Radiographic, Computed Tomographic and Cellular Phenotypic Features of Primary Nasal Transmissible Venereal Tumors in Four Dogs

Muhammad Waseem Aslam (dr.waseemaslam@gmail.com)  
Faculty of Veterinary Medicine, Universiti Putra Malaysia (UPM), 43400 UPM, Serdang, Selangor, Malaysia. https://orcid.org/0000-0002-4256-5961

Seng Fong Lau (lausengfong@hotmail.com)  
Faculty of Veterinary Medicine, Universiti Putra Malaysia (UPM), 43400 UPM, Serdang, Selangor, Malaysia. https://orcid.org/0000-0003-1283-4355

Puteri Azaziah Megat Abdul Rani  
Faculty of Veterinary Medicine, Universiti Putra Malaysia (UPM), 43400 UPM, Serdang, Selangor, Malaysia.

Ikhwan Saafi Ahamad Azahari  
Faculty of Veterinary Medicine, Universiti Putra Malaysia (UPM), 43400 UPM, Serdang, Selangor, Malaysia.

Case Report

Keywords: Canine transmissible venereal tumor, modified Adams staging, computed tomography, vincristine sulphate, cellular phenotype

DOI: https://doi.org/10.21203/rs.3.rs-62779/v1

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Abstract

Primary nasal canine transmissible venereal tumor (CTVT) is a rare disease, developed by allografted transmission of neoplastic cells in the nasal cavity. The disease reported quite uncommonly in free roaming dogs with social behaviour of excessive licking and vigorously sniffing the affected parts of the other dogs in an endemic community. A non-resolving chronic epistaxis and/or serosanguinous discharge from nares is a common historical complaint. Usually, cytology of the nasal discharge/epistaxis or fine-needle aspiration (FNA) of nasal tissue is sufficient for definitive diagnosis. Currently, computed tomography scan (CT-scan) is the best modality to check the invasiveness of the disease and perform modified Adams staging of canine nasal tumors. In present study, all four dogs have stage-4 nasal tumors, due to the complete or partial lysis of the cribiform plate and lymphocytoid plasmacytoid (mixed) phenotype of the neoplastic cells based on the cellularity of cytological samples. All four dogs responded well to five cycles of vincristine sulphate and recovered completely from presented clinical signs. Prognosis is good based on the findings of present study.

Introduction

Canine transmissible venereal tumor (CTVT) is the oldest known, evolved thousands of years ago, continuously passed somatic cell lineage. It is also known as sticker's sarcoma, transvenereal sarcoma, infectious sarcoma, canine condyloma, transmissible lymphosarcoma, venereal granuloma and contagious venereal tumor. CTVTs are distributed globally, predominantly in tropical and subtropical regions. It is naturally occurring, horizontally transmitted, parasitic-like, infectious neoplasia of dogs. Because of the uncertainty in its origin, it has been described as lymphatic, reticuloendothelial, macrophage or myeloid, and histiocytic origin tumors in previous studies. Other than this ambiguity, it is considered one of the most common round cell tumors in dogs. The most common mode of transmission is coitus, although it can spread through biting, licking, and sniffing of the neoplastic sites of the dog's body.

Exfoliation of living neoplastic cells and allogenic transplantation across abraded mucosa is mandatory to develop genital or extragenital disease. Studies on experimental transplantation stated three distinct phases of growth for the CTVT: (1) progressive phase, (2) static phase and (3) regressive phase. The cells of a CTVT avoid detection due to downregulation of the major histocompatibility complex I (MHC-I) by secreting inhibitory cytokines such as transforming growth factor beta 1 (TGFβ-1) and interleukin 6 (IL-6) molecules, and there is no MHC-II activity. In an experimental model, during the initial proliferative phase of tumor growth, little MHC class I or II was detected, but at 12 weeks, MHC expression increased remarkably, and lymphocytes stimulated MHC expression, resulting in regression of the tumor. In previous studies, spontaneous regression due to the immune response (immunoglobulin G formation, lymphocyte-mediated cytotoxicity) has been documented after the tumor age of 2 to 9 months.

In the past, some studies overrepresented male or female populations. Gender bias was not observed in recent case reports, and a survey study was conducted on a larger scale. Adult and intact dogs of reproductive age (2 to 8 years) are more prone to this disease, although there are some reports on neutered and old dogs (11 years).

Extragenital primary sites have been documented for CTVT in previous studies, where the nasal cavity is the second most common site (5 to 13% of all CTVT cases), followed by the skin, oral cavity, eyes and rectum. Additionally, it is overrepresented in adult male dogs. The most common historical findings associated with the nasal form of CTVT are sneezing, snoring, inspiratory dyspnea, bilateral epistaxis, sanguinopurulent nasal discharge, submandibular/mandibular lymphadenopathy, nasal deformation, and soft fleshy swelling at the level of the nasal bone area.

Grossly, the tumor can be soft to firm in consistency and single or multinodular, sessile or pedunculated, with or without ulcerative surface in both genital and extragenital form. Tumor size can be up to 15 cm in diameter in the genital form of the disease. Microscopically, plasmacytoid, lymphocytoid and mixed phenotypes have been described in detail in previous studies. Generally, it is a large but uniform and round to ovoid or polyhedral-shaped cell tumor resembling lymphocytes, and its cytoplasm is pale blue with distinct peripheral cytoplasmic vacuolization. Bunicleation, mitotic figures, and single or multiple nucleoli are also observed quite often in cytology samples. Definitive diagnosis can be made based on the cytological findings of sterile cotton swab samples, impression smear, fine-needle aspirated samples, and histopathology of the biopsy tissue. PCR of the rearranged LINE-c-myc gene can be a suitable option in cases where definitive diagnosis is difficult based on cytology or histopathology results.

Radiographs are quite helpful to see deformities, including soft tissue or fluid opacity (radiopaque) of the nasal cavity and frontal sinuses. Computed tomography scan is currently the best available supportive modality to see aggressiveness of the changes in the nasal cavity and frontal sinuses, including bone lysis and metastasis in neighbouring areas, before and after treatment. Additionally, it is quite useful to perform CTVT staging by a modified Adams staging system. Chemotherapy with vincristine or doxorubicin is the most common treatment used and suggested in previous studies of dogs diagnosed with the nasal form of the disease. A fatal outcome and high metastasis risk (up to 5% in routine cases of CTVT) is documented in puppies and immunosuppressed adult dogs.

The present report describes the radiographic, computed tomographic and cellular phenotypic features of four dogs affected with stage 4 intranasal CTVTs. All dogs were treated successfully with medical management. Two out of four dogs underwent follow-up scanning after chemotherapy.

Materials And Methods

The retrospective data of four dogs definitively diagnosed with primary intranasal CTVT at University Veterinary Hospital (UVH) of Universiti Putra Malaysia were analysed for history, diagnostics, clinical findings and treatment related to final outcome. Telephonic interviews were conducted with the owners regarding the current status of the dogs and any further history of tumor recurrence. All dogs were tested serologically for Ehrlichia canis (E. canis) with an
enzyme-linked immunosorbent assay (ImmunoComb® Canine Ehrlichia Antibody Test Kit) and microscopically for other common blood parasites, such as Babesia canis vogeli and Babesia gibsoni, from peripheral blood smears. Complete blood count (CBC) and selected parameters from the serum biochemistry panel were also tested in all four cases.

Radiographs of the skull, mainly the nasal cavity, with left and right lateral and ventrodorsal views were taken for all dogs. Contrast-enhanced CT images were acquired for all four dogs using a cone beam CT scanner (Fidex; Animage; Pleasanton, CA) and based on results "modified Adams staging" criteria used to stage the nasal tumor. Criteria adapted from Adams et alK where stage 1 is confined to the unilateral nasal passage, paranasal sinus, or frontal sinus without any bony involvement beyond nasal turbinates. Stage 2 is confined to any bony involvement beyond nasal turbinates without any evidence of orbital, subcutaneous, or submucosal mass. Stage 3 is confined to the orbit or nasopharyngeal or submucosal mass involvement, and finally, stage 4 is indicated when the tumor is causing lysis of the cribriform plate. Rigid rhinoscopy was performed in Dog-2. Follow-up CT scans were performed for Dog-3 and Dog-4 after the completion of five cycles of intravenous chemotherapy.

Tissue biopsy samples were collected by punch biopsy from Dog-1 only at the level of the left maxillary gum caudal to the canine teeth. Impression smears and sterile cotton swab samples of nasal secretions were collected for cytology and culturing of pathogenic bacteria and fungi, respectively, in all four dogs. Blood agar and MacConkey agar were used for primary bacterial culture, and Sabouraud dextrose agar was used to detect fungi in samples. Fine needle aspiration (FNA) samples were collected from the left side of the hard palate in Dog-1, soft swelling at the nasal bridge in Dog-2, intranasal soft tissue mass in Dog-3 and soft swollen mass at the right side of the hard palate in Dog-4.

Results

Signalement

Two dogs were mixed breeds (Dog-2 and Dog-3), one Spitz (Dog-1) and another Siberian Husky (Dog-4). All dogs were young adult males. One was neutered, and the remaining three were intact. The "mean ± standard error" (range) age and body weight of these dogs were 2.5 ± 0.46 (1.5 to 3.5 years) and 18.4 ± 2.14 (12.4 to 22.4 kg), respectively. All four dogs were raised in a free roaming lifestyle [Table 01].

Clinical Findings

The summary and duration of the detailed clinical signs before the first visit to UVH for individual dogs are summarized in [Table 01]. The most remarkable presenting complaint was chronic bilateral epistaxis in all four dogs, which started unilaterally in Dog-1 and Dog-3 but was reported bilaterally at the time of presentation. In addition to epistaxis, the second most remarkable finding was concurrent ocular manifestations in all four cases. Dog-1 showed left-sided mild epiphora, while Dog-2 and Dog-3 manifested right-sided epiphora, conjunctivitis and left-sided prolapsed third eyelid, respectively. Dog-4 manifested mild epiphora, while Dog-2 and Dog-3 manifested right-sided epiphora, conjunctivitis and left-sided prolapsed third eyelid, respectively. Dog-4 manifested mild epiphora, while Dog-2 and Dog-3 manifested right-sided epiphora, conjunctivitis and left-sided prolapsed third eyelid, respectively. Dog-4 manifested mild epiphora, while Dog-2 and Dog-3 manifested right-sided epiphora, conjunctivitis and left-sided prolapsed third eyelid, respectively. Dog-4 manifested mild epiphora, while Dog-2 and Dog-3 manifested right-sided epiphora, conjunctivitis and left-sided prolapsed third eyelid, respectively. Dog-4 manifested mild epiphora, while Dog-2 and Dog-3 manifested right-sided epiphora, conjunctivitis and left-sided prolapsed third eyelid, respectively. Dog-4 manifested mild epiphora, while Dog-2 and Dog-3 manifested right-sided epiphora, conjunctivitis and left-sided prolapsed third eyelid, respectively.

Haematology and selected biochemistry parameters were tested in all four dogs [Table 2]. Cross verification of all haematology reports and examination of routine blood parasites was performed through blood smears. The most remarkable findings in haematology were [mean ± SE (reference range)] leucocytosis 24.14 ± 2.89 (6 – 17) with band neutrophilia 0.53 ± 0.21 (<0.3), segmented neutrophilia 16.57 ± 1.90 (3 – 11.5), and monocytes 2.46 ± 0.71 (0.2 – 1.4) in all four dogs. Regarding the biochemistry parameters, major changes were seen in total proteins 78.08 ± 4.96 (55 – 75) with hypoalbuminemia 24.83 ± 0.59 (25 – 40) and hyperglobulinaemia 56.6 ± 5.74 (25 – 45), consequently reducing the albumin to globulin ratio 0.47 ± 0.07 (0.5 – 1.2).

Serologically, all dogs were tested for E. canis. Dog-1 was treated with doxycycline before presentation and reported negative on testing. Dog-2 showed a serologically very high antibody titre (scale 5/6) and was treated with doxycycline in the initial management of epistaxis with poor outcome. Dog-3 and 4 tested negative for E. canis but managed with doxycycline with poor outcome in the initial course of the disease diagnosis while dealing with epistaxis.

Radiology and Rhinoscopy

A detailed summary of radiographic and computed tomographic findings with staging of nasal tumor has been outlined in [Table 3]. All four dogs fell into stage 4 of the modified Adams staging for canine nasal tumors because of the involvement of the cribriform plate. The radiographic appearance of the neoplasia in Dog-2 has been shown and explained in detail in [Figure 02]. The pre- and post-treatment CT scan appearance of the nasal passages of Dog-3 and Dog-4 have been demonstrated with underlying relevant details in [Figure 03 and 04]. Rhinoscopy was performed on Dog-2 for detailed examination of the nasal cavity and to rule out the possibility of any foreign body.

Cytology and Histopathology

Cytology was performed in all four dogs, and phenotypically, all samples had identical findings. A mixed plasmacytoid and lymphocytoid population of cells was noticed in impression smears and FNA samples of intranasal, paranasal and invasive soft tissue swelling of the oral cavity. Characteristically, round to ovoid or polyhedral cells with distinct boundaries were noticed in all four dogs. Round nuclei containing prominent angular nucleoli and slight basophilic cytoplasm with distinct vacuolation were also observed. Mitotic figures were noticed in all four cytological samples as shown in [Figure 05].
Only Dog-1 had a histopathology report for a specimen consisting of few pieces of whitish tissue measuring 1.8 x 1.5 x 0.2 cm in aggregate. Characteristically, neoplastic cells identical to cytology samples were identified in nasal mucosa arranged in sheets with fibrous septa, separating the tumor into vague nodules. Occasional mitotic figures and subepithelial lymphocytic infiltration were also observed in the histopathology samples.

**Treatment and Outcome**

A detailed summary of treatment and outcome is presented in [Table 04](#). All four dogs achieved complete resolution of clinical signs as shown in Figure 1 C&F with vincristine sulfate (Vincristine Sulfate®; 1 mg/ml; Korea United Pharm. Inc.) at a dose rate of 0.025 mg/kg q7days intravenously in five cycles without any obvious adverse reactions or side effects. Hematology was repeated at every follow-up for each case before administration of the chemotherapeutic agent. The most common finding was thrombocytosis in all these cases. Furthermore, all dogs responded well to this therapy and were still alive without any recurrence of clinical signs, confirmed during subsequent follow-up post-treatment protocols, by detailed telephone interviews with the clients and CT scans for Dog-3 and Dog-4. The last case in the present study was treated approximately 5 months ago. Although CT for Dog-4 questionable the state of remission [Figure 3], no clinical signs were observed upon check-up and as reported by the owner.

**Discussion**

The most remarkable historical findings in the present study are the presentation of young adult male dogs with chronic (2 – 5.5 months duration) epistaxis and/or serosanguinous nasal discharge, which is quite consistent with previous case studies of primary nasal CTVT where nasal discharge was reported from one month to one year. Although some concurrent oral and ocular manifestations were also noticed in all dogs during physical examination, these findings are also quite consistent with previously reported cases where allografted transmission causes an invasive nature of the disease spreading to surrounding areas of the nasal cavity. Mild, microcytic, non-regenerative anaemia (PCV at low normal) was noticed in Dog-1, 2 and 4, likely due to prolonged bleeding as a result of chronic epistaxis, which is in agreement with the previous study of primary nasal CTVT. Nevertheless, a similar finding was absent in Dog-3, where the PCV was at mid-range, possibly due to compensatory polycythaemia induced by increased erythropoietin, endogenously produced by the tumour. All four dogs had mild-to-moderate leukocytosis, which could occasionally be present as a result of possible inflammation of the tumour surface.

Following definitive diagnosis of these cases, CT findings [Table 03] revealed remarkable lysis of nasal turbinates, septum and nasal bone in all four dogs. Palatine bone lysis was noticed in Dogs 1, 3 and 4, which is conclusive of oral cavity contamination with neoplastic tissue. The lysis of the orbital process of palatine bone was noticed in Dogs 2, 3 and 4, causing manifestation of ocular signs. Since bony lysis is quite significant in all these cases, the external and internal tables of the cribiform plate and frontal sinuses, separating sinuses from the nasal cavity, were also affected and allowed discharge and/or neoplastic tissue to spread into these areas. These findings indicated stage 4 of the “modified Adams staging” used for staging of the primary nasal CTVT in the present study. Staging with the same criteria has been done recently in a case study of four dogs diagnosed with primary nasal CTVT where only one dog was categorized in stage 4 based on CT scan findings. Interestingly, in the same case report, the aggressive nature of CT scan findings was noticed in the male population only, whereas another 2 males were categorized as stage 3, and the only female was categorized as stage 1.

The primary nature of the disease was considered based on the absence of genital form and/or metastasis of the primary tumor from another site, history and clinical findings related to nasal CTVT. Additionally, free roaming lifestyle and social behaviour, such as excessive licking of genital organs of affected animals and vigorous sniffing habits, can be a possible mode of allografted transmission. Definitive diagnosis can be made based on cytology only because of the typical characteristics of neoplastic cells seen in this study, but it can be further ensured with PCR and histopathology. In the present study, all four dogs were diagnosed mainly through cytology, and histopathology was performed in Dog-1 only. Contrary to a recent study on primary nasal CTVTs in which the lymphocytoid phenotype was considered less aggressive than the plasmacytoid phenotype with aggressive lytic changes in the nasal cavity, the present study had a mixed phenotype (none of the samples demonstrated more than 60% single phenotype) with aggressive changes recorded from CT scans, as mentioned in the preceding paragraph [Table 03].

Complete remission can be seen on follow-up CT images of Dog-3 [Figure 03 (c,d)], however, it is questionable in Dog-4. It is unknown whether the remaining soft tissue density lesion [Figure 04 (c,d)] comprises residual biologically active tumour or the tumour to be in a possible sterile or regressive state. It can be differentiated by performing positive emission tomography (PET) imaging; however, it is not regularly available in veterinary medicine. Alternatively, post-treatment sequential CT scans can be performed to evaluate disease progression, recurrence and remission. Several studies have proven the evidence of nasal turbinate regrowth in cases of brachycephalic dogs undergoing laser-assisted turbinectomy, pigs with atrophic rhinitis, and cats and dogs following intranasal polyps and angioleiomyoma removal, respectively. This remains uncertain, as recent and present studies showed persistent lysis of turbinate and adjacent bones upon follow-up CT scans. Interestingly, partial restoration of the right horizontal plate and right orbital process of the palatine bone can be seen in Dog-3 and Dog-4, respectively, but not the turbinate. These occurrences warranted further studies involving characterization pertaining to lysis and regrowth of the turbinate and adjacent bones affected by intranasal CTVT, which could possibly be achieved via sequential advanced imaging such as CT.

All four dogs are free of clinical signs until now with five cycles of vincristine sulfate. A positive response to therapy in this phenotype with variety of bony changes in all these cases gave impression that staging would be more related to local tissue changes rather than duration of treatment and outcome. Ojeda et al. also suggested similar results regarding the correlation of the staging system with treatment and outcome. Radiotherapy and surgical excision can be an option but not as monotherapy because of the poor remission period. Uncommonly, if it occurs, metastasis usually involves regional lymph nodes. In the present study, Dog-2 had unilateral left-sided submandibular lymphadenomegaly, but unfortunately, it was not tested for metastasis.

By comparing previous and present primary nasal CTVT reports, vincristine sulfate is still an effective monotherapy to achieve full recovery, although the number of cycles can vary, possibly depending on the expressed phenotype. In the past, resistance to this drug was reported in few cases, especially with
the plasmacytoid phenotype. In such cases, alternatives such as doxorubicin or a combination of surgical strategies can be adopted to achieve complete remission.\textsuperscript{24} Prognosis is not correlated to the staging system; it is quite variable and documented good to poor in previous studies.\textsuperscript{5,14,30} Based on the results of the present study, prognosis seems good with vincristine sulfate usage in mixed phenotype cases.

Declarations

Acknowledgements

We would like to thank the dog owners for answering the follow-up phone calls and provided necessary information for this study. Additionally, Muhammad Waseem Aslam and Lau Seng Fong have made equal contributions to the major drafting of this article.

Conflict of interest

The authors declare no potential conflicts of interest with respect to this case report, authorship, and/or publication of this article.

Funding

The authors received no financial support for the data analysis, authorship and publication of this article.

Declarations

This work involved the use of non-experimental animals only (owned) and followed established internationally recognised high standards (‘best practice’) of individual veterinary clinical patient care. Ethical approval from a committee was not necessarily required.

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Tables

| Case No. | Breed | Sex | Age (Years) | B.Wt (Kg) | Primary complaint/s and remarkable clinical findings on first and subsequent visits | Duration of clinical signs |
|---------|-------|-----|-------------|-----------|----------------------------------------------------------------------------------|-------------------------|
| Dog-1   | Spitz | M   | 2Y          | 12.4      | Occasional profuse bleeding or blood clots from nares. Serosanguinous discharge from left nares. 2-cm mass present at left maxillary gum with ulcerative mark on the surface. Slight bulging at the level of left lateral nasal bone surface. Left sided epiphora. | 5-months |
| Dog-2   | Mixed | MN  | 3Y          | 22.4      | In past, had history of genital-organ TVT but treated. Presented with bilateral epistaxis. Asymmetrical face because of the distorted nasal bone with a small soft lump on dorsal surface. Right-sided epiphora with conjunctivitis. Small growth at the level of right upper premolar. Discoloration of nasal planum. Left sided sub-mandibular lymphadenomegaly. | 4-months |
| Dog-3   | Mixed | M   | 1Y          | 20        | Started as unilateral epistaxis and turned into bilateral just one week before presentation. Continuous blood mixed mucoid nasal discharge from left nares and occasional bleeding from right nares when patient being subjected to physical stress. Prolapsed third eyelid of left eye. | 5.5-months |
| Dog-4   | Siberian Husky | M   | 3Y          | 18.8      | Epistaxis from both nares. Serosanguinous discharge from medial canthus of right eye without any sign/history of injury, started one day before presentation. Slight bulging-out of right eye globe. Another bulging noticed at the level of right lateral nasal bone surface. A 1.5 x 1.5 cm mass observed on right side of hard palate. | 2-months |

B. Wt: Body weight; TVT: Transmissible Venereal Tumor; M: Male; MN: Male Neutered; FR: Free roamer
### Table 02: Haematological and biochemistry parameters of four dogs diagnosed with primary nasal CTVT.

| Parameters (Units)       | Dog-1 | Dog-2 | Dog-3 | Dog-4 | Reference Range |
|--------------------------|-------|-------|-------|-------|-----------------|
| Erythrocytes x10^{12}/L  | 6.84  | 6.59  | 7.34  | 6.54  | 5.5 – 8.5       |
| Hemoglobin g/L           | 156   | 144   | 164   | 138   | 120 – 180       |
| PCV L/L                  | 0.35  | 0.38  | 0.45  | 0.35  | 0.35 – 0.55     |
| MCV fl                   | 51    | 58    | 61.6  | 54    | 60 - 77         |
| MCHC g/L                 | 446   | 379   | 363   | 394   | 320 – 360       |
| CWCC x10^{9}/L           | 26.8  | 29.3  | 24.48 | 15.99 | 6 - 17          |
| Band-neutrophils x10^{9}/L | 0.54 | 0.88  | --    | 0.16  | < 0.3           |
| Segmented-neutrophils x10^{9}/L | 16.62 | 21.68 | 15.36 | 12.63 | 3 - 11.5        |
| Lymphocytes x10^{9}/L    | 3.75  | 2.34  | 5.13  | 1.60  | 1.5 - 4.8       |
| Monocytes x10^{9}/L      | 2.68  | 4.10  | 2.40  | 0.64  | 0.2 - 1.4       |
| Eosinophils x10^{9}/L    | 3.22  | 0.29  | 1.55  | 0.96  | 0.1 - 1.3       |
| Basophils x10^{9}/L      | 0     | 0     | 0.04  | 0     | Rare            |
| Thrombocytes x10^{9}/L   | 316   | 243   | 485   | 318   | 200 - 500       |
| Sodium mmol/L            | --    | 141   | 152   | 143   | 140 - 155       |
| Potassium mmol/L         | --    | 6.7   | 5.5   | 5.4   | 3.7 - 5.5       |
| Chloride mmol/L          | --    | 108   | 117   | 107   | 96 - 122        |
| Calcium mmol/L           | 2.75  | 2.5   | 2.6   | --    | 2 - 2.8         |
| Inorganic phosphate mmol/L | --  | 1.3    | 1.63  | --    | 0.8 - 2.5       |
| Urea mmol/L              | 3.7   | 7.3   | 2.9   | 8.6   | 3 - 7.5         |
| Creatinine μmol/L        | 103   | 92    | 79    | 85    | 88 - 176        |
| Total bilirubin μmol/L   | --    | 3     | 3     | --    | 1.7 - 17        |
| ALT U/L                  | 35.4  | 25    | 41    | 22    | 5 - 90          |
| ALP U/L                  | --    | 70    | 72    | --    | 40 - 100        |
| GGT U/L                  | --    | --    | 9     | --    | 0 - 11          |
| Total Protein g/L        | 68    | 82.5  | 72    | 89.8  | 55 - 75         |
| Albumin g/L              | --    | 24.4  | 26    | 24.1  | 25 - 40         |
| Globulin g/L             | --    | 58.1  | 46    | 65.7  | 25 - 45         |
| A:G Unit                 | --    | 0.4   | 0.6   | 0.4   | 0.5 - 1.2       |

PCV = Packed Cell Volume; MCV = Mean Corpuscular Volume; MCHC = Mean Corpuscular Haemoglobin Concentration; CWCC = Complete White Cell Count; ALT = Alanine Transaminase; ALP = Alkaline Phosphatase; GGT = Gamma-Glutamyl Transferase; A:G = Albumin: Globulin Ratio

### Table 03: Summary of radiographic and CT scan findings in all four dogs and staging of primary nasal CTVT
Case | Radiographic Findings | Computed tomography findings at different regions of nasal cavity | Modified Adams Staging
--- | --- | --- | ---
Dog-1 | Abnormally radiopaque nasal cavity in both lateral and VD views, partial loss of nasal turbinates and cribriform plate detail | Rostral region: Soft tissue density filled cavity with nasal bone and septum lysis | Maxillary 4th premolar region: Lysis of septum, turbinates and palatine bone, soft tissue density invading from right to left nasal passage | Frontal sinuses region: Soft tissue density filled (partial) right rostral frontal sinus, partial cribriform lysis | Stage 4

Dog-2 | Abnormally radiopaque nasal cavity in both lateral and VD views, loss of nasal turbinates and cribriform plate detail | Rostral region: Soft tissue density filled cavity with nasal bone and septum lysis | Maxillary 4th premolar region: Bilateral soft tissue density, right orbit involved, septum and turbinate lysis | Frontal sinuses region: Soft tissue density filled right frontonal sinuses, prominent cribriform lysis | Stage 4

Dog-3 | Abnormally radiopaque nasal cavity in both lateral and VD views, loss of nasal turbinates and cribriform plate detail | Rostral region: Soft tissue density filled cavity with nasal bone and septum lysis | Maxillary 4th premolar region: Right orbit involved, lysis of septum, turbinates and palatine bone (orbital process). Soft tissue density invading from right to left nasal passage | Frontal sinuses region: Soft tissue density filled right frontonal sinuses, prominent cribriform lysis | Stage 4

Dog-4 | Abnormally radiopaque nasal cavity in both lateral and VD views, loss of nasal turbinates and cribriform plate detail | Rostral region: Soft tissue density filled cavity with nasal bone and septum lysis | Maxillary 4th premolar region: Both orbit involved, lysis of septum, turbinates, perpendicular plates (palatine) and palatine bone itself, soft tissue density filled both nasal passages | Frontal sinuses region: Soft tissue density in both frontonal sinuses. Massive lysis of the orbital process, perpendicular plate (palatine) and cribriform | Stage 4

**Table 04** Diagnostic confirmation, drug of choice, outcome and follow-up data of four dogs diagnosed with primary nasal CTVT

| Case | Diagnostic Confirmation | Treatment | Follow-up | Final Outcome |
|------|-------------------------|-----------|-----------|---------------|
| Dog-1 | Cytology (Mixed) and Histopathology | Vincristine chemotherapy, q7days for 5 weeks | Still alive after 37 months of last treatment without recurrence | Recovered |
| Dog-2 | Cytology (Mixed) | Vincristine chemotherapy, q7days for 5 weeks | Still alive after 19 months of last treatment without recurrence | Recovered |
| Dog-3 | Cytology (Mixed) | Vincristine chemotherapy, q7days for 5 weeks | Still alive after 10 months of last treatment without recurrence | Recovered |
| Dog-4 | Cytology (Mixed) | Vincristine chemotherapy, q7days for 5 weeks | Still alive after 08 months of last treatment without recurrence | Recovered |

Mixed: phenotypically plasmacytoid and lymphocytoid cell population of cytological sample

**Figures**
Figure 1

(a, b) Dog-4 presented with epistaxis and serosanguinous discharge from the medial canthus of the right eye and bulging-out of the right dorsolateral nasal bone surface, diagnosed with primary nasal CTVT. (c) Same dog on follow-up, after successful treatment. (d, e) Dog-2 presented with epistaxis and soft swelling at the level of the dorsal nasal surface causing asymmetry of the face, diagnosed with primary nasal CTVT. (f) Same dog on follow-up, after successful treatment.
Figure 2

(a, b) Right lateral and ventrodorsal (VD) radiographs of the skull, including the nasal cavity, in Dog-2 diagnosed with primary nasal CTVT. An abnormally radiopaque (especially on right side compared to left in VD view) nasal cavity with loss of the nasal conchae and turbinates detail and bony lysis of cribiform plate noticed in both lateral and VD views.
Figure 3

(a, b, c, d) Sagittal and dorsal pre-contrast bone reconstruction images of Dog-3 before and after chemotherapy. The right side is denoted by “R”, and window level and width are labeled. (a, b) A large isoattenuating region occupies a major portion of the right nasal passage, (b) causing left-side deviation of the nasal septum and lysis of the cribriform plate [highlighted in (a)] including surrounding bony structures. (c, d) Nasal passage is clear post-chemotherapy. However, permanent loss of the nasal turbinates is observed, predominantly in the right nasal passage.
Figure 4

(a, b, c, d) Sagittal and dorsal pre- and post-contrast, soft tissue (a, b) and bone (c, d) reconstruction images of Dog-4 before and after chemotherapy. The right side is denoted by “R”, and window level and width are labelled. (a, b) A large mixed (iso, hyper, and hypo) attenuating region occupies the entirety of both nasal passages and (b) further infiltrates into right lateral nasal soft tissue, (b) causing significant left-side deviation of the nasal septum and lysis of the cribriform plate, including surrounding bony structures. (c, d) Nasal passages are clear post-chemotherapy. However, permanent loss of the nasal turbinates is noticed in both the left and right nasal passages.
Figure 5

FNA of the intranasal mass of Dog-3 diagnosed with primary nasal CTFT. The phenotype is mixed by classification containing plasmacytoid (red arrow) and lymphocytoid (green arrow) cell populations. Numerous round to ovoid cells are observed with distinct cellular margins, cytoplasmic vacuolation, round nuclei with large angular nucleoli and coarse chromatin. A mitotic figure is also noticed in this smear, as shown in section (A) 400x. (Modified Giemsa Stain)