is even more rare and those cases mimic a plasma cell neoplasm (PCN) (6). In a study of 27 cases with either IgA or IgG secretion, Qiu *et al* (6) reported that all patients had a median bone marrow involvement of 10%, light chain was identified in 96% of the cases measured by flow cytometry, while *MYD88* mutation was detected in 17 of 24 cases (71%). The neoplastic plasma cells were positive for CD45 (100%), CD19 (96%), CD81 (89%), CD27 (83%), CD56 (16%), whereas CD117 was consistently negative (6). As differential diagnostic features of LPL over PCN, the authors point the characteristic immunophenotypic profile and the presence of *MYD88* and/or *CXCR4* mutations. In a study comparing non-IgM LPL cases and WM controls matched by age and sex, the presence of extramedullary disease was higher in cases, while neuropathy and hyperviscosity was higher in controls (7). A recent study using next-generation sequencing approach reported *MYD88* to be the most common mutation

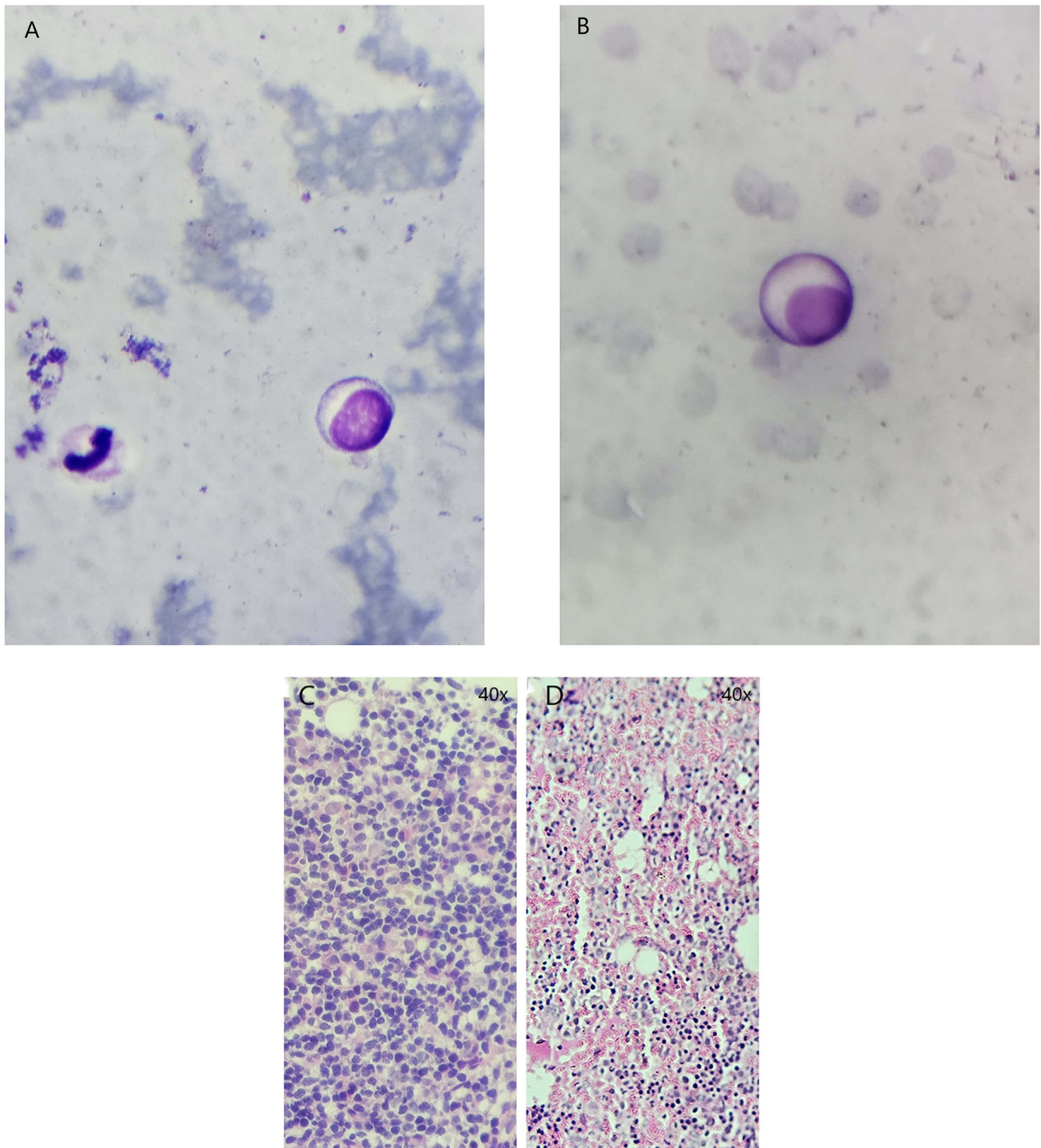


Figure 1. (A and B) Staining of the bone marrow (magnification, x100) and (C and D) staining with hematoxylin-eosin (magnification, x40). (A and B) Cells typical for LPL, bearing marks of both lymphocytes and plasma cells: Round to oval eccentric nucleus, clumped or condensed chromatin and basophilic cytoplasm with perinuclear clear zone. Images (C) before chemotherapy and (D) after chemotherapy showing the presence of mature lymphocytes, lymphoplasmacytic cells and plasma cells, which is characteristic of LPL. (D) A slight change in the amount of the lymphoplasmacytic population was observed after 4 courses of immunochemotherapy. LPL, lymphoplasmacytic lymphoma.

in non-IgM LPL patients (70%), followed by *CXCR4* (20%), *KMT2D* (10%) and *ARID1A* (10%). Mutant allele frequency in *MYD88* L265P did not differ significantly between WM and non-IgM-type LPL. Most mutations detected by NGS were subclonal following *MYD88* L265P. Those results proved similar genetic characteristics in the two subsets of LPL patients (8).

Nearly 90% of IgM secreting LPL develop a somatic mutation in the gene *MYD88*, and even rarer, in *CXCR4* (1). *MYD88* is a driver gene in hematologic B-cell malignancies and the missense mutation (L265P) is a single causative mutation transforming IgM-producing B cells into malignant B cells (9). It constitutively activates NF- $\kappa$ B and its associated signaling pathways, thereby promoting B-cell proliferation



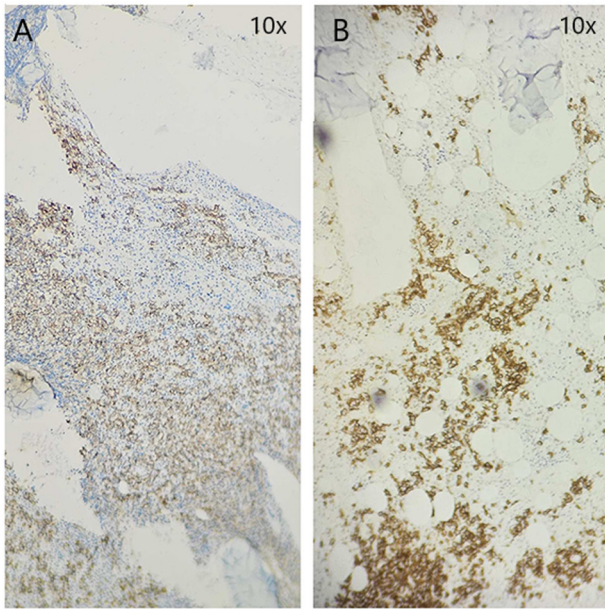


Figure 2. IHC of CD138. Immunohistochemical staining of 8- $\mu$ m thick formalin-fixed paraffin-embedded sections was performed using an antibody against CD138 marker (magnification, x10) (Roche Diagnostics for usage with BenchMark Ultra IHC/ISH System), showing a decrease of the infiltration (A) before and (B) after four courses of immunochemotherapy. CD138 is an IHC marker indicating the plasma cell population in the bone marrow. VENTANA primary antibodies are developed for use on BenchMark instruments in combination with Roche Tissue Diagnostics detection kits and accessories. The parameters for the automated procedure are edited in each detection kit according to the procedure in the instrument used guide. All used antibodies are intended for *in vitro* diagnostic purposes. The antibody is optimized for use on BenchMark IHC/ISH instrument in combination with VENTANA detection kit and no dilution or titration is required. Primary antibody is incubated for 16 min at 37°C, counterstain is with hematoxylin II (8 min), post counterstain with Bluing (4 min). The staining pattern has been analyzed on BOND-MAX automated IHC and ISH staining system (Leica Biosystems GmbH).

and survival (10). It is a missense gain-of-function mutation in myeloid differentiation changing the amino-acid leucine to proline at position 265 of MYD88 (11). MYD88 is playing the role of an adaptor molecule in the canonical NF- $\kappa$ B pathway coordinating the assembly of a multisubunit complex of IRAK1 and IRAK4 (IL-1 receptor-associated kinases), which through TRAF6, activate TAK1 (TGF $\beta$ -activated kinase 1). The activated NF- $\kappa$ B increases signaling of IL-6 and IL-10, which further promotes B-cell proliferation and survival via JAK/STAT signaling cascade (10).

MYD88 L265P is a somatic mutation (9,12) identified in ~90% of WM, but the demonstration of this mutation is also a necessary tool for the right WHO diagnosis of LPL (12,13). It is usually found in blood and/or the bone marrow. However, there are unusual places of its expression, as the skin in cutaneous form of WM (14). MYD88 L265P is usually used to discriminate WM and non-IgM LPL from other B-cell disorders (15). However, there are several studies discussing the potential of the mutation as a prognostic biomarker. It was previously revealed that MYD88 expression was an independent prognostic factor affecting overall survival in diffuse large B cell lymphoma (16,17). It was positively correlated with high Ki-67 expression and promotes tumor proliferation (17). Pham-Ledard *et al* (18) reported that MYD88 L265P

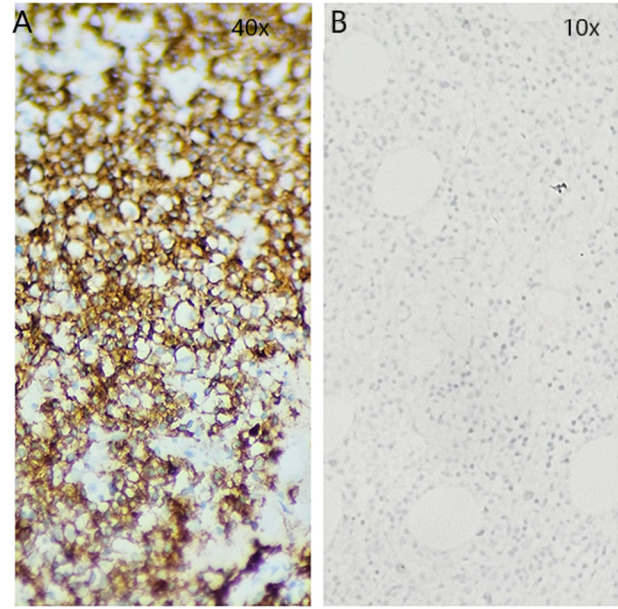


Figure 3. Immunohistochemical staining using an antibody against CD20 marker (Roche diagnostics for BenchMark Ultra IHC/ISH system). (A) Diffuse CD20-positive cells at diagnosis (magnification, x40). (B) No positive staining for CD20 (magnification, x10)-a very favorable response to the treatment with Rituximab. The recommended staining protocol for anti-CD20 antibody with DAB IHC Detection Kit on BenchMark instrument includes primary antibody incubation for 16 min at 36°C. Counterstain was performed with Hematoxylin II (4 min), post-counterstain with Bluing (4 min). The staining pattern has been analyzed on BOND-MAX automated IHC and ISH staining system (Leica Biosystems GmbH).

was associated with a poorer outcome of patients with large B-cell lymphoma. Previous studies could not engage with a statement about the prognostic impact of the mutation (19,20). In LPL/WM, there is no consensus about the role of MYD88 L265P as prognostic biomarker. LPL/WM patients harboring the MYD88 L265P mutation show clues of longer survival compared with wild-type cases (21). In IgM-secreted monoclonal gammopathies, the mutation behaves like an adverse risk factor and exhibits a 5-fold increased risk of progression to LPL/WM (22). According to other authors, the identification of the MYD88 L265P gene mutation represented a major advance in the diagnosis of LPL (3,13). Rossi (23) stated that the presence of this mutation is just an indicative of a more accurate diagnosis of LPL and maybe just accompanies the tumor burden on predicting the disease progression. Cautha *et al* (2) reported a non-IgM rare case of LPL with lambda light chain paraprotein expression positive for MYD88 L265P mutation. It was stated that non-IgM LPL has a poorer outcome yet does not infer the prognosis to the mutational presence (2). In the present study, the patient shows a favorable recovery yet, according to the authors, this is rather due to the treatment strategy than to the prognostic indication of MYD88 L265P mutation.

Major clinical complications of non-IgM-secreting LPL have been described as anemia associated symptom (53.8%), mucocutaneous hemorrhage and superficial lymphadenopathy (15.4%). At the same time, clinical and biological differences between non-IgM LPL and WM have not been identified (24). One of the serious complications associated with high levels of paraproteins in patients with hematological malignancies

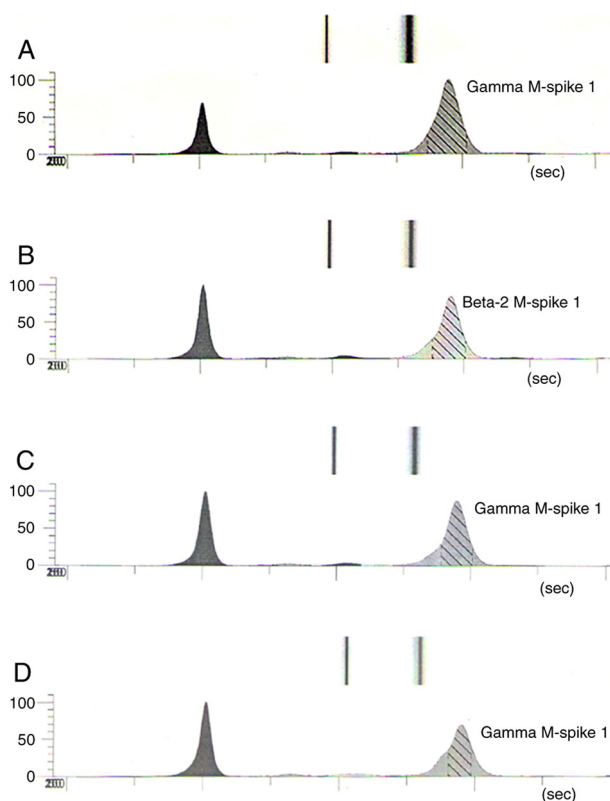


Figure 4. Results of the IEF at different stages of the treatment process. The band shown on the left side represents the levels of the serum albumin. (A) IEF of blood serum in the beginning of the treatment (after one course immune-chemotherapy), showing paraprotein type IgA/kappa at the level of 63.96 g/l. (B) An IEF after 4 rounds of immune-chemotherapy (44 g/l; partial response). (C) IEF after six courses of Bendamustin/Rituximab (44,57 g/l), which prompted a change in the therapeutic plan and the addition of Ibrutinib 420 mg/daily as second-line of treatment. (D) An IEF after 4 months of treatment with Ibrutinib (29.27 g/l), demonstrating a decrease in the level of IgA/kappa paraprotein. IEF, isoelectric focusing.

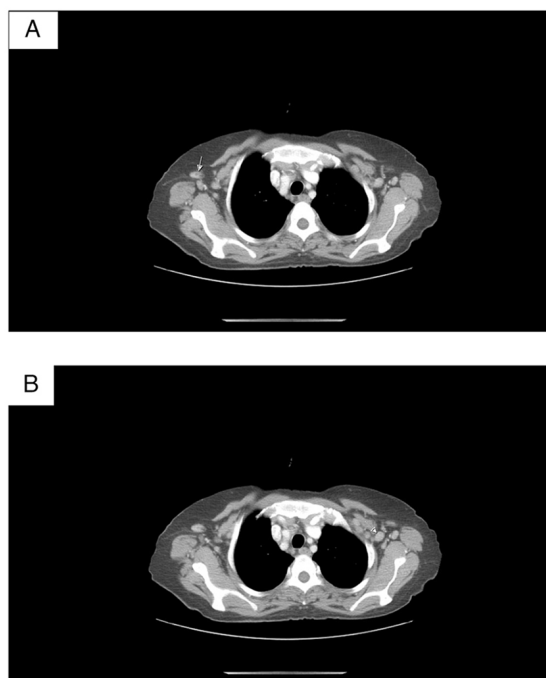


Figure 5. Computer tomography data of (A) right and (B) left axial lymphadenopathy.

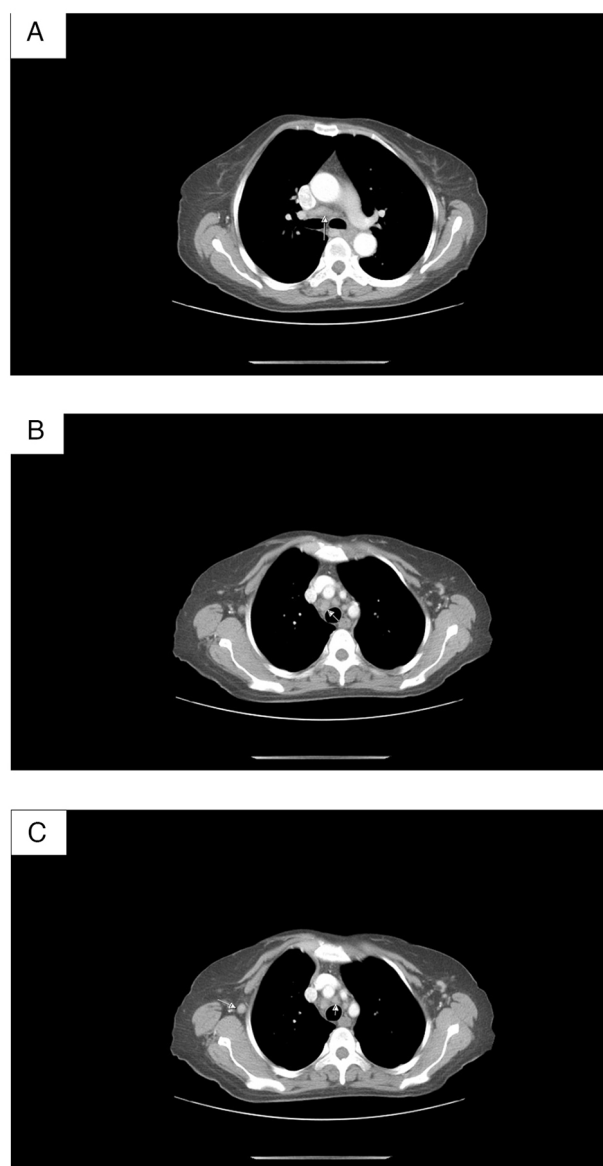


Figure 6. Computer tomography (CT) images indicating enlarged mediastinal lymph nodes (indicated by arrows from different angles). (A) CT scan image showing subcarinal lymph nodes in the mediastinum, forming a conglomerate. (B) CT scan image showing an enlarged lymph from the upper paratracheal group in the mediastinum. (C) CT scan image showing an enlarged lymph node in the upper paratracheal group in the mediastinum (right arrow) and an enlarged axillary lymph node (left arrow).

is the hyperviscosity syndrome (HVS). It is demonstrated by symptoms, including nosebleeds, blurring vision, dizziness, headaches and shortness of breath (1). The treatment of WM (IgM LPL) mainly aims to monitor the disease and keep it under stable control. In case of serious symptoms, HVS or deviations from the normal blood indicators (anemia, neutropenia or thrombocytopenia), the usual starting treatment consists of a combination of a chemotherapeutic and an antibody (Rituximab). The common regimens include either DRC (Dexamethasone, Rituximab and Cyclophosphamide) or Benda-R (Bendamustine and Rituximab). In the current presented case, the second treatment option was preferably used. In some cases, Bruton tyrosine kinase (BTK) inhibitors or proteasome inhibitors give promising results but in specific

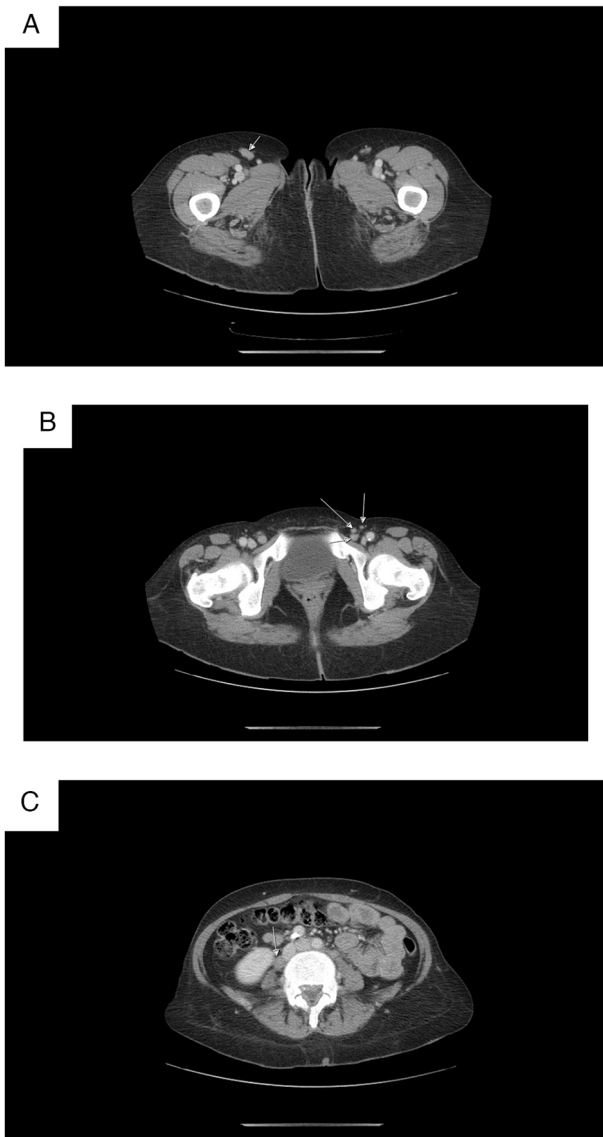


Figure 7. Computer tomography images indicating (A and B) inguinal and (C) abdominal lymphadenopathy.

circumstances (relapsed lymphoma or lack of response to previous treatment). When trying to discriminate non-IgM LPL and WM, there were no discovered differences in both response and overall survival and they are similar between the two groups (7). However, a study from 2018 in Korean patients, reported that patients with non-IgM LPL demonstrated a higher 5-year mortality rate and more adverse prognostic factors than those with LPL/WM (25). Another study of non-WM LPL cases identified the most common paraprotein being IgG (54%), followed by IgA (15%) and non-secretory (12%). The authors reported more adverse prognostic factors such as elevated LDH, anaemia and lymphocytosis at diagnosis but no difference in overall survival (26). As the combination of Bendamustine and Rituximab in the present case did not produce the desired effect, Ibrutinib (IMBRUVICA®) was included in the treatment protocol.

Ibrutinib has been approved in combination with Rituximab for the treatment of adults with WM in 2018. From that moment on, several studies reported the overall efficacy

Table I. Whole blood count of the patient upon her acceptance in the Hematology ward of 'St. Ivan Rilski' University hospital.

Cell populations	Result	Units	Reference ranges
WBC	1.25	$\times 10^9/l$	3.5-10.8
RBC	3.52	$\times 10^{12}/l$	3.76-5.34
HGB	113	g/l	115-150
HTC	0.305	l/l	0.350-0.490
MCV	86.8	fL	85.2-98.5
MCH	32.0	pg	28.4-34.5
MCHC	368	g/l	325-356
PLT	137	$\times 10^9/l$	112-330
LYM%	41.9	%	15.2-41.9
MONO%	21.4	%	4.9-12.6
EO%	1.7	%	Up to 6.2
BASO%	0.5	%	Up to 1.3
NEUT%	34.5	%	37.6-78.7
LYM	0.52	$\times 10^9/l$	1.0-4.5
MONO	0.27	$\times 10^9/l$	0.4-1.1
EO	0.02	$\times 10^9/l$	0.04-0.5
BASO	0.01	$\times 10^9/l$	Up to 0.1
NEUT	0.43	$\times 10^9/l$	2.0-7.0
RDW	14.9		11.5-14.0
MPV	7.5	fL	6.2-10.6
Sedimentation rate	91	mm/h	Up to 30
Glucose	5.54	mmol/l	3.5-6.1
Creatinine	57.0	$\mu\text{mol/l}$	Up to 96
Total protein	87.67	g/l	64.0-83.0
$\beta 2$ microglobulin-serum	2.8	mg/l	0.97-2.64

WBC, white blood cells; RBC, red blood cells; HGB, hemoglobin; HTC, hematocrit; MCV, mean corpuscular volume; MCH, mean hemoglobin concentration; MCHC, mean corpuscular hemoglobin concentration; PLT, platelets; LYM%, percentage of lymphocytes; MONO%, percentage of monocytes; EO%, percentage of eosinophils; BASO%, percentage of basophils; NEUT%, percentage of neutrophils; LYM, MONO, EO, BASO, NEUT, absolute values of the respective cell populations; RDW, red blood cells distribution width; MPV, mean platelet volume.

of Ibrutinib treatment. In a study of 2017, Helber *et al* (27) reported the clinical effect of Ibrutinib on 23 patients with LPL (most with IgM and one with IgG secretion). The median maximum IgM decrease was 67%, as for IgG-the decrease was 37%. It was underlined that the response to Ibrutinib requires long-term continuation of treatment in most of the patients (27). According to the approved therapeutic indications of the drug, it is recommended for the treatment of elderly patients with CLL (in combination with Bendamustine and Rituximab) who have received at least one preceding therapy or for patients with WM (in combination with Rituximab). In a previously reported case of non-IgM LPL and lambda light chain expression, the authors reported that, even in case of an initial response, the treatment of Ibrutinib and Rituximab did not lead to an improve (the patient succumbed after 8 months

Table II. Whole blood count (WBC) of the patient after her discharge from the Hematology ward of 'St. Ivan Rilski' University hospital (at her last control examination).

Cell populations	Result	Units	Reference ranges
WBC	1.68	x10 <sup>9</sup> /l	3.5-10.8
RBC	4.11	x10 <sup>12</sup> /l	3.76-5.34
HGB	124	g/l	115-150
HTC	0.370	l/l	0.350-0.490
MCV	89.9	fL	85.2-98.5
MCH	30.2	pg	28.4-34.5
MCHC	336	g/l	325-356
PLT	243	x10 <sup>9</sup> /l	112-330
LYM%	26.1	%	15.2-41.9
MONO%	17.2	%	4.9-12.6
EO%	5.2	%	Up to 6.2
BASO%	1.3	%	Up to 1.3
NEUT%	50.3	%	37.6-78.7
LYM	0.44	x10 <sup>9</sup> /l	1.0-4.5
MONO	0.29	x10 <sup>9</sup> /l	0.4-1.1
EO	0.09	x10 <sup>9</sup> /l	0.04-0.5
BASO	0.02	x10 <sup>9</sup> /l	Up to 0.1
NEUT	0.85	x10 <sup>9</sup> /l	2.0-7.0
RDW	15		11.5-14.0
MPV	9.5	fL	6.2-10.6

WBC, white blood cells; RBC, red blood cells; HGB, hemoglobin; HTC, hematocrit; MCV, mean corpuscular volume; MCH, mean hemoglobin concentration; MCHC, mean corpuscular hemoglobin concentration; PLT, platelets; LYM%, percentage of lymphocytes; MONO%, percentage of monocytes; EO%, percentage of eosinophils; BASO%, percentage of basophils; NEUT%, percentage of neutrophils; LYM, MONO, EO, BASO, NEUT, absolute values of the respective cell populations; RDW, red blood cells distribution width; MPV, mean platelet volume.

of diagnosis) (2). To the best of the authors' knowledge, there is only one more case in literature, reporting the usage of Ibrutinib in a refractory IgA LPL carrying MYD88 L265P gene mutation (3). In the cited study, the patient benefited from Ibrutinib treatment for a period of 4-6 weeks following treatment and the PR was maintained for ~1 year of therapy. Therefore, the present case is the second reported kappa positive LPL case positively influenced by Ibrutinib treatment and the response was detected at the fourth month following treatment. In the current case, the patient showed a substantial improvement in her condition and the level of the IgA paraprotein was decreased ~50% after four months of treatment with the triple combination (Bendamustine, Rituximab and Ibrutinib). Therefore, the reported data confirms previously reported single observations and adds a relevant knowledge to those challenging-to-diagnose and rare cases of non-IgM IgA kappa secreting LPLs.

In conclusion, the case presented by our team describes a very rare hematological malignancy; IgA-secreting LPL resembling PCN. The processes of the disease diagnosis and treatment

were reported, highlighting the effectiveness of the triple treatment protocol (Benda-R plus BTK) in the patient of the present case report. Regardless of the observed improvement, there is a necessity for a long-term monitoring of the patient condition to prove the suitability of the selected treatment option.

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#### Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

#### Authors' contributions

DN designed the study, analyzed and interpreted the data, and drafted the manuscript. AY, LS and AM acquired the data and participated in the analysis. DN, AR and AM interpreted the data. AR critically revised the manuscript and made final suggestions. AY, AM, LS and AR treated and cared for the patient. AY and AR confirm the authenticity of all the raw data. All authors read and approved the final version of the manuscript.

#### Ethics approval and consent to participate

Not applicable.

#### Patient consent for publication

The patient provided written informed consent upon admission to the University Hospital 'St. Ivan Rilski' for publication of the data and associated images.

#### Competing interests

The authors declare that they have no competing interests.

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