ESVCP Mystery Case 2022

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SIGNALMENT:

2 years-old neutered female Small Munsterlander dog.

HISTORY AND CLINICAL FINDINGS:

The dog was presented to the emergency care unit (of the National Veterinary School of Toulouse) after an insect bite on the lips. It had just spent five days in a dog boarding facility during which anorexia, diarrhea and one episode of vomiting were reported. Weight loss was also noticed by the owners.

On physical examination, the dog was underweighted (body condition score 3/9), dehydrated, and presented a generalized lymphadenopathy. Splenomegaly and intra-abdominal lymphadenopathy were also suspected on abdominal palpation.

LABORATORY FINDINGS

Complete blood cell count (CBC) with blood film and SNAP test 4Dx Plus® (Idexx), biochemistry and hemostasis panels, urinalysis, peripheral lymph nodes fine needle aspiration and serum protein electrophoresis were performed. Results are in tables 1 and 2, and in figures 1-4. Hemostasis panel was unremarkable except mild fibrin degradation products increase (5 < FDPs < 20 mg/L; RI < 5 mg/L). Complete urinalysis was unremarkable.

Table 1: Hematology results (Sysmex XN-V®, Sysmex)

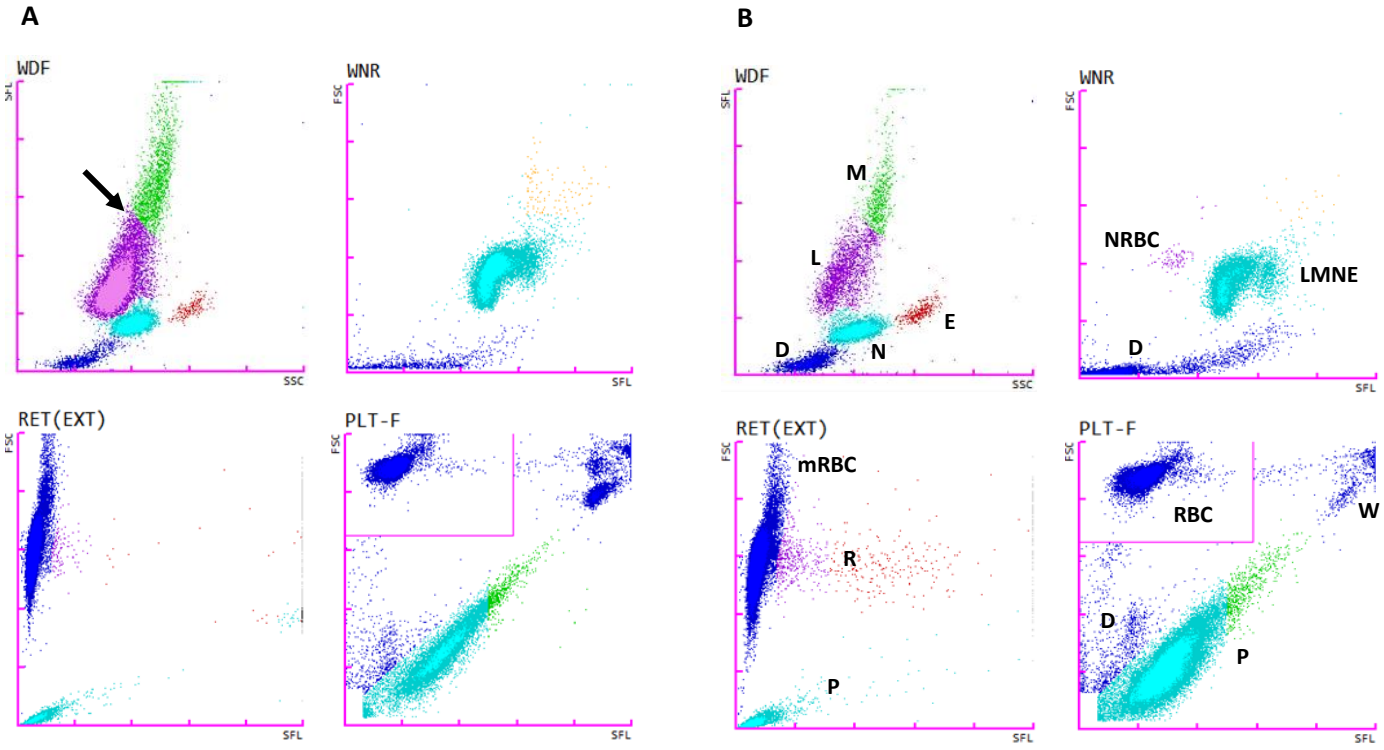
Analytes	Data	Reference Interval	Alarm
HGB (g/dL)	15.5	12.4-19.2	
RBC (.10^{12}/L)	6.72	5.20-7.90	
HCT (L/L)	0.45	0.35-0.52	
MCV (fL)	67.0	60.0-71.0	
MCH (pg)	23.1	21.9-26.3	
MCHC (g/dL)	34.4	34.4-38.1	
RDW-SD (fL)	30.7	31.1-38.9	
RDW-CV (%)	13.2	13.2-19.1	
PLT-I (.10^{9}/L)	181	64-613	
PLT-O (.10^{9}/L)	195	108-562	
WBC-WDF (.10^{9}/L)	37.79	5.60-20.40	Leukocytosis
WBC-WNR (.10^{9}/L)	34.37		
Neutrophils (.10^{9}/L)	7.82	2.90-13.60	

Lymphocytes (.10^9/L)	24.53	1.10-5.30	Lymphocytosis
Monocytes (.10^9/L)	1.72	0.40-1.60	Monocytosis
Eosinophils (.10^9/L)	0.19	< 3.10	
Reticulocytes (10^9/L)	10.10	19.40-150.10	
Reticulocytes (%)	0.15	0.30-2.37	
SNAP test 4 Dx Plus® (Idexx) (*Dirofilaria immitis, Ehrlichia canis, Ehrlichia ewingii, Anaplasma phagocytophilum, Anaplasma platys,* and *Borrelia burgdorferi*)	Negative	Negative	

Table 2: Biochemistry results (Vitros®, Ortho Clinical Diagnostics Inc.)

Analytes	Data	Reference Interval
Color of the plasma	Clear	Clear
Glucose (mmol/L)	5.6	3.7-8.2
Urea (mmol/L)	6.0	1.6-10.9
Creatinine (µmol/L)	71.0	44.0-133.0
AST (U/L)	154	1-37
ALT (U/L)	357	3-50
PAL (U/L)	151	20-155
GGT (U/L)	< 10	5-25
CK (U/L)	86	25-467
Total Bilirubin (µmol/L)	3.0	1.7-12.0
Total Protein (g/L)	64	48-66
Albumin (g/L)	29	23-39
Albumin to protein ratio	0.82	> 0.80
Ionized calcium (mmol/L)	1.33	1.20-1.50
CRP (mg/L)	22.5	0.5-10.0

Figure 1: Sysmex XN-V® cytograms from peripheral blood sample.



A: 2 years-old Small Munsterlander dog**. B**: Healthy dog for cell identification.

WDF, WBC differential scattergram; WNR, WBC count scattergram; RET (EXT), Reticulocyte extended scattergram; PLT-F, platelet scattergram with optic-fluorescent analysis; D, debris; E, eosinophils; L, lymphocytes; M, monocytes; mRBC, mature RBC; N, neutrophils; NRBC, nucleated red blood cells; P, platelets; R, reticulocytes; RBC, red blood cells; W, white blood cells.

Figure 2: Photomicrographs of the peripheral blood smear of the dog (modified May-Grünwald Giemsa stain, A: x 200; B: x 500; C: x 1000, oil).

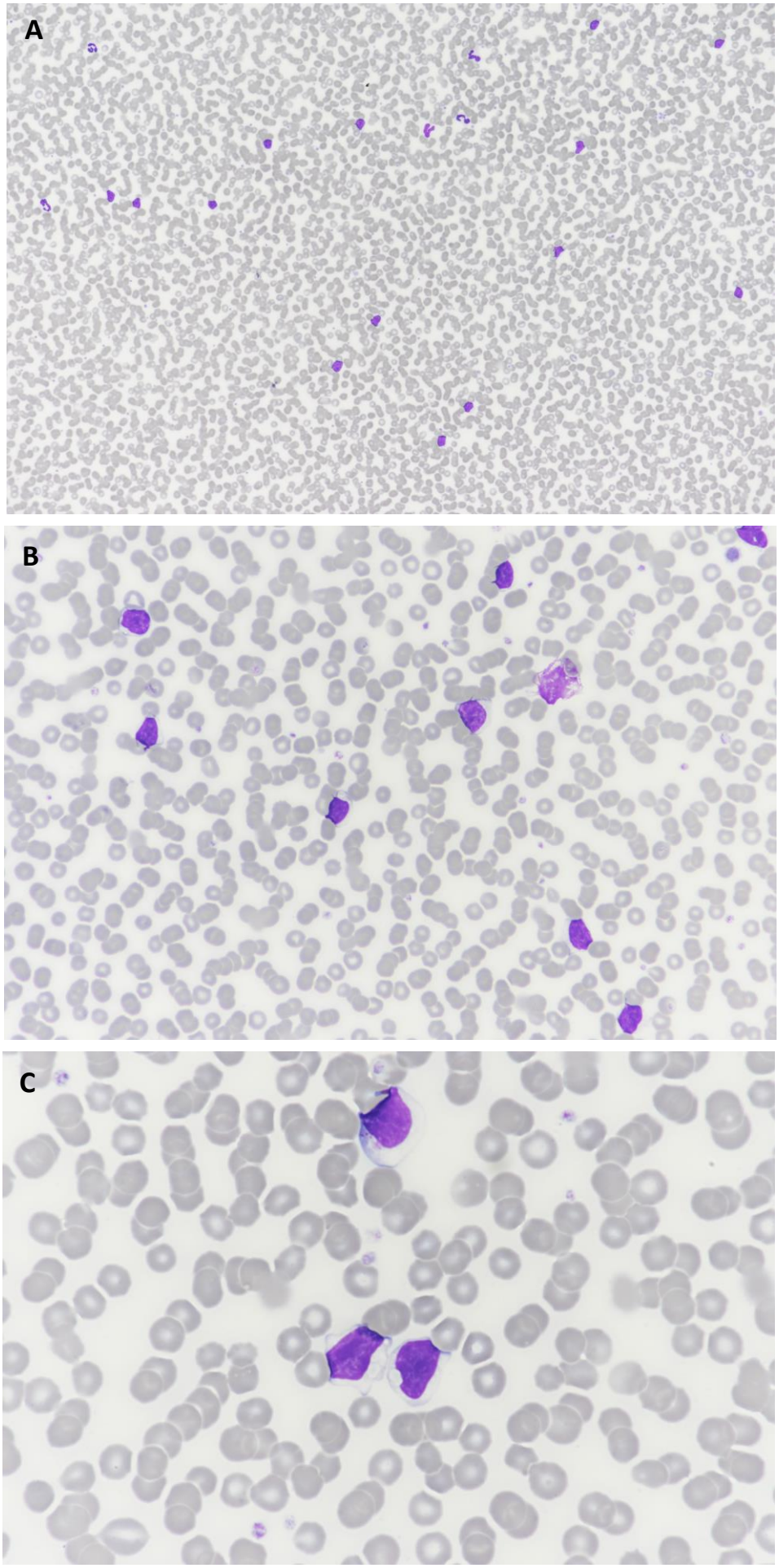


Figure 3: Photomicrograph of a prescapular lymph node aspiration of the dog (modified May-Grünwald Giemsa stain, A: x 500; B: x 1000, oil)). Popliteal and iliac lymph nodes were very similar.

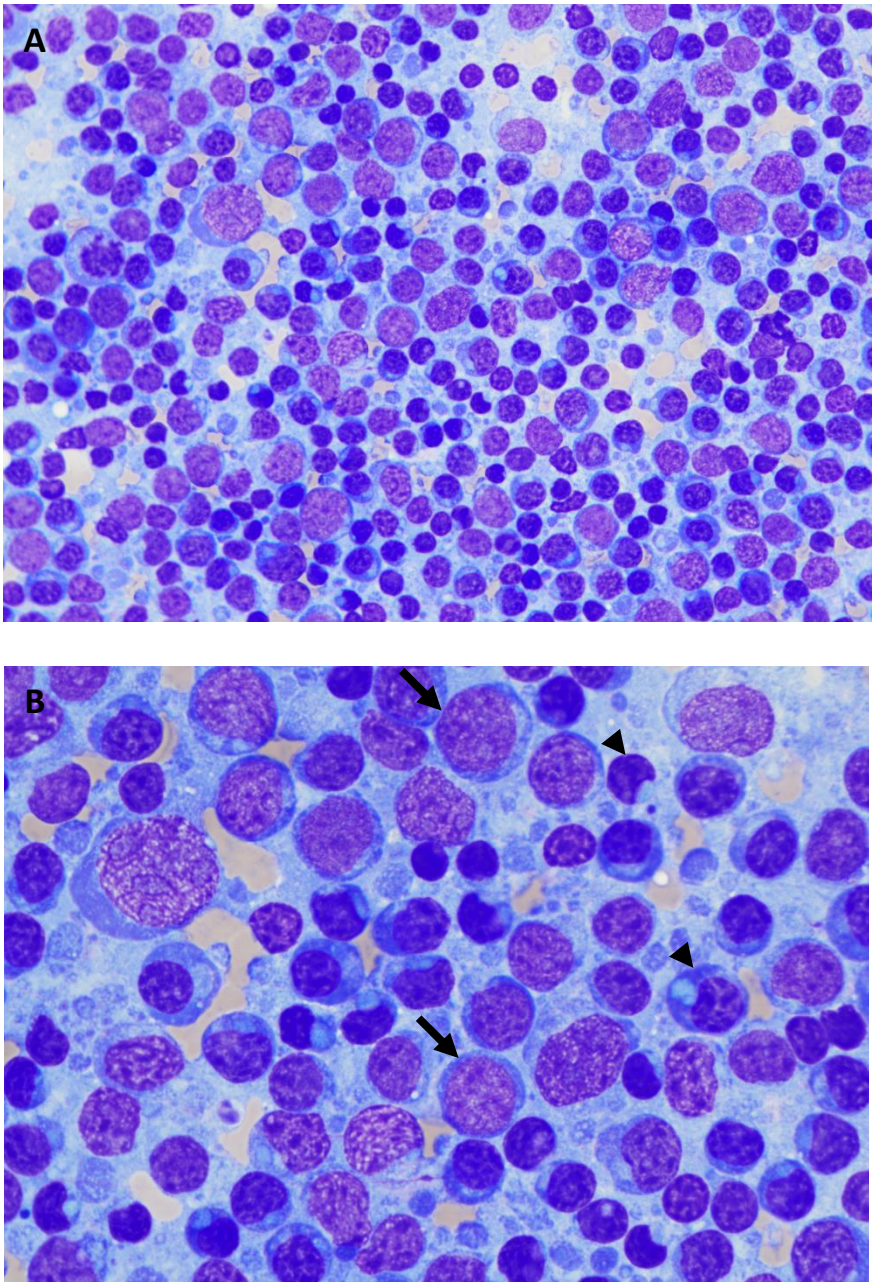
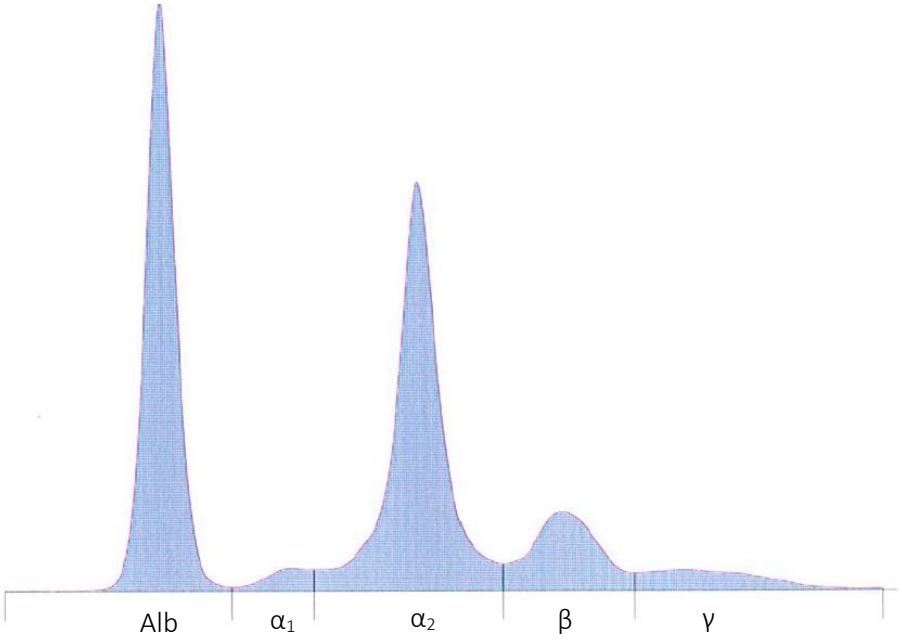


Figure 4: Serum protein electrophoresis (agarose gel Hydragel – Hydrasys2scan - SEBIA®)



Protein fractions	% [RI]	g/L [RI]
Total proteins (Vitros ®)	100	67 [48-66]
Albumin	39.4 [59.8-72.4]	26.4 [24.0-46.0]
α_1 globulins	2.3 [1.0-3.2]	1.5 [1.3-2.8]
α_2 globulins	41.3 [7.4-12.6]	27.7 [6.0-13.0]
β globulins	11.7 [7.5-12.9]	7.8 [6.9-19.6]
γ globulins	5.3 [8.0-15.8]	3.6 [3.5-9.4]

QUESTIONS:

Question 1: Based on CBC results and blood smear examination, what is the differential diagnoses for rouleaux formations?

Question 2: Based on lymph node cytological examination, what is the differential diagnoses and which additional tests do you propose?

Question 3: Based on serum protein electrophoresis, what is the most likely final diagnosis?

CLINICO-PATHOLOGICAL FINDINGS:

CBC results obtained with the Sysmex XN-V® analyzer revealed a marked leukocytosis and lymphocytosis with a mild monocytosis. On the WDF scattergram, the lymphoid population was predominant. A large and extended population was observed at the lymphocytes and monocytes position and mainly identified as lymphocytes (pink dots) and in a lesser extent as monocytes (green dots), with an arbitrary separation between those two populations. Neutrophils and eosinophils dot plots were unremarkable. On the WNR scattergram, the cluster of leukocytes little extended to the upper right part of the scattergram (turquoise and yellow dots).

On the blood smear, the semi-quantitative evaluation of the WBC count was increased and consistent with the WBC-WNR channel count. The manual differential count was in agreement with the WBC differential given by the WBC-WDF channel, and was mainly composed of lymphocytes (76.0% manual *vs.* 71.4% automated) and in a lesser extent of neutrophiles (17.0% manual *vs*. 22.7% automated) and monocytes (5.0% manual *vs*. 5.0% automated) with rare eosinophils (1.0% manual *vs*. 0.6% automated) and basophils (1.0% manual).
The most significant abnormalities were, firstly, the abundant and monomorphic population of medium-sized mature lymphocytes (nucleus size about 1.5-2 RBC) with clumped chromatin and scant to moderate amount of pale blue cytoplasm. Increased cytoplasmic basophilia and small clear vacuoles were occasionally noticed; secondly, the marked rouleaux formation. Numerous naked nuclei, occasional granular lymphocytes and lymphocytes with intensely basophilic cytoplasm and rare mitosis were also noticed. Some basophils and lysed erythrocytes were noticed. No significant change was observed for the platelets population. Based on CBC and blood smear examination, a lymphroliferative disorder was suspected, although an inflammatory process with a reactive lymphocytosis could not be excluded.

Cytology examination of a fine needle aspirate from enlarged popliteal and prescapular lymph nodes revealed an atypical bimorphic lymphoid population. The first population consisted of small lymphocytes with plasmacytoid appearance. The nucleus was dark, round, eccentrically placed with highly condensed chromatin and was about 1 to 1.5 times RBC size. Cytoplasm was scant, deep blue, with frequently single or sometimes multiple, small well defined clear blue round vacuoles displacing the nucleus. This population composed about 44% of the total nucleated cell population. The second population consisted of medium to large lymphoid blastic cells. The nucleus was round, eccentrically placed and was about 1.5 to more than 3 times RBC size. The chromatin was coarsely stippled to clumped with multiple small round to ovoid discreet nucleoli. Cytoplasm was scant and pale blue with occasional round vacuole as previously reported. A low number of mitotic figures were observed. This population composed about 35% of the total nucleated cell population. Some plasma cells, occasional classical Mott cells and a residual mature lymphoid population were also observed and composed about 21% of the total nucleated cell population. Proportions could vary according to the area observed. Scattered inflammatory cells mainly composed of phagocytic macrophages with few neutrophils and eosinophils were also noticed. Based on lymph node cytological examination, lymphoma with lymphoplasmacytic differenciation was suspected as first hypothesis, although an atypical reactive population could not be excluded.

Some vector borne diseases were excluded as possible infectious causes based on the negative Snap test 4Dx Plus® (Idexx, USA) result (Table 1) and a quantitative serology for leishmaniosis and erhlichiosis.

PCR for antigen receptor gene rearrangement (PARR) was performed on unstained peripheral lymph node and whole blood EDTA smears, and revealed a clonal BCR gene rearrangement and a polyclonal TCR gene rearrangement in both locations.

Flow cytometry was performed on peripheral lymph node aspirate, blood and bone marrow aspirate. Lymph node sample was composed by a mixed population including 10% small-sized T-cells and 25% small sized B-

cells staining positive for CD21, CD79a and MHC II, and a third population (60%) of medium-sized B-cells with staining positive for CD79a, but negative for MHC II and CD21. Blood and bone marrow samples were composed of a dominant population of small-sized B-cells staining positive for CD21 and MHC II.

Morphology, clonality testing and immunophenotype were suggestive of leukemic B cell lymphoma with lymphoplasmacytic appearance.

Based on rouleaux observation, dysprotidemia was suspected, and although the patient did not have a hyperglobulinemia, serum and urine protein electrophoresis were pursued two days after initial presentation to investigate paraproteinemia. Agarose gel serum electrophoresis revealed decreased albumin/globulin ratio and markedly increased $\alpha_2$globulinemia with an atypical restricted peak. Immunofixation electrophoresis was submitted to Nantes University's Veterinary Biological Laboratory (LabOniris), and revealed monoclonal IgM gammopathy.

Though complete urinalysis was unremarkable, UPC was increased (2.4 > 0.5) and urinary protein electrophoresis revealed a tubular proteinuria, wich was further characterized as lambda free light chains by immunofixation (Laboniris) and was so suggestive of a Bence Jones proteinuria.

Abdominal ultrasound revealed splenomegaly with multiple hypoechoic nodules, mild hepatomegaly, multiple enlarged visceral lymph nodes with heterogeneous and hypoechoic patterns. Fine needle aspiration of spleen and liver revealed infiltration by the same previously reported atypical bimorphic lymphoid population, with mild to moderate hepatocellular cytoplasmic rarefaction, which could explain ALT and AST increased activities. Although no radiographic bone survey was conducted, no bone lesion was observed on thoracic radiographs, nor later on head computed tomography.

Bone marrow aspiration was also performed and revealed mildly increased lymphocytes and plasma cells, with an infiltration by the same previously reported atypical bimorphic lymphoid population (2.4% of small lymphocytes with plasmacytoid appearance).

INTERPRETATION/DIAGNOSIS:

Based on cytologic examination, clonality testing and immunophenotyping, a diagnosis of leukemic B cell lymphoma with lymphoplasmacytic appearance was established. The combination of lymphoplasmacytic neoplastic cell morphology, monoclonal IgM paraproteinemia, spleen, liver, lymph nodes and bone marrow infiltration was consistent with a diagnosis of Waldenström's macroglobulinemia.

CLINICAL OUTCOME AND FOLLOW-UP:

Eight months after initial presentation the dog is still alive. Although the disease has progressed, based on cutaneous and mucosal infiltration observed on nasopharyngeal, gingival, tonsil and clitoral cytological examination, it remains stable and is treated with Melphalan chemotherapy. The dog had thereafter an episode of azotemia and diarrhea, which both resolved after a short hospitalisation and symptomatic management. Periodontal disease was treated with antibiotherapy.

ANSWERS TO QUESTIONS:

Question 1: Based on CBC results and blood smear examination, what is the differential diagnoses for rouleaux formations?

Rouleaux formation are commonly observed under physiological conditions in some species such as horses and cats. Otherwise, rouleaux occur secondary to elevated plasma protein concentration such as globulin proteins (fibrinogen, haptoglobin, immunoglobulins) in inflammatory conditions or in some lymphoproliferative disorders with paraprotidemia. Rouleaux should also be distinguished from agglutination and can be disrupted with saline agglutination test. (1, 2)

In our case, fibrinogen concentration was within reference range, and CRP was mildly increased.

Abnormal WBC scattergrams suggested a possible atypical lymphoid population. In acute leukemia or leukemic lymphoma, the absence of clear separation between the different leukocytes populations **(arrow)** and presence of cells with a higher fluorescence activity such as reactive, atypical or blastic lymhoid cells in the monocyte position have been reported with the Sysmex XT-2000iV® in dogs, the Sysmex XN-V® in people and more recently with the Sysmex XN-V® in dogs (3, 4). The few events observed in the upper right area on the WNR scattergram have also been reported previously in canine leukemia cases with the Sysmex XT-2000iV®, and more recently the Sysmex XN-V®, cells in this location were designated as lysis resistant cells (4, 5).

Lymphocytosis with the abundant monomorphic population of medium-sized lymphocytes observed on blood smear, numerous naked nuclei and rare mitosis, leads to suspect lymphoid neoplasia as the first hypothesis (leukemic lymphoma, chronic lymphocytic leukemia) although a reactive lymphocytosis cannot be excluded (chronic inflammatory or infectious disorders). Further tests are needed to distinguish reactive from neoplastic lymphoid expansion.

Question 2: Based on lymph node cytological examination, what is the differential diagnoses and which additional tests do you propose?

On cytological examination of fine needle aspirate from enlarged peripheral lymph nodes, an atypical bimorphic population of lymphocytes was observed and consisted of medium to large immature cells **(arrow)** with smaller plasmacytoid cells with dark nuclei and cytoplasmic inclusions **(arrow head)**. Some plasmocytes, occasional classical Mott cells and a residual normal lymphoid population were also observed but were a minority. Based on cytology, differential diagnoses included lymphoid neoplasia (lymphoma with plasmacytoid differenciation, myeloma related disorder, leukemia) or lymphoid hyperplasia with atypical plasma cells (ie. inflammation, autoimmune disorders or sustained antigenic stimulation secondary to an infectious disease such as *E. canis* infection).
Further tests are needed to distinguish reactive from neoplastic lymphoid population expansion.
A PCR for antigen receptor gene rearrangement (PARR) assay was pursued to assess cellular clonality. PARR perfomed on unstained peripheral lymph node and whole blood smears revealed a clonal BCR gene rearrangement and a polyclonal TCR gene rearrangement in both locations, suggestive of B-cell neoplasia.

Flow cytometry immunophenotyping was pursued to investigate a phenotypically homogeneous expanded lymphocyte population and was performed on peripheral lymph node, blood and bone marrow. Blood and bone marrow samples were composed of a dominant population of small-sized B-cells staining positive for CD21 and MHC II, suggestive of B-cell neoplasia (chronic lymphocytic leukemia or stage V lymphoma

lymphoma). Lymph node sample contained a majority of medium-sized B-cells staining positive for CD79a but negative for MHC II and CD21, primarily compatible with a second neoplastic B-cell clone although reactive population could not be excluded.

Since clonal and phenotypically homogeneous lymphocytosis may also occur with reactive proliferation against a specific antigen, some vector borne diseases were investigated (6). Notably *E. canis* infection in dogs can cause an homogeneous expansion of CD8+ T cells, which was not observed in our case, with also a clonal expansion in rare cases (7). A snap test 4Dx Plus® (Idexx, USA) and a quantitative serology for leishmaniosis and erhlichiosis were negative.

Morphology, clonality testing, immunophenotyping, spleen, liver and bone marrow involvement were primarily suggestive of leukemic B-cell lymphoma with lymphoplasmacytic appearance.

Question 3: Based on serum protein electrophoresis, what is the most likely final diagnosis?

Although the dog was normoprotidemic at the initial presentation, serum protein electrophoresis was performed and revealed an increased α_2-globulin fraction with an atypical restricted peak. Increased α_2-globulin fraction is observed in acute inflammatory phase response (ie: haptoglobin, ceruloplasmin) or nephrotic syndrome (α_2-lipoprotein, α_2-macroglobulin), unlikely in our case (8, 9). As the dog was diagnosed with a B-cell lymphoproliferative disease, monoclonal gammopathy with spurious migration was suspected. Immunofixation electrophoresis was performed to further investigate the atypical restricted peak, and identified a monoclonal IgM with lambda light chains paraprotidemia. Urinary protein electrophoresis was also performed and revealed a tubular proteinuria wich was further characterized as lambda free light chains by immunofixation, and was so suggestive of a Bence Jones proteinuria.

The combination of laboratory testings was suggestive of a leukemic lymphoplasmacytic lymphoma with splenic, hepatic and bone marrow infiltration, IgM paraprotidemia and Bence Jones proteinuria. According to WHO classification, a diagnosis of Waldenström's macroglobulinemia (WM) was established.

DISCUSSION

To our knowledge, this is the first report of Waldenström's macroglobulinemia (WM) with plasmacytoid differenciation and atypical cytoplasmic inclusions.

The lymph nodes were composed of an atypical bimorphic neoplastic population of small mature lymphocytes with cytoplasmic vacuolisation and medium to large-sized blastic/immature cells. This unusual bimorphic population have been previously described in two cases of canine lymphomas, one case was reported in a 7-year-old Jack Russel Terrier and the other in a 5-year-old Australian Sheperd dog (10, 11). As the nodal lymphoid population was bimorphic, atypical reactive process could not be excluded, and clonality testing with immunophenotyping were required to demonstrate a clonal lymphoid expansion with a uniform immunophenotype. PARR and flow cytometry immunophenotyping performed on lymph node sample revealed a clonal B-cell expansion, with a dominant medium-sized B-cells population staining positive for CD79a but negative for MHC II and CD21, and in a lesser extent a small sized B-cells staining positive for CD21, CD79a and MHC II. Nodal immunophenotyping was also performed on the two previous reports via immunocytochemistry or immunohistochemistry. In one case both morphologically distinct cells were notably positive for CD79a, CD21, MCH II and MUM-1 (10), and also positive for CD79a and MUM-1 in the

second case (11). The first hypothesis for the two B-cells immunophenotype patterns observed in our case was the presence of a second neoplastic clone having undergone plasmacytoid differentiation.

Interestingly, the monomorphic lymphoid population in the peripheral blood was quite morphologically different from the neoplastic cells of the lymph node, which was also reported in a previous case (10). So, clonality and immunophenotyping were performed on blood sample. PARR confirmed that lymphocytes observed in peripheral blood were also a clonal population. Flow cytometry revealed dominant small-sized B-cells positive for CD21 and MHC II, as previously reported (10), and exhibit the same pattern as one of the populations observed in the lymh node. Thus, clonality and immunophenotyping were necessary to confirm blood involvement of the lymphoma with a morphologically different lymphoid population from that observed in solid lesions.

A few previous studies also reported cases of B-cells lymphomas with Mott-cell differenciation (MCL) in 7 dogs, one cat and one ferret (12-18). Cytomorphology with numerous Mott cells and free globules on the background differs from that observed in this present case. MCL in dogs was first described as a cytomorphologically unique form of primary gastrointestinal lymphoma lacking neoplastic M-protein synthesis (12). Even if most cases of MCL actually involved digestive tract, the most recent cases also involved liver, spleen, peripheral or visceral lymph nodes and tonsils without consistently a primary digestive infiltration. In this current case, no gastrointestinal lesion was observed on abdominal ultrasound.

Though the dog was normoprotidemic at the initial presentation, given rouleaux formations, lymphocytosis and the abnormal bimorphic lymph node cytomorphology, dysprotidemia was suspected. Serum protein electrophoresis (SPE) was performed and revealed an atypical restricted peak in α_2-globulin fraction, identified by immunofixation electrophoresis (IFE) as monoclonal IgM with lambda light chains. All clinical and clinico-pathological findings were consistent with Waldenström macroglobulinemia (WM). WM is an uncommon syndrome in human and veterinary medicine. According to WHO classification, WM is defined as a subset of lymphoplasmacytic lymphoma with bone marrow involvement and an IgM monoclonal gammopathy (macroglobulinemia) (19). In the two previous studies exhibiting the same bimorphic cytomorphology as in this present case macroglobulinemia was not reported, dogs were normoprotidemic, but nor SPE nor IFE were performed so M proteins could not be excluded (10, 11). In two of the most recent cases of canine MCL, dogs were normoprotidemic or slightly hypoprotidemic, variable peaks were observed in the α_2 region on SPE, however lower than in our case, and was primarily attributed to acute phase response while IFE revealed the presence of M proteins in both cases, monoclonal Ig A and Ig M respectively (12). The authors suspected that α_2 peaks were in fact due to M proteins and possibly masked by APP in one case. In other cases of MCL, no SPE was performed and no dysprotidemia was observed (13-18). M proteins usually migrate in γ or β regions in normal SPE tracing. Rare cases of M proteins migration in α_2 region have been reported in human literature and were predominantly represented by monoclonal IgA (20, 21). Authors hypothesis for this atypical migration were protein complex formation with other plasma components, high carbohydrate contents, or IgA properties. In our case, normoprotidemia admixed with this unusual SPE migration pattern emphasizes the importance of immunofixation to detect monoclonal gammopathy, as recommended by recent studies (22).

To conclude, we report an atypical case of canine stage V B-cell lymphoma consistent with a Waldenström macroglobulinemia with a bimorphic population of plasmacytoid cells characterized by cytoplasmic inclusions and associated with a monoclonal IgM gammopathy.

REFERENCES:

1. Schalm's Veterinary Hematology, 7th Edition. Chapter 24, Erythrocyte Morphology, Barger A;188-189.
2. Harvey J, Veterinary Hematology. A Diagnostic Guide and Color Atlas. Chapter 4, Evaluation of erythrocytes;59.
3. Bauer N, Nakagawa J, Dunker C. Evaluation of the automated hematology analyzer Sysmex XT-2000iV compared to the ADVIA (R) 2120 for its use in dogs, cats, and horses. Part II: Accuracy of leukocyte differential and reticulocyte count, impact of anticoagulant and sample aging. J Vet Diagn Invest. 2012;24:74- 89.
4. Grebert M, Granat F, Braun JP, Leroy Q, Bourgès-Abella N, Trumel C. Validation of the Sysmex XN-V hematology analyzer for canine specimens. Vet Clin Pathol. 2021; 50:2:184-197.
5. Gelain ME, Rossi G, Giori L. Identification of neoplastic cells in blood using the Sysmex XT-2000iV: a preliminary step in the diagnosis of canine leukemia. Vet Clin Pathol. 2010; 39: 169-179.
6. Schalm's Veterinary Hematology, 7th Edition. Chapter 62, Determination of clonality, Goto-Koshino Y, Tsujimoto H;502.
7. Avery PR, Avery AC. Molecular methods to distinguish reactive and neoplastic lymphocyte expansions and their importance in transitional neoplastic states. Vet Clin Pathol. 2004; 33:196-207.
8. Schalm's Veterinary Hematology, 7th Edition. Chapter 144, Electrophoresis and acute-phase proteins. Giordano A;1320-1330.
9. Tothova C, Nagy O, Kovac G. Serum proteins and their diagnostic utility in veterinary medicine: a review. Veterinarni Medicina. 2016; 61: 475-496.
10. Kol A, Christopher MM, Skorupski KA, Tokarz D, Vernau W. B-cell lymphoma with plasmacytoid differentiation, atypical cytoplasmic inclusions, and secondary leukemia in a dog. Vet Clin Pathol. 2013 Mar;42(1):40-6.
11. Snyman HN, Fromstein JM, Vince AR. A rare variant of multicentric large B-cell lymphoma with plasmacytoid and mott cell differentiation in a dog. J Comp Pathol. 2013 May;148(4):329-34.
12. Seelig DM, Perry JA, Zaks K, Avery AC, Avery PR. Monoclonal immunoglobulin protein production in two dogs with secretory B-cell lymphoma with mott cell differentiation. J Am Vet Med Assoc. 2011 Dec 1;239(11):1477-82.
13. Gupta A, Gumber S, Schnellbacher R, Bauer RW, Gaunt SD. Malignant B-cell lymphoma with Mott cell differentiation in a ferret (Mustela putorius furo). J Vet Diagn Invest. 2010 May;22(3):469-73.
14. Stacy NI, Nabity MB, Hackendahl N, Buote M, Ward J, Ginn PE, Vernau W, Clapp WL, Harvey JW. B-cell lymphoma with Mott cell differentiation in two young adult dogs. Vet Clin Pathol. 2009 Mar;38(1):113-20.
15. Kanehara T, Matsui N, Murakami M, Maruo K, Mori T, Hirata A, Yanai T, Sakai H. B-cell lymphoma with Mott cell differentiation in a cat. Vet Clin Pathol. 2016 Jun;45(2):356-360.
16. De Zan G, Zappulli V, Cavicchioli L, Di Martino L, Ros E, Conforto G, Castagnaro M. Gastric B-cell lymphoma with Mott cell differentiation in a dog. J Vet Diagn Invest. 2009 Sep;21(5):715-9.
17. Kodama A, Sakai H, Kobayashi K, Mori T, Maruo K, Kudo T, Yanai T, Masegi T. B-cell intestinal lymphoma with Mott cell differentiation in a 1-year-old miniature Dachshund. Vet Clin Pathol. 2008 Dec;37(4):409-15.
18. Tang K. Mystery Case - A jejunal mass in a 2-year-old dog. ECVCP congress oct 2021.
19. Swerdlow SH, et al. Lymphoplasmocytic lymphoma. In: Swerdlow SH, Campo E, Harris NL, et al, eds. World Health Organization Classification of Tumours of Haematopoietic and Lymphoid Tissues. Revised 4th ed. Lyon, France: IARC Press; 2017:232-235.

20. Chari A, Eisenberger A, Pesce M. Monoclonal Immunoglobulins of Alpha-2 Mobility on Protein Electrophoresis: A Case Series. Blood. 2007; 110 (11): 4753.
21. Dash NR, Mohanty B. Multiple myeloma: a case of atypical presentation on protein electrophoresis. Indian J Clin Biochem. 2012 Jan;27(1):100-2. doi: 10.1007/s12291-011-0178-3.
22. Moore AR, Harris RA, Jeffries C, Ashton L, Avery PR. Diagnostic performance of routine electrophoresis and immunofixation for the detection of immunoglobulin paraproteins (M-Proteins) in dogs with multiple myeloma and related disorders: Part 1 - Current performance. Vet Clin Pathol. 2021 Jun;50(2):240-248.