Secondary Multicentric B-cell Lymphoma after Intestinal T-cell Lymphoma in a Dog

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Introduction

Secondary malignant neoplasm is rarely reported in veterinary medicine, especially two kinds of different lymphoid tumors in a dog. Here we report a dog who had secondary multicentric B-cell lymphoma after solitary intestinal T-cell lymphoma, which had been surgical excised and followed by adjuvant chemotherapy for fifteen months. Histopathology, immunohistopathology, flow cytometry, and PCR for antigen receptor rearrangement (PARR) had performed in the surgical, cytological, and necropsy specimens. This is the first case report for secondary malignancy of multicentric B cell lymphoma after intestinal T cell lymphoma in a dog.

Materials and methods

Case History

- Patient: A 14-year-old spayed mixed-breed female dog suffered from chronic diarrhea, hematochezia, and hypoalbuminemia.
- First malignancy: A small intestine mass was detected by ultrasound and removed through surgery, identified as Intestinal large-cell T-cell lymphoma.
- Treatment: Chemotherapy followed the surgery, initially CHOP for a month and then cyclophosphamide for 11 months. Complete remission was achieved.
- Second malignancy: New clinical presentations emerged at 5 months, including diarrhea, thickened intestinal walls and generalized lymphadenopathy. Initially, the lymphadenopathy was initially suspected as distant metastasis of intestinal T cell lymphoma (stage IV), but it was later diagnosed as multicentric B cell lymphoma (stage III) based on flow cytometry.
- Treatment: Chemotherapy was administered using a CHOP-based protocol for 7 months. Complete remission was achieved.
- Follow-up: Tumor relapse in after 3 months, necessitating reinduction chemotherapy followed by rescuer chemotherapy based on response.
- Necropsy: The dog died due to tumor progression. Blood tests showed anemia, leukocytosis, and elevated liver enzymes.

Methods

- Surgical and necropsy pathology
- Immunohistochemistry (IHC) and flow cytometry to analyze the lymphoid lineage in the clinical and histological specimens.
- PCR for antigen receptor rearrangement (PARR) to analyze the clonal rearrangement of the variable regions of the T cell receptor (TCR) gene and immunoglobulin heavy chain (IgH) genes in clinical and histopathological specimens.

Results

Day 1: First malignancy

- Clinical presentation: Intestinal mass
- Pathological diagnosis: Intestinal large T-cell lymphoma

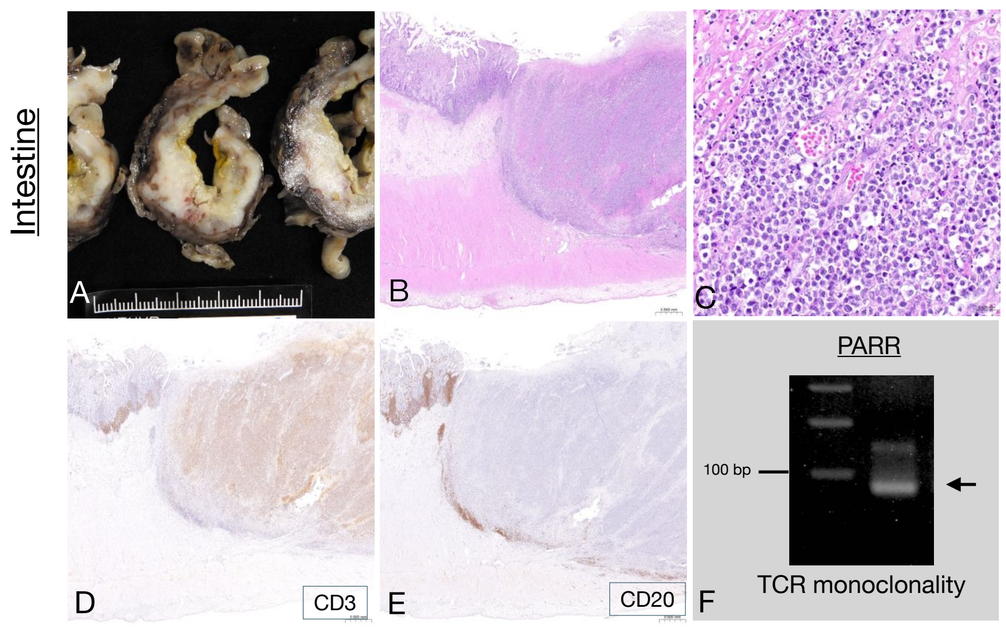

Fig.1 The intestinal mass was diagnosed as intestinal large T-cell lymphoma based on pathological, phenotyping and clonality examination. A) The intestinal mass were non-encapsulated and poorly circumscribed with a generally beige color, transverse section, formalin-fixed specimen. B-C) Large lymphocytes expended and infiltrated in the mucosa to submucosa. H&E stain, 20x and 400x. D) Neoplastic cells with immunolabeling for CD3, 20x. E) Neoplastic cells without immunolabeling for CD20, 20x. E) Monoclonality of T cell receptor-gamma (TCRγ) was detected in PARR.

Day 518: Second malignancy

- Clinical presentation: Generalized lymphadenopathy
- Clinical diagnosis: Multicentric B cell lymphoma, stage III

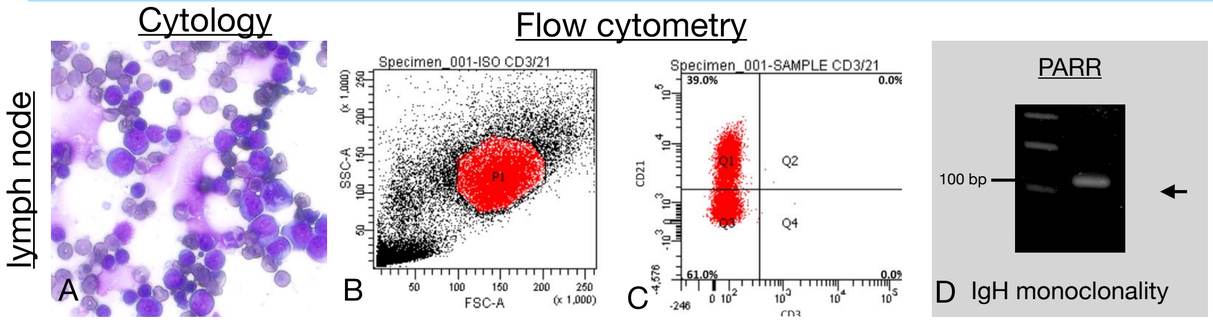

Fig. 2 The enlarged lymph nodes were diagnosed as large B cell lymphoma based on cytological exam, flow cytometry and PARR. A) About 60% to 70% medium to large lymphocyte, fine-needle aspiration of popliteal lymph node. B-C) The cell population present CD20% of CD21+ and 0% of CD3+ lymphocytes, scatter-plot of flow cytometry. D) Monoclonality of immunoglobulin heavy chain (IgH) was detected in PARR.

Day 931:Necropsy

- Pathological diagnosis: B cell lymphoma with multiple organ involvement, including peripheral lymph node, intestine, liver, spleen and lung

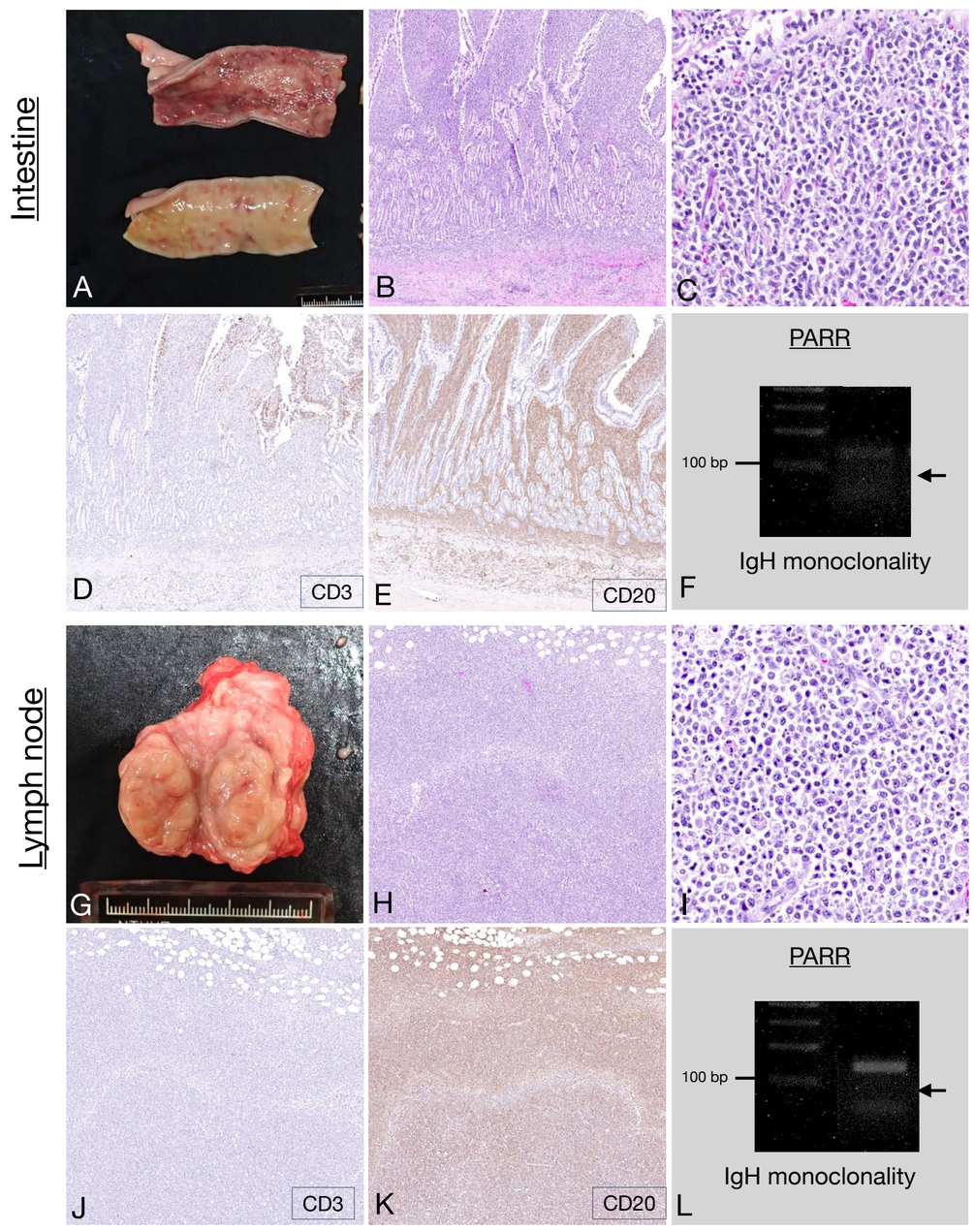

Fig.3. Large B cell lymphoma was diagnosed and invaded in the intestine (A-F) and peripheral lymph node (G-L) based on pathological, phenotyping and clonality examination.
A) The mucosa displayed diffusely redness lesion, intestine. B-C) Numerous medium to large lymphocytes infiltrated in the mucosa to serosa of small intestine.
G) Marked enlargement with necrotic component, cut section of popliteal lymph node. H-I) The nodal structure was effaced and replaced by neoplastic cells, popliteal lymph node
D, J) Immunolabeling for CD3. E, K) Immunolabeling for CD20. F, L) Monoclonality of immunoglobulin heavy chain (IgH) was detected in PARR.

Conclusion and Discussion

- This is the first case report for secondary malignancy of multicentric B cell lymphoma after intestinal T-cell lymphoma in a dog by fully investigate the immunolabeling and clonality of lymphocytes in clinical, surgical and necropsy pathological specimens.
- Intestinal T-cell lymphoma have been reported has poor outcome, but in this case, surgical resection of solitary intestinal lymphoma accompanied with chemotherapy may encourage a good prognosis.
- The survival time for intestinal T-cell lymphoma and multicentric diffuse large B cell lymphoma were 931 and 319 days, respectively.
- The cause of secondary malignancy is still unknown. In this case, it may be related to chronic usage of cytotoxic dosage of cyclophosphamide which may caused transient myelodysplasia.

References

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2. Waugh, E. M., et al. (2016). "Optimisation and validation of a PCR for antigen receptor rearrangement (PARR) assay to detect clonality in canine lymphoid malignancies." Veterinary Immunology and Immunopathology 182: 115-124.