



วารสารสัตวแพทยศาสตร์ มข.

KKU Veterinary Journal

ISSN 0858-2297



CASE REPORT

Canine perivascular wall tumors with bone metastasis of the proximal humerus in a Golden Retriever dog

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Received 11 January 2025, Revised 16 August 2025 Accepted 25 October 2025, Published 20 December 2025

Abstract

A 10-year-old male Golden Retriever dog presented with a two-week history of right forelimb lameness and shoulder pain. Initial examination revealed knuckling and muscle atrophy. Radiography and computed tomography scan results revealed severe osteolysis at the proximal humerus. Forequarter amputation was performed, and a bone biopsy confirmed a perivascular wall tumor with bony metastasis. Adjuvant metronomic chemotherapy was administered. Two months postoperatively, diffuse pulmonary nodules and visceral masses were detected, with no local recurrence. Despite palliative care, the dog succumbed to the disease 169 days after the initial diagnosis. This case underscores the aggressive nature of perivascular wall tumors and the challenges in managing advanced metastatic disease. Early detection and aggressive therapy are crucial for better outcomes in similar cases in veterinary practice.

Keywords: Chemotherapy, hemangiopericytoma, myopericytoma, perivascular wall tumor, soft tissue

Introduction

Canine perivascular wall tumors (cPWTs) are a group of soft tissue sarcomas (STS) that develop from mesenchymal neoplasms, originating from parts of vascular mural cells. The term hemangiopericytoma (HPC) was used to categorize all canine perivascular wall tumors. Since 2007, a subclassification based on immunophenotype markers and histologic patterns has been used to classify specific types of cPWTs, including angioleiomyoma, angioleiomyosarcoma, myopericytoma, angiofibroma, angiomatofibroma, adventitial tumors, and hemangiopericytoma (Avallone et al., 2007; Godizzi et al., 2023).

Histologic vascular patterns described for cPWTs include perivascular whorling, placoid growth, interlacing bundles, and staghorn vessels (Avallone et al., 2007). The cPWTs are commonly found in the cutaneous and subcutaneous tissues (Avallone et al., 2007; Kravitz et al., 2019). However, primary cPWTs and HPC have been reported in various locations, including the orbit (Pucket et al., 2017), nasal cavity (Kluthcovsky et al., 2021), nasopharynx (Carpenter and Hamilton, 1995), lungs (Vignoli et al., 2008), spleen (Kim et al., 2012), mesentery (Katsuta et al., 1998), pelvic cavity (Cho and Park, 2006), and brain (Cohn-Urbach et al., 2015). A comprehensive search on Google Scholar, PubMed, CAB Abstracts, Web of Science, and Scopus, using search terms such as “perivascular wall tumor,” “myopericytoma,” “hemangiopericytoma,” “bone,” “dog,” “canine,” “invasion,” and “metastasis,” in various combinations did not yield any reported cases of canine perivascular wall tumors with bone invasion. This indicates that such cases have not been documented in the existing literature.

Clinical history and symptoms

A 10-year-old intact male Golden Retriever, weighing 48.4 kg, presented with a 2-week history of right forelimb lameness, without crepitus or soft tissue swelling. The dog exhibited pain upon palpation of the shoulder joint. Initial physical and neurological examinations were unremarkable. The dog was initially treated with a non-steroidal

anti-inflammatory drug. However, after one month, the condition worsened, with knuckling and muscle atrophy of the right forelimb. Regional lymph nodes were not enlarged. A complete blood count indicated mild anemia (packed cell volume 36%; reference range 38-55%), while clinical serum biochemistry was within normal limits.

Radiographs revealed a moth-eaten pattern of severe osteolysis at the proximal humerus, particularly at the neck, with no evidence of periosteal reaction, measuring 67 mm in length and 22 mm in diameter. No abnormalities were noted in other bones (Fig 1). A computed tomography scan showed extensive destruction of the right proximal humerus with an inconspicuous soft tissue mass and no evidence of metastasis (Fig 2).

Diagnosis and treatment

An initial bone biopsy diagnosed angiosarcoma, which led to a right forequarter amputation. A full circumferential specimen of the proximal humerus was collected, fixed in 10% neutral buffered formalin, and examined under a microscope. The dog recovered completely without complications.

Histologic lesions of a hard and black mass in the right proximal humerus revealed a poorly defined, unencapsulated tumor with dense, irregular interlacing bundles, and whorl formations with central blood slits. Moreover, the tumor invaded deep subcutaneous tissue, periosteum, and medullary bone marrow. The neoplastic cells were large, spindle-shaped with prominent nucleoli, and showed moderate anisocytosis and anisokaryosis. Areas displayed interlacing bundles of collagen, spindle cells, fibroblasts, and bony matrix destruction with new bone formation (Fig 3). The diagnosis was confirmed as a malignant perivascular wall tumor with bony metastasis.

The immunohistochemical analysis revealed strong positivity for vimentin and smooth muscle actin (SMA) in spindle-shaped tumor cells, indicating a mesenchymal and myofibroblastic origin. Endothelial cells showed strong positivity for factor VIII and some spindle cells were positive for CD31. Negative staining was observed for desmin, Special AT-rich sequence-binding protein 2 (SATB2), S-100

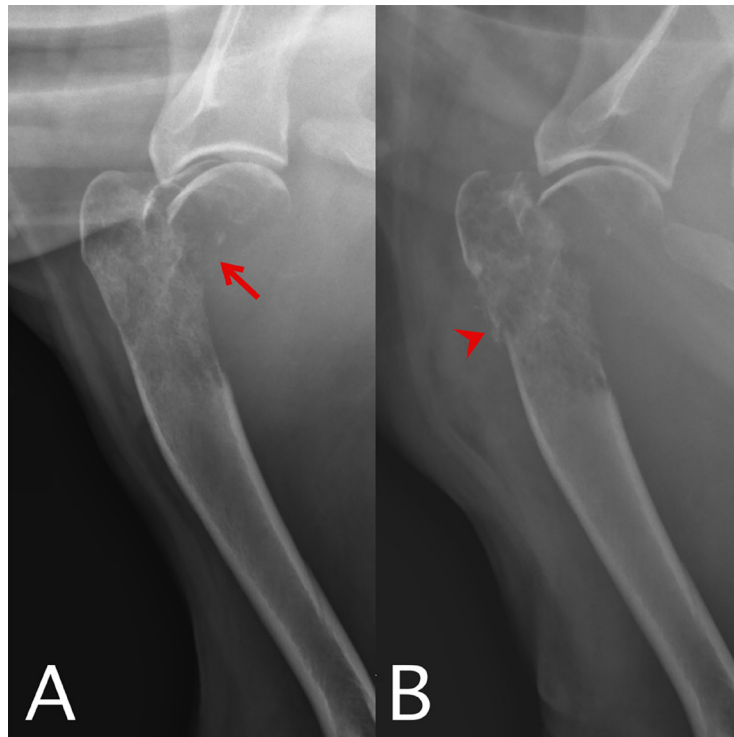


Figure 1. Radiographs of the right proximal humerus. A. A progressively worsening lesion was seen at the proximal humerus, with an invasive osteolytic lesion (arrow). B. The radiograph showed a significant lytic lesion at the neck of the proximal humerus one month later (arrowhead).

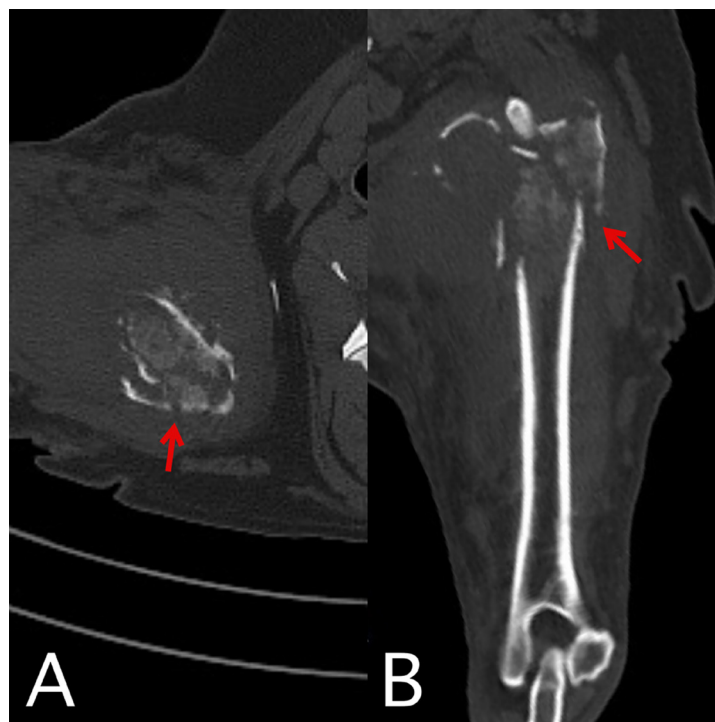


Figure 2. CT scan of the right humerus shows severe bone destruction of the proximal humerus (arrow), A. Transverse plane. B. Cranial plane.

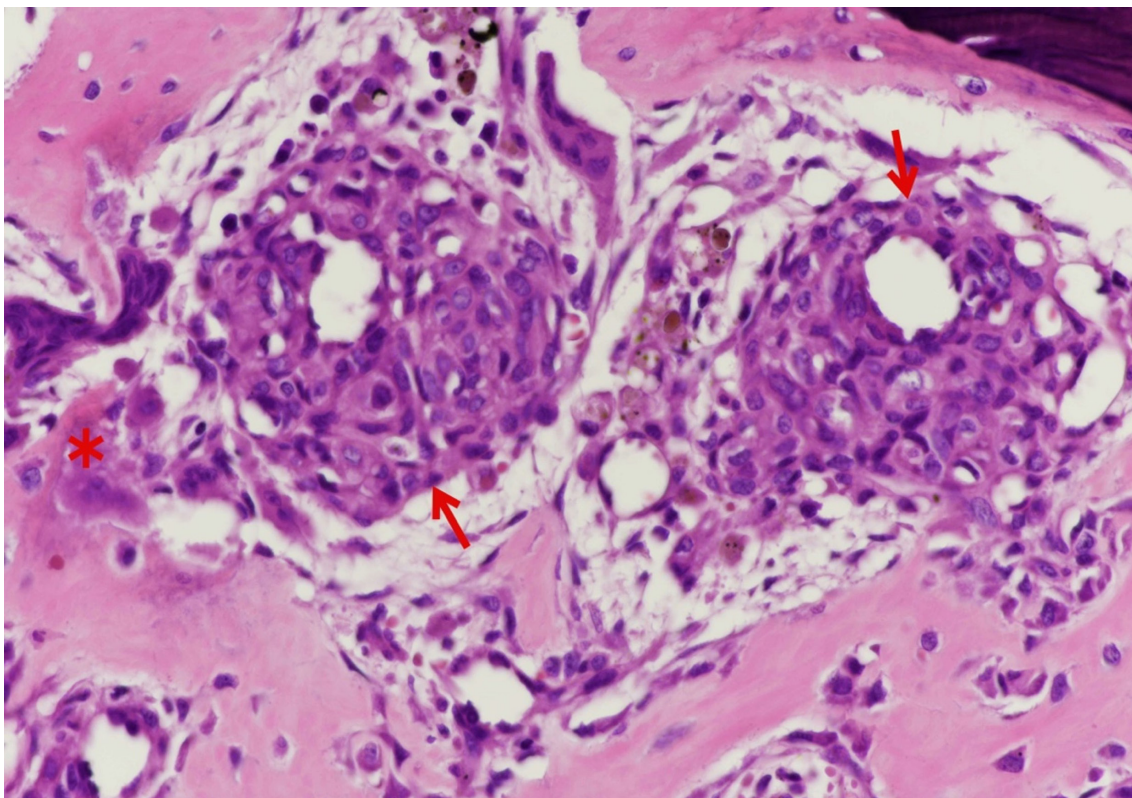


Figure 3. Histopathology of the right proximal humerus mass shows proliferation of pericytes surrounding small blood vessels (arrow), invading beneath the mature bony matrix (asterisk) (H&E staining, 40x magnification)

protein, and neuron-specific enolase (NSE). These findings are consistent with a diagnosis of myopericytoma, characterized by its distinct immunohistochemical profiles (Fig 4).

Metronomic chemotherapy, including chlorambucil 4 mg/m² PO (Leukeran; Aspen, Excella GmbH & Co. KG, Feucht, Germany) and firocoxib at 5 mg/kg SID PO (Previcox; Boehringer-Ingelheim GmbH, Rhein, Germany), was chosen as adjuvant treatment. At the follow-up, two months postoperatively, diffuse pulmonary nodules were detected on the thoracic radiograph, with no evidence of local recurrence (Fig 5). B-mode ultrasonography using a 15-mm micro-convex transducer with a frequency range of 2.6 - 12.8 MHz was performed, revealing a heterogeneous mass within visceral organs, including the liver, spleen, and renal cortices (Fig 6). A complete blood count showed severe anemia (pack cell volume 17%; reference range 38-55%). Clinical serum biochemistry indicated elevated blood urea nitrogen (18.42 mmol/L; reference range

3.5-9 mmol/L) and serum creatinine (210.39 μ mol/L; reference range 20-150 μ mol/L). Routine urinalysis demonstrated proteinuria with a urine protein-creatinine ratio of 2.56. Ultimately, palliative care was requested by the owner. Unfortunately, the dog passed away one month later, with a total survival time of approximately 169 days.

Discussion

Soft tissue sarcomas are varied tumors originating from mesenchymal cells, showing similar histopathological patterns such as liposarcoma, fibrosarcoma, myxosarcoma, peripheral nerve sheath tumors (PNSTs), and perivascular wall tumors. Diagnosing cPWTs involves recognizing vascular patterns like interlacing bundles and whorls. The histologic classification of cPWTs and PNSTs remains debated because of overlapping microscopic features. While PNSTs usually display whorls around a collagenous center, cPWTs show whorls centered on small vascular structures (Silva et al., 2014). Immunohistochemistry and

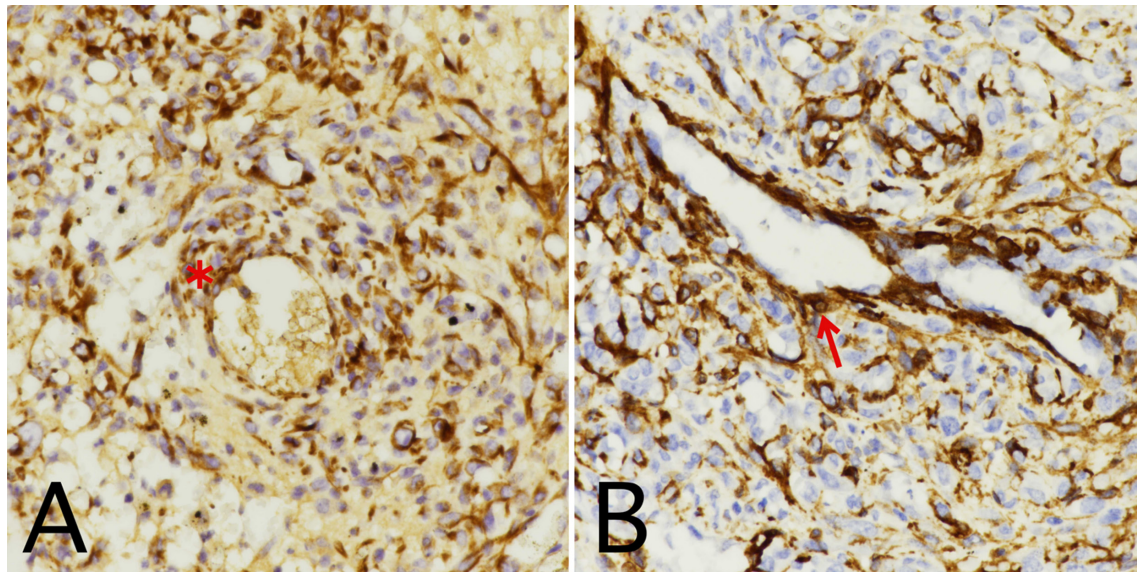


Figure 4. Immunohistochemistry of the right proximal humerus mass showing intense cytoplasmic positive staining of spindle-shaped tumor cells. A. Vimentin confirms the mesenchymal origin of the cells (asterisk). B. Smooth muscle actin confirms myofibroblastic cells (arrow). (IHC, LSAB counterstained with Meyer's, Hematoxylin, 40x magnification)

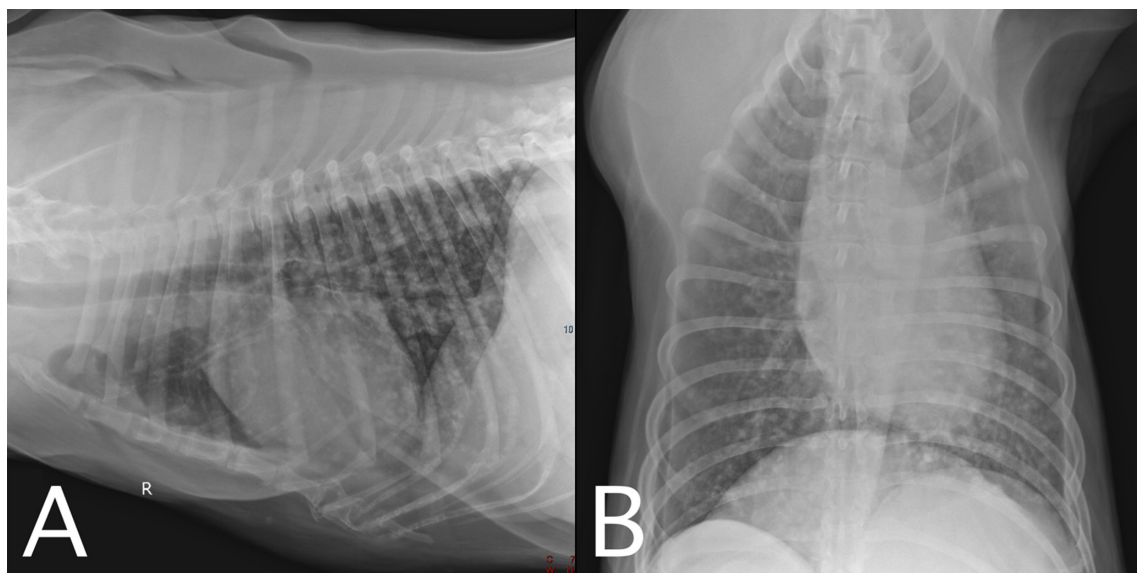


Figure 5. A structured interstitial lung pattern visible on the thoracic radiograph. A. Right lateral view. B. Ventrodorsal view.

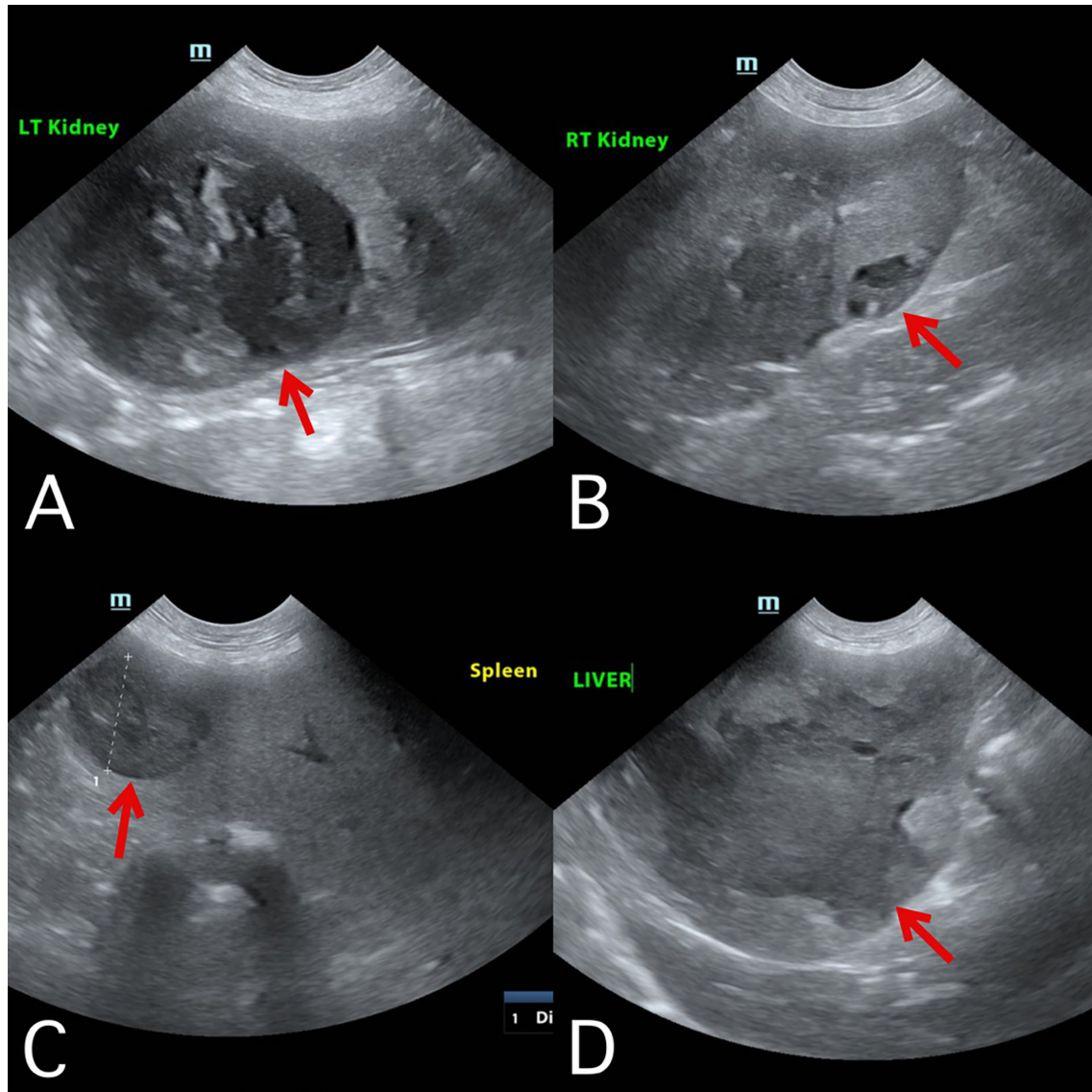


Figure 6. Abdominal ultrasound images show a heterogeneous nodular structure suspected of metastasis (arrow). A. Left kidney. B. Right kidney. C. Spleen. D. Liver.

ultrastructural analysis assist in accurately subtyping these tumors (Avallone et al., 2007; Loures et al., 2019; Palmieri et al., 2013)

Myopericytoma is mainly characterized by pericapillary whorls. The diagnostic criteria include strong positivity for vimentin, SMA, calponin, and pan-actin, with variable expression of desmin. It is negative for S-100 and NSE (Avallone et al., 2014, 2007; Loures et al., 2019; Sisó

et al., 2023).

In this case, the forequarter amputation was regarded as a radical surgical removal aimed at preventing the local recurrence of tumors. At follow-up, no local recurrence was seen after surgery. For STS, radical or wide surgical removal is recommended; several studies indicate that radical and wide excision approaches have the lowest recurrence rates (Chiti et al., 2021).

Conventional chemotherapy with maximum tolerated doses (MTD) of doxorubicin and carboplatin targets rapidly dividing tumors; however, it can cause toxicity and drug resistance. Adjuvant doxorubicin for STS resulted in a median disease-free interval of 724 days, while carboplatin alone in mesenchymal tumors had a mean time to progression of 42 days (Pritchard et al., 2023).

Adjuvant treatment was planned to be administered postoperatively as metronomic therapy. Several studies have indicated that metronomic chemotherapy serves as an alternative delivery method at doses below MTD, without extended drug-free breaks. (Leach et al., 2012) There are various protocols for metronomic therapy in STS, including the use of either chlorambucil or cyclophosphamide in combination with piroxicam. In a previous study, the chlorambucil protocol resulted in a median survival time of 153 days (Leach et al., 2012), while the cyclophosphamide protocol given to dogs with hemangiosarcoma achieved an overall survival time of 178 days (Lana et al., 2007). Several studies have demonstrated that the use of COX inhibitors is effective in managing cancer pain and tends to enhance the activity of chemotherapeutic agents (Leach et al., 2012).

Conclusion

Although the estimated survival time was 169 days, the tumor showed aggressive metastatic behavior in this case. The prognosis for cPWTs with bony metastasis remains uncertain due to limited available data. Multiorgan metastasis may indicate a late stage of cPWTs progression and could serve as additional evidence of the tumor's aggressiveness, resulting in shorter survival times.

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