

FidoCure[®] Case Study: Adley Hurwitz

Pulmonary Carcinoma

Madison Luker, DVM Candidate 2024,
UC Davis School of Veterinary Medicine

Dr. Garrett Harvey, VMD
Veterinary Affairs, FidoCure[®]

After six months of FidoCure[®] enabled therapy, Adley showed no evidence of pulmonary mass recurrence.



Introduction

Primary lung carcinoma is an uncommon tumor usually affecting middle to older age dogs. Compared to humans, the prevalence of this type of tumor in dogs is still very low.^{1,2} Interestingly, there has been an increase in diagnosed cases in recent years indicating a potential increase in incidence.¹ Affected dogs show clinical signs such as coughing, tachypnea, dyspnea, lethargy, exercise intolerance, hyporexia, and anorexia, but these may vary according to tumor location, tumor size and number of lesions.¹⁻³ Thoracic radiographs are a diagnostic technique frequently used to identify lung masses. This is usually followed by a computed tomography (CT) scan for a more precise evaluation of the lung parenchyma, which helps identify smaller lesions and lymph nodes involvement.² When a solitary tumor is detected, the treatment option often recommended is complete surgical removal. However, pulmonary carcinomas can spread locally throughout the lungs and even with a complete lobectomy, all neoplastic lesions may not be fully excised.² In veterinary medicine there have been a few published reports on the use of injectable chemotherapy for the treatment of pulmonary adenocarcinoma, and until now, no benefit of adjuvant treatment has been noticed.⁴ Results have been disappointing, especially for advanced tumors with reported survival times for those dogs with stage III and IV disease of 72–158 days and 26–58 days, respectively.^{1,3,4} Those dogs in stage I and II who have been submitted to a complete surgical excision have a better prognosis and can achieve a survival time longer than 658 days.⁴

In humans, tyrosine kinase inhibitors are frequently used to treat primary pulmonary carcinomas. They are recommended based on genetic characterization of fusion and activating mutations of EGFR, ALK, ROS1, HER2, BRAF and RET genes.⁵ In dogs, HER2 point mutations have also been identified in 38% of primary pulmonary adenocarcinoma.⁶ These are hotspot mutations at the V695E position in 93% of HER2 mutated cases. The mutation is localized in the transmembrane domain of the protein, representing an important opportunity for targeted therapy in affected dogs.⁷

History, Initial Assessment, and Surgery

Adley Hurwitz, a 6.5-year-old female spayed Rhodesian Ridgeback mix, was presented to her primary veterinarian on January 28, 2020 due to a progressive cough occurring over a period of approximately one and a half months. During a physical exam, two nodules were identified in the right cranial abdominal mammary gland. Fine needle aspiration of the mammary nodules and chest radiographs were performed. Cytology evaluation of the nodules confirmed presence of mammary and inflammatory cells. On pulmonary radiographs, a solitary lung mass was identified, suggesting a diagnosis of mammary tumor metastasis or a concomitant primary lung tumor. To better characterize the lung mass and its possible spread, a full body CT scan was performed on January 30, 2020. The scan confirmed the presence of a single pulmonary lung nodule with no apparent lymph node involvement.

On February 4, 2020, a right cranial lung lobectomy was performed, and a 60mm lung mass was completely excised. Histopathologic evaluation revealed a grade I pulmonary carcinoma removed with marginal excision. Another surgical intervention was performed to remove the two mammary nodules on March 10, 2020, which included a multilobulated mammary gland nodule (15 mm) and one soft subcutaneous nodule (10 mm) adjacent to it. Both nodules were completely excised. Histopathology revealed epithelial cells forming tubulopapillary sheets associated with myoepithelial proliferation. A mitotic index of 10 in 10 high-power fields was characterized. Results were consistent with a complex mammary carcinoma mixed type, and a ductal hyperplasia. Following both surgeries, no adjuvant treatment was elected.

Post-Operative Evaluation and Treatment Plan

During Adley's three month re-staging, a new lesion was suspected in the right middle lung lobe via thoracic radiographs. A chest CT scan was performed and although there was no evidence of regrowth from the primary lung tumor, the CT scan revealed a right caudal pulmonary mass, which was likely a secondary or metastatic lesion. At this time Adley showed an enlarged lymph node, suggesting lymphatic tumor spread from the primary pulmonary carcinoma that was previously removed. At this point, treatment options for Adley were discussed including systemic therapy.

FidoCure[®] Analysis

After consideration of all treatment options, Adley's family elected to enroll in the FidoCure[®] Precision Medicine Platform. Based on the high incidence of HER2 V695E mutation previously published and tumor cases database, the tyrosine kinase inhibitor lapatinib was recommended for Adley's treatment.

Lapatinib is a small molecule used in humans to target ERBB1 (EGFR) and ERBB2 (HER2) membrane receptors by selective binding to the adenosine triphosphate (ATP) binding pocket and preventing receptor activation. This tyrosine kinase activity prevents downstream signaling resulting in inhibition of tumor cell proliferation and survival.⁷

FidoCure[®] Treatment

As the genomic results from FidoCure[®] analysis indicated the potential benefit of targeted therapy use, the following targeted therapies were prescribed by the patient's treating veterinary oncologist:

- Lapatinib
200 mg, orally, once a day (5.7 mg/kg)

Beginning in late May 2020 this medication was administered orally by the pet owners at home.

Two months after starting lapatinib therapy, repeat thoracic radiographs revealed that the nodule which had previously been identified within the right caudal lung lobe had completely resolved without any new appreciable lesions in the lung field. After six months of FidoCure[®] enabled therapy, Adley still showed no evidence of disease recurrence.

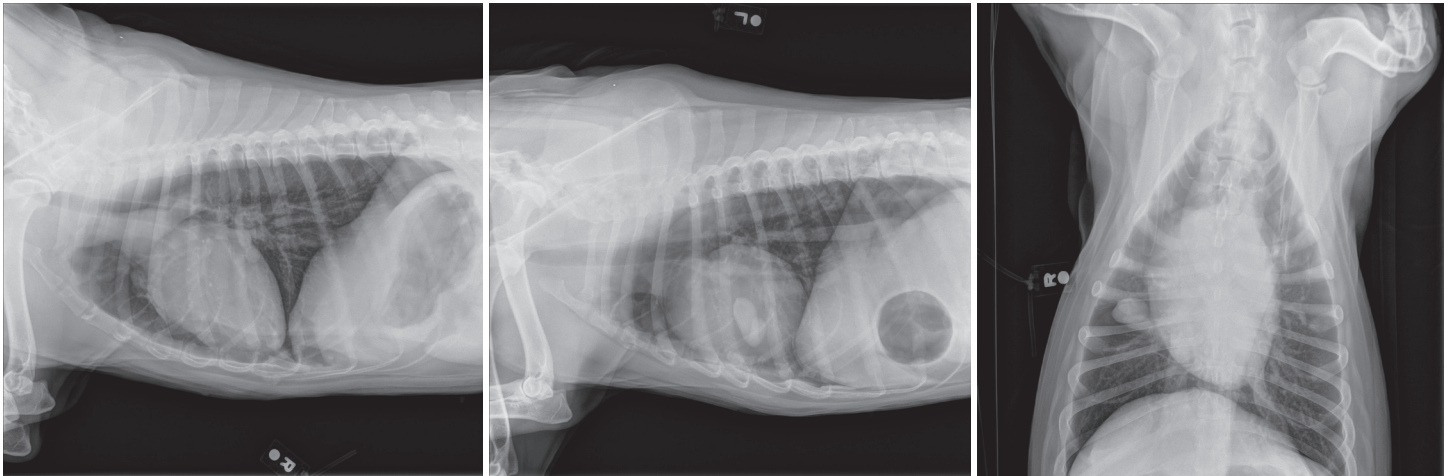
Her treatment has been continued on the same dosage of lapatinib. She showed unremarkable blood work and maintained a positive quality of life with no side effects reported.

Conclusion

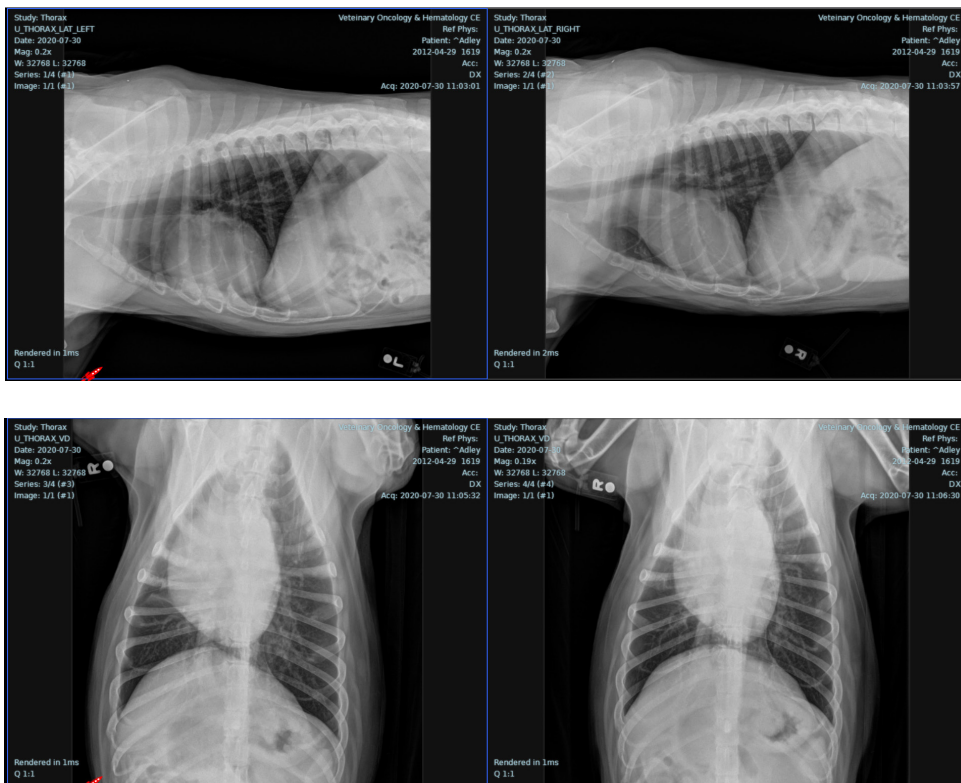
After FidoCure® enabled treatment, there was no evidence of Adley's secondary pulmonary mass.

Six months into FidoCure® enabled therapy, Adley has continued to thrive. There was resolution of the recurrent pulmonary mass two months into taking lapatinib. Adley has maintained a positive quality of life (including no reported side effects) and extended time with her pet owners.

Radiographs April 2020 (before)



Radiographs July 2020 (after)



What Adley's Parents Say



Adley, aka Addie Bear, was diagnosed with a lung tumor in January 2020. After removal of the first tumor, a second tumor, found about a month later, was found to be inoperable. We were given several choices for chemotherapy. After consideration, we decided to go with FidoCure[®], mostly because of the extent of their research and experience with lung cancer in dogs. While we were initially told that chemo would only slow the tumor, subsequent scans have shown that the tumor is gone. Addie has been on chemo for over a year now and is feeling great — energy and appetite haven't changed. I can't thank FidoCure[®] enough!

— Laura Hurwitz



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