Unique Papillary Thyroid Cancer (PTC) Metastasis to the Skin: A Case Report

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ABSTRACT

Cutaneous metastasis of papillary thyroid cancer (PTC) is an unusual phenomenon with limited documented cases in medical literature. PTC is the most common of the thyroid cancers. Typically characterized by slow growth and a favorable prognosis, PTC is confined primarily to the thyroid gland and regional lymph nodes. However, in rare instances, aggressive behavior may lead to distant metastases, with the lungs and bones being the most affected sites. Nevertheless, the skin is an infrequent location for thyroid cancer dissemination. This case report presents a unique clinical scenario involving a patient diagnosed with papillary thyroid cancer who developed skin metastases. We aim to contribute to the growing body of knowledge concerning this uncommon manifestation of PTC by describing this patient's clinical presentation.

CASE REPORT

INTRODUCTION

A 77-year-old female with a history of PTC presented with a progressively enlarging, pruritic, skin nodule to her parietal scalp in May 2015. She described the nodule as an itchy, bleeding sore. An excisional biopsy of the nodule was taken including the subcutaneous tissue, from which the diagnosis of papillary thyroid cancer metastasis was determined (Figures 1,2). In April 2016 at a dermatology follow up, the patient was noted to have a 1 cm exophytic nonhealing sore to the right parietal scalp. Due to its non-healing nature, the lesion was excised in April 2016 (Figure 3) and found to be metastatic papillary thyroid cancer. Additionally, in October 2022, the patient reported a pruritic, gradually growing lesion on her scalp for the past six months. This lesion was biopsied and determined to be metastatic carcinoma consistent with metastatic papillary thyroid carcinoma (Figure 4), and immunohistochemical staining was positive for TTF-1 and thyroglobulin.

The patient was initially diagnosed with a 3.2 x 1.5 cm nodule in the left lobe papillary thyroid carcinoma in 1992 and a left thyroid lobectomy was performed. In 1993, a right thyroid lobectomy was performed followed by I-131 therapy. In September of 2002, the patient had hemoptysis and recurrent papillary carcinoma was revealed with bronchoscopy and biopsy. In November of 2002, the patient was treated with 200 millicuries of I-141 and then again in January 2004 was treated with 100 millicuries of I-131. Reevaluation was done in 2006 and 2007 with the recommendation to proceed with targeted therapy. A Chest CT in August 2008 (Figure 5) numerous pulmonary nodules and masses in both lungs, consistent with metastasis, as well as a sclerotic lesion in the L2 vertebral body, question of metastatic lesion. In April 2013, the patient had a negative I-131 scan (Figure 6) and CT imaging demonstrated increasing size of pulmonary lesions.

From 2013-2023, there was significant disease progression; the patient had positive skin metastasis, metastases to the lung, bones and pleura as well as presumed metastasis to the spleen, brain, kidney, liver, and soft tissue, and pancreas (Figures 7-18). The patient began sorafenib treatment in February 2014 and continued this until March 2018 when treatment was changed to lenvatinib and denosumab was added. The patient died in September of 2023 at age 84 with a 31-year history of recurrent PTC with known metastasis to numerous locations including the scalp, pleura, lungs, and bones as well as presumed metastases to the spleen, kidney, brain, liver, and pancreas.

DISCUSSION

Papillary thyroid cancer (PTC) is the most common classification of thyroid malignancy, accounting for approximately 80% of all thyroid cancer cases [1]. Typically characterized by slow growth and a favorable prognosis; PTC is confined primarily to the thyroid gland and regional lymph nodes [2,3]. However, in rare instances, aggressive behavior

may lead to distant metastases, with the lungs and bones being the most affected sites [2,4]. One exceptionally atypical presentation of PTC metastasis is to the skin. Representing approximately 1% of all metastases, the skin is an infrequent target for thyroid cancer dissemination [5-7]. This case report presents a unique clinical scenario involving a patient diagnosed with papillary thyroid cancer who developed distant metastases to the bones and lungs as well as rare metastases notably to the skin and pleura, with presumed metastases to the liver, kidney, brain, soft tissues, spleen, and pancreas.

Less than 10% of patients with differentiated thyroid cancer develop distant metastases and the incidence and prevalence of metastases to rare sites are not yet completely known [8]. Madani et al. reported a systematic review of rare metastases of differentiated thyroid cancers, consisting of 42 case series and 197 case reports, (57% papillary carcinoma, 39% follicular, and 4% Hurthle cell carcinomas). Of these rare metastatic presentations of thyroid carcinoma, there was a prevalence of brain metastases (44%), followed by skin (17%) and liver metastases (8%). Additional rare metastases were also found including kidney, soft tissues, adrenal gland, eye, pancreas, spinal cord, endobronchial, breast, dura, gastrointestinal, ovary, vascular, thymus, parotid submandibular, pleura, spleen, oral cavity, and the less common penis metastasis [8,9].

In a review of 43 cases of reported skin metastases from thyroid carcinoma, papillary carcinoma was the most common (41%), followed by follicular (28%), anaplastic (15%), and medullary carcinomas (15%) [7]. Additionally, in agreement with Dahl et. al, our patient presented with metastasis to the scalp which is reported as the most probable site of skin metastases, with almost all skin metastases of papillary cancer reported in head-and-neck areas [10]. It is generally believed that the mechanisms of PTC skin metastasis include direct diffusion, hematogenous diffusion, lymphatic diffusion, and tumor cell implantation during biopsy or surgery. The scalp, face, and neck are rich in dermal capillary network providing a suitable environment for the formation of metastatic foci; however, the exact mechanism of skin metastasis is not fully understood [8,11].

Cutaneous metastases are often slow-growing erythematous nodules or plaques [5,6]. These metastases can occur as single lesions, as in our case, or with multiple lesions. Though these lesions are usually asymptomatic [8], in both occurrences our patient described pruritis to the lesion, which was described to progressively enlarge over six months. Additionally, the first nodule had associated bleeding, which contrasts with literature data showing that ulceration is uncommon [8,12].

The two cardinal morphological features of conventional PTC are the papillae and the nuclear changes. The papillae are composed of a central fibrovascular stalk covered by a neoplastic epithelial lining. The papillae may be long, straight, or arborizing; arranged in a parallel, regimented fashion; short and stubby, or tightly packed. Though immunohistochemistry is seldom of value in diagnosing PTC, it can play a role in diagnosis of metastatic disease. The neoplastic cells are strongly and diffusely immunoreactive with keratin, CK7, thyroglobulin, TTF-1, and PAX-8 [1], as evidenced by positive staining in patient samples (Figure 3,9) which were positive for TTF-1 as well as thyroglobulin and PAX-8 respectively. Without a clinical history, the diagnosis of papillary thyroid carcinoma metastatic to the skin can be difficult because primary cutaneous neoplasms may have similar histopathologic features. Apocrine tumors, such as hidradenoma papilliferum and syringocystadenoma papilliferum, also can exhibit well-formed papillary structures and may be confused with a metastatic thyroid neoplasm [7].

In the literature, it is reported that patients with skin metastases usually present 2–20 years after papillary thyroid cancer diagnosis [13,10] with an interval of five years from the initial diagnosis to the skin metastases being common [14]. However, our patient's skin metastases were reported 23 and 30 years after her initial diagnosis, providing a distinctive presentation.

Despite the overall survival rates of papillary thyroid cancer being quite high; the average survival period is relatively low in PTC with skin metastases. Previous literature states that skin metastasis appearance suggests a poor prognosis, the presence indicating aggressiveness and spreading of the disease [15]. In Dahl et al. reported case series [7], the average survival of patients with cutaneous metastases was 19 months after the first diagnosis in five lethal cases. Though, according to Shon et al. [12] and Aghasi et al. [16], the average life expectancy after the diagnosis of cutaneous metastasis is less than a year. In significant contrast, the patient in this case report survived for an additional eight years following her initial skin lesion diagnosis in 2015, a point that emphasizes the uniqueness of this case.

CONCLUSION

Although skin metastasis is a rare presentation of papillary thyroid carcinoma, skin metastasis of PTC demonstrates disseminated disease and may serve as a useful signifier of prognosis. This represents an important clinical opportunity for clinicians to consider metastasis upon lesion detection and reflects the importance of close, prolonged follow-up in patients with a previous diagnosis of thyroid cancer.

With this case report, we hope to raise awareness among clinicians about the possibility of papillary thyroid cancer metastasizing to the skin. By sharing our clinical experience and insights from the literature, we seek to improve clinical decision-making and provide better care for patients facing this rare and challenging condition.

TEACHING POINT

Cutaneous metastasis of papillary thyroid cancer (PTC) is an

unusual presentation, typically associated with high mortality within one year. This case report presents a unique clinical scenario involving a patient diagnosed with papillary thyroid cancer who developed skin metastases and survived 8 years after diagnosis of first skin lesion and 31 years after initial PTC diagnosis.

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FIGURES

Figure 1: Disease progression and management timeline

CLINICAL & IMAGING FINDINGS:

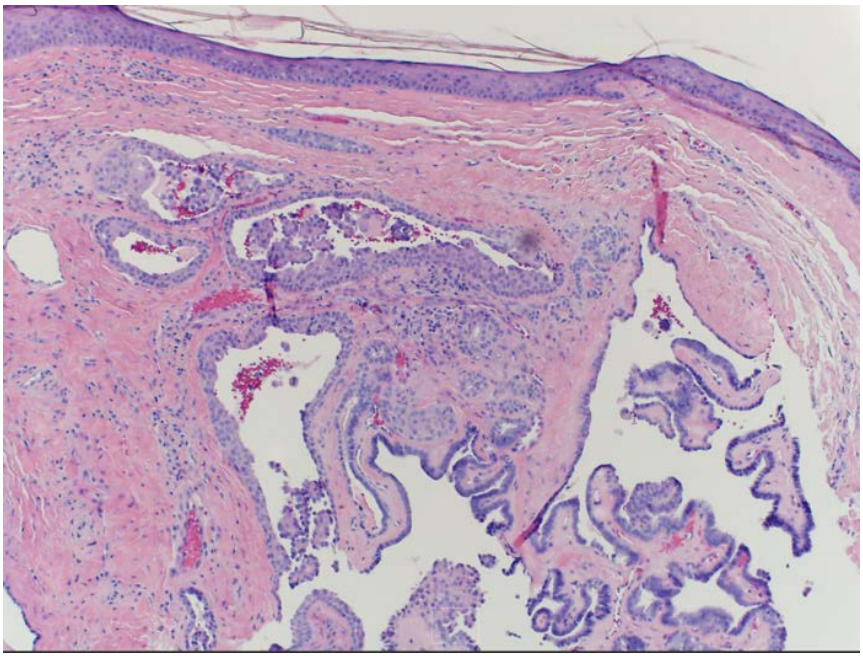

Figure 2: May 2015 scalp nodule: H and E stain 10x. Dermal involvement by PTC with focal papillary architecture.

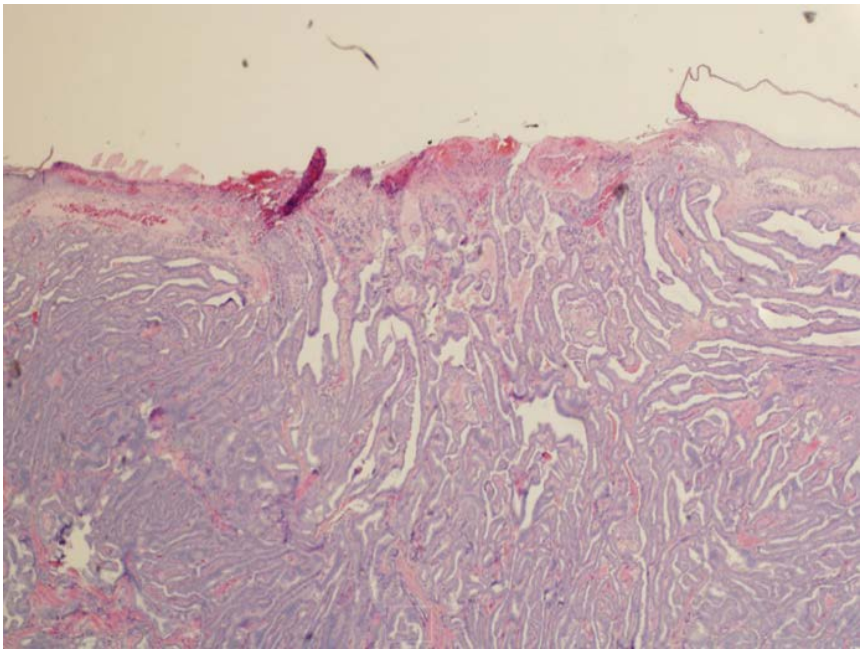

Figure 3: April 2016 ulcerative scalp lesion: H and E stain 4x. Ulcerative epidermis with dermal involvement by PTC with classic cytologic features.

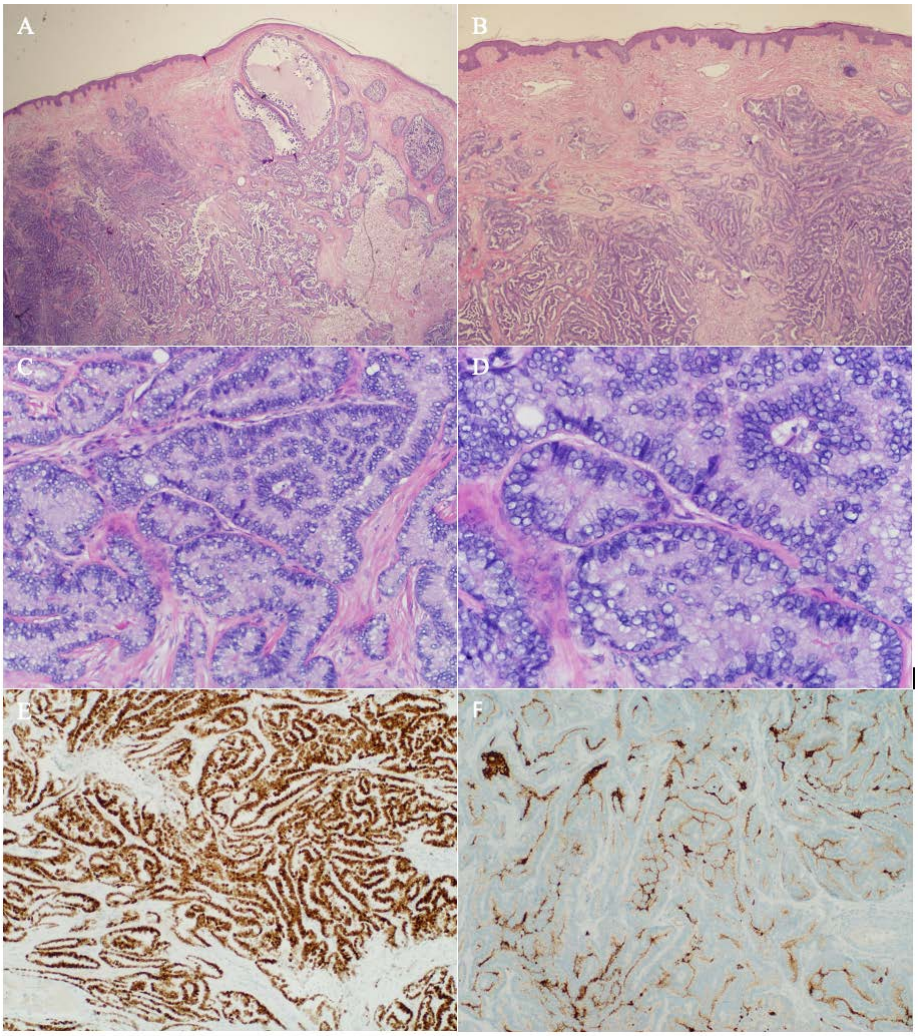

Figure 4: October 2022 scalp nodule. Dermal involvement-cutaneous metastases of PTC showing nuclear clearing and grooves. A. H and E stain magnification 2x B. H and E stain magnification 4x C. H and E magnification 20x D. H and E magnification 40x
F. Immunohistochemical staining positive for thyroid transcription factor-1 (TTF-1) magnification 10x E. Immunohistochemical staining positive for thyroglobulin magnification 10x

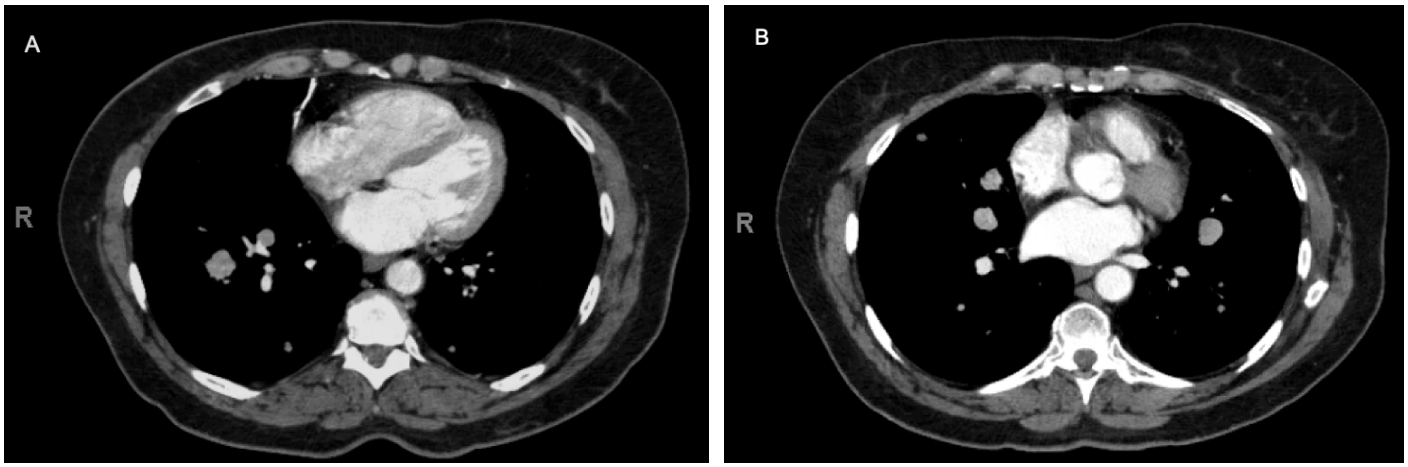

Figure 5: August 2008. Chest CT with contrast. Axial view. Pulmonary metastasis, with numerous pulmonary nodules and masses in both lungs. A. The largest mass on the right measures 1.9 x 1.7 cm. B. The largest mass on the left measures 1.8 x 1.7 cm.

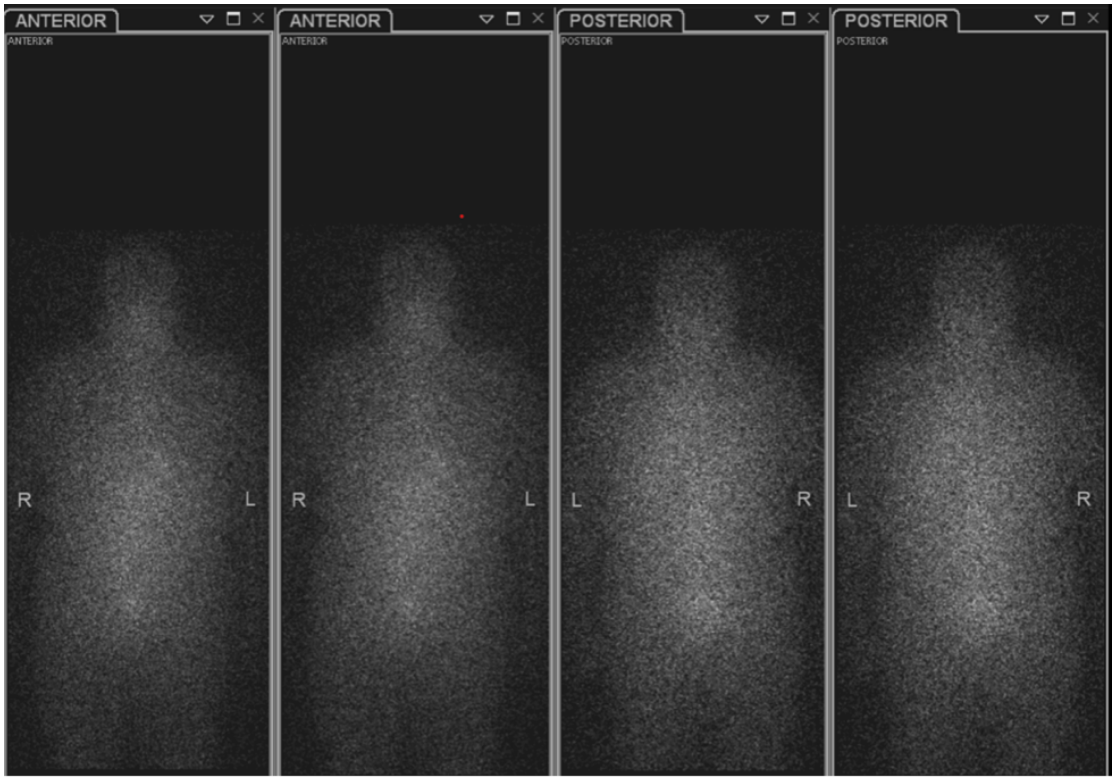

Figure 6: April 2013. Negative I-131 WBS scan. Anterior and posterior views.

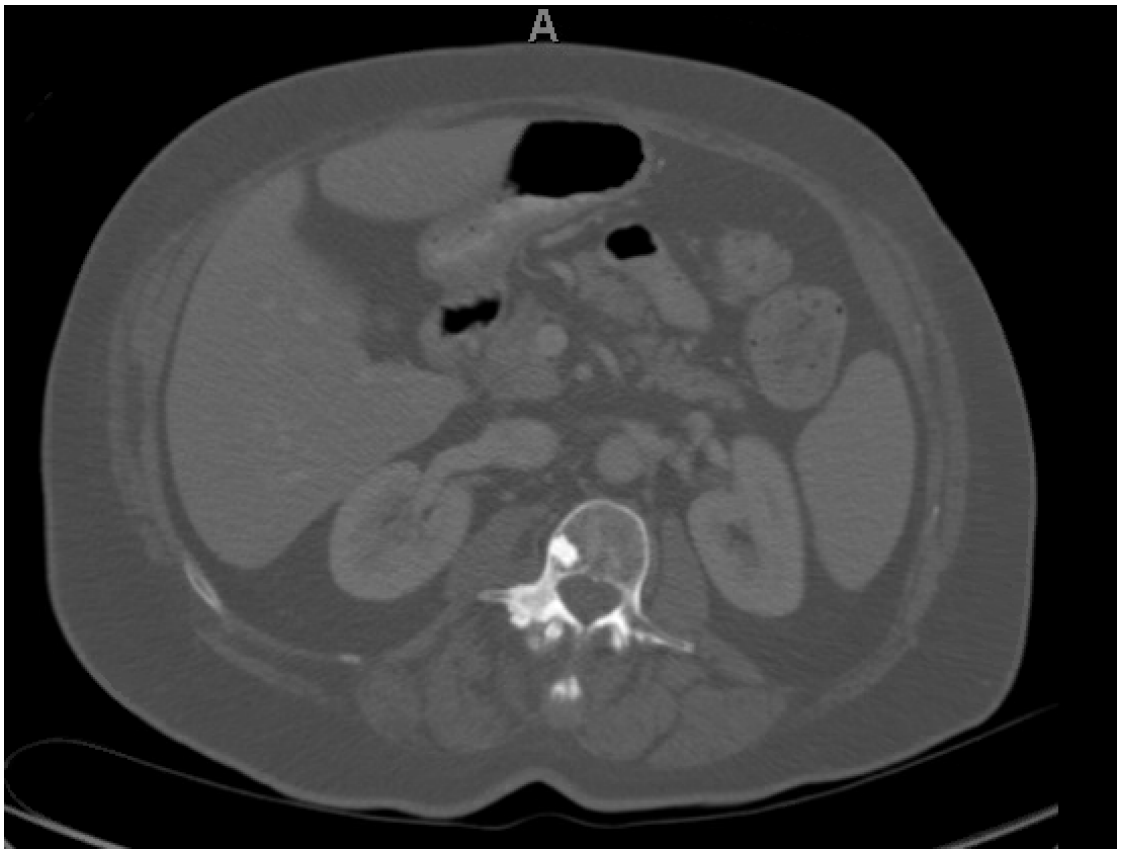

Figure 7: June 2013. CT chest abdomen pelvis with contrast. Axial view. Sclerotic areas in the L2 and L4 vertebral bodies cut, which could represent metastasis.

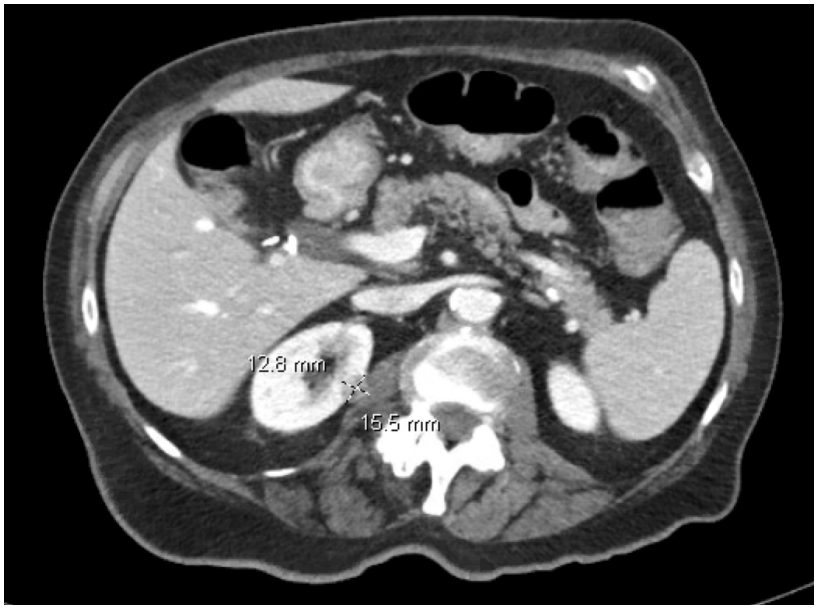

Figure 8: July 2016. CT chest abdomen pelvis with contrast. Axial view. Enhancing mass in mid-portion of right kidney medially which measures 1.6 x1.3 cm. Differential includes solid renal neoplasm versus metastasis.

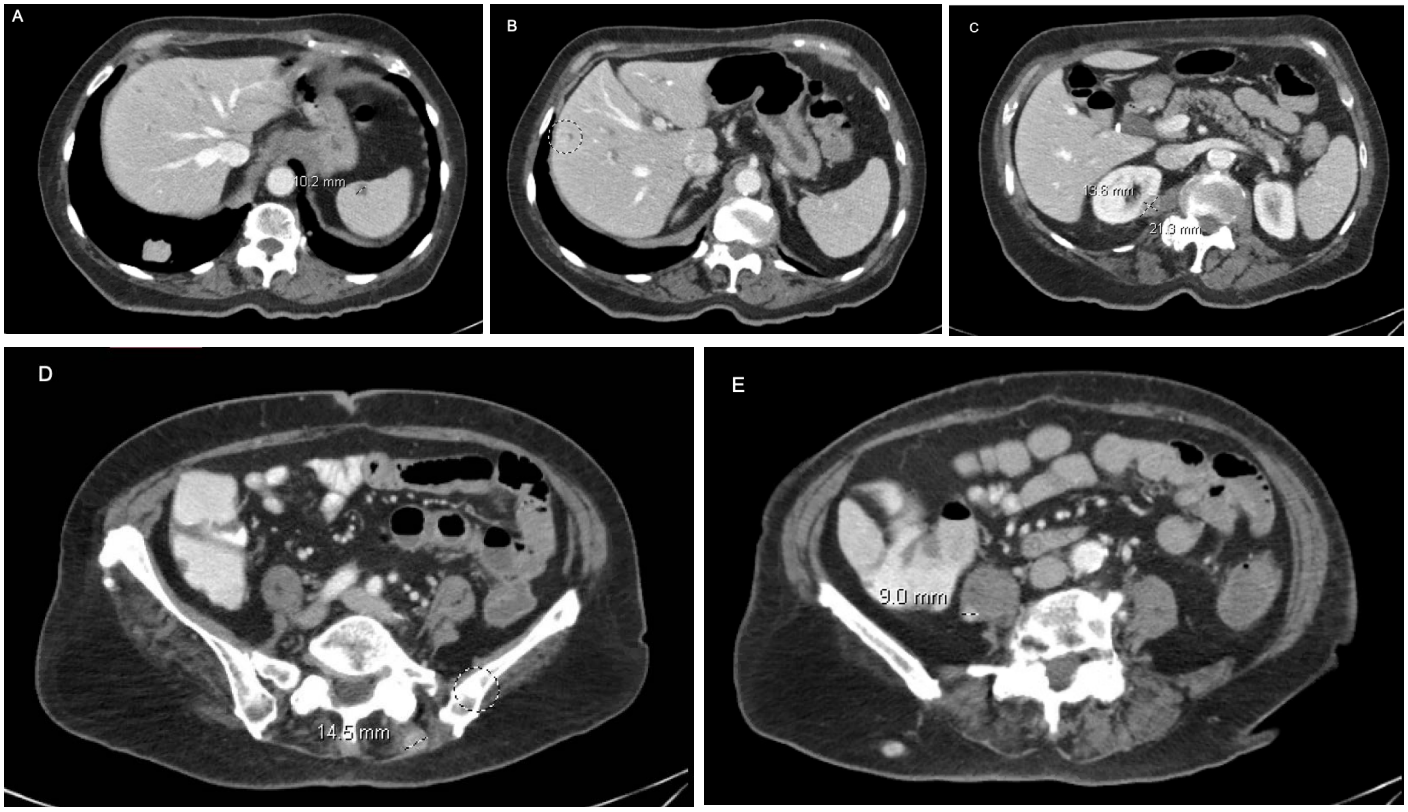

Figure 9: February 2018. CT chest abdomen pelvis with contrast. Axial view. Progression with new splenic and liver lesions, kidney, soft tissue, and pancreatic lesions suspicious for metastases.

A. Interval increases in size of low attenuation lesion in the spleen with a second low attenuation lesion slightly decreased in size, appearance worrisome for metastases.

B. New small subcapsular region in the right hepatic lobe is suspicious for small metastasis.

C. Lesion in the pancreatic head is somewhat ill-defined, however is grossly unchanged from prior and is suspicious for metastasis. Solid mass in right kidney measures 2.1 x 1.4 cm, slightly increased in size may represent metastasis or primary renal cell carcinoma.

D. Enhancing inferior left paraspinous musculature. Compatible with soft tissue metastases.

E. Enhancing lesion in right iliopsoas muscle measures 0.9 cm. Compatible with soft tissue metastases.

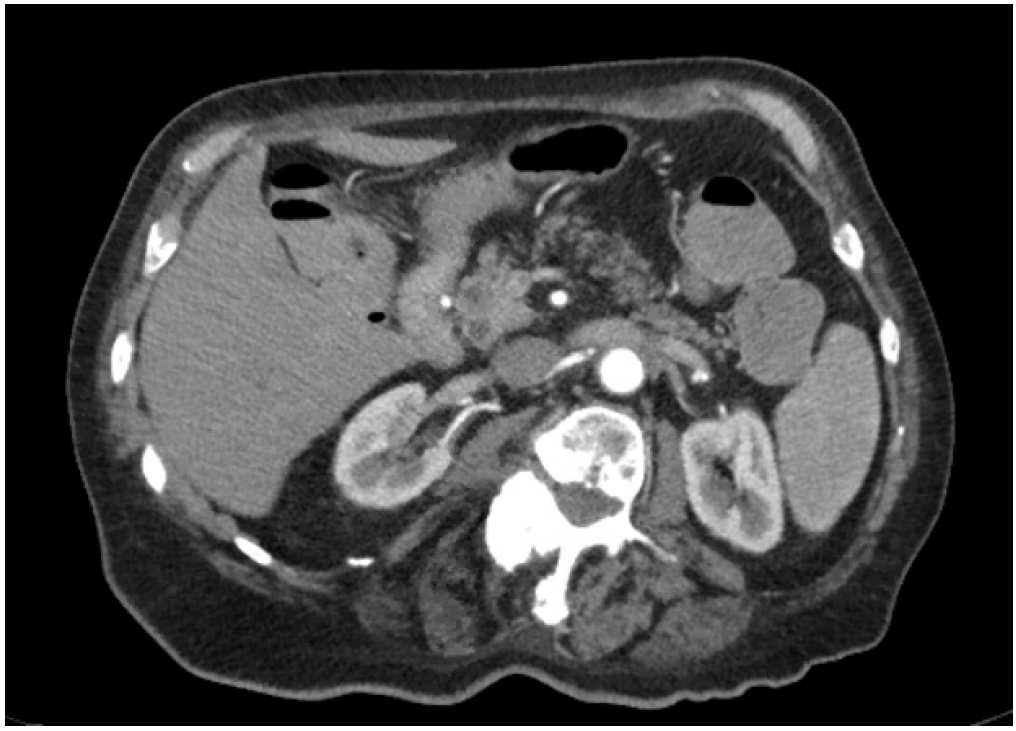

Figure 10: January 2020 CT chest, abdomen, and pelvis with contrast. Axial view. Stable pulmonary nodules, multiple lesions in the spleen, and multiple sclerotic and lytic lesions are present in lumbar spine, bony pelvis, and left proximal femur. Stable small 12 cm pancreatic head hypodense mass.

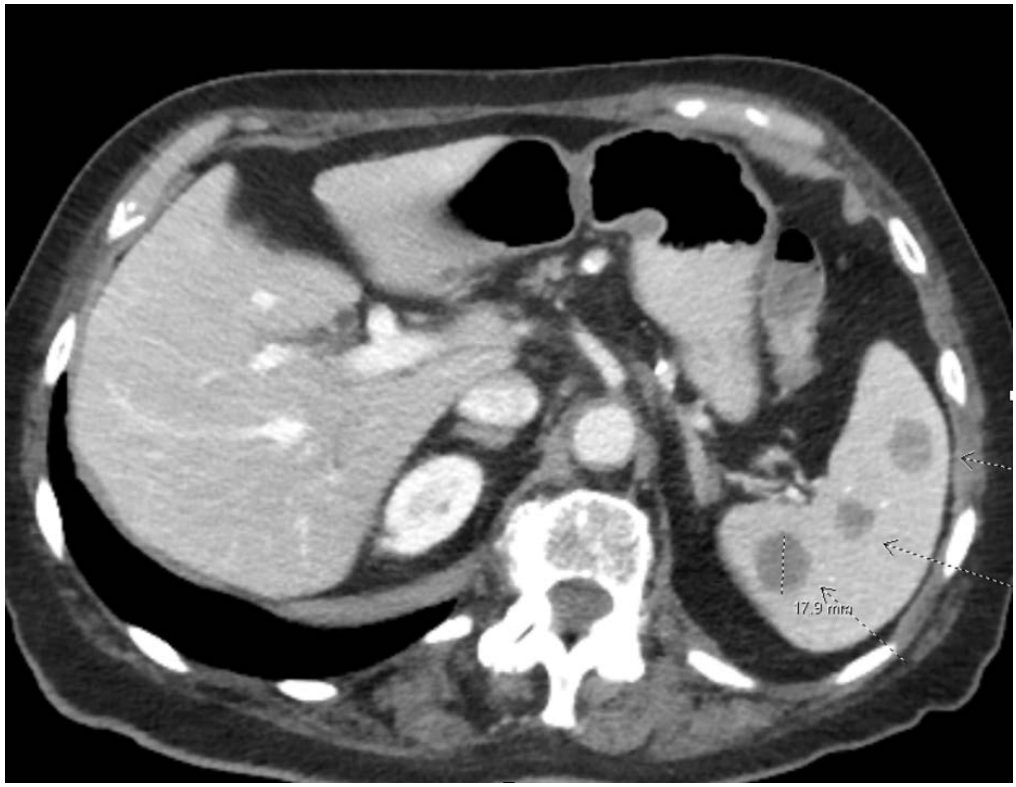

Figure 11: February 2021. CT chest abdomen pelvis with contrast. Axial view.
Multiple low-attenuation masses in the spleen. Some of these masses are slightly increased in size with representative lesion measuring 1.5 cm compared to prior measurement of 1.2 cm. Additional lesion measuring 1.8 cm, previously measured 0.6 cm. Additional lesions are not significantly changed. Tiny low-attenuation lesion in the subcapsular right hepatic lobe is stable. Rounded low-attenuation lesion in the pancreatic head is not significantly changed. Multiple low-attenuation lesions in both kidneys.

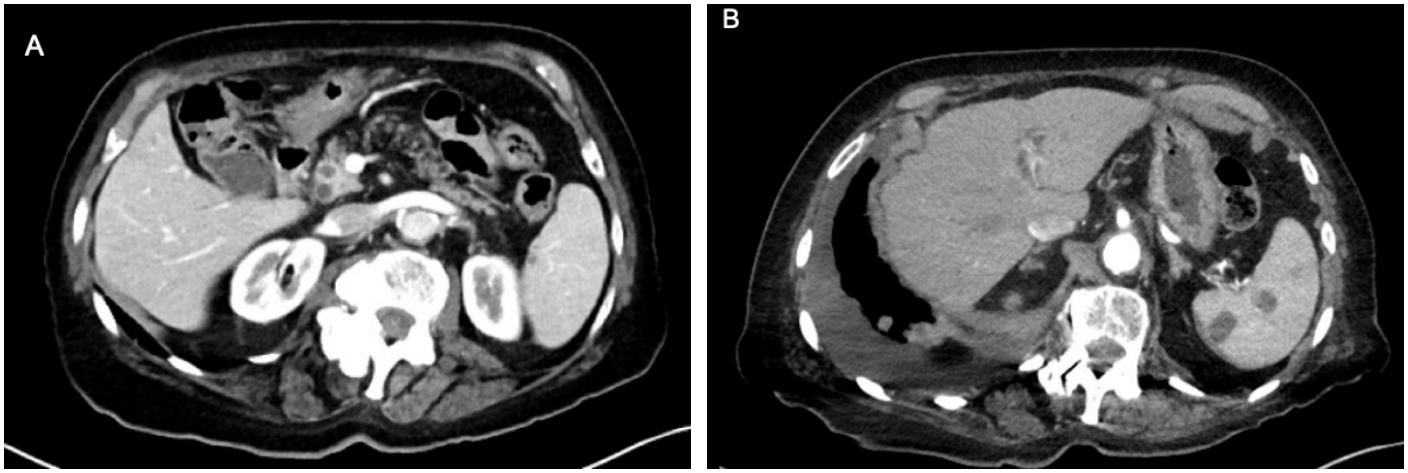

Figure 12: May 2021. CT abdomen pelvis with contrast. Axial view.
Pancreatic atrophy. A.Cystic mass in the pancreatic head measures 0.9 cm and has decreased in size since prior exam when it measured 1.3 cm. This could represent metastasis. B. Diffuse splenic metastases have progressed measuring up to 2 cm.

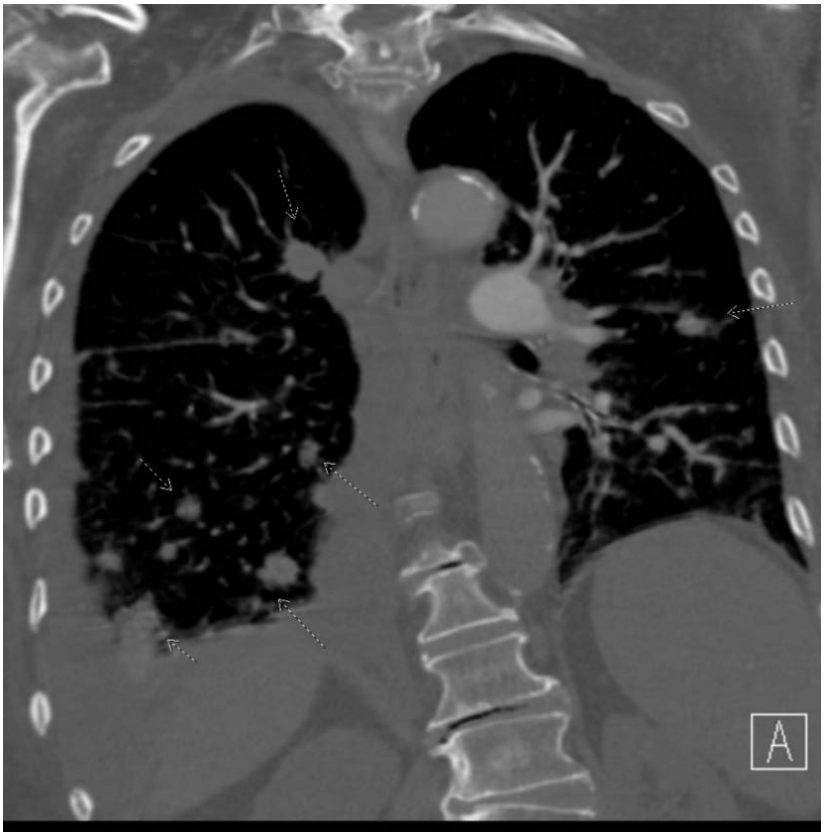

Figure 13: March 2023. CTA chest with contrast. Coronal view. Revealed worsening metastases including increased size and number of pulmonary metastases with involvement of the pleura.

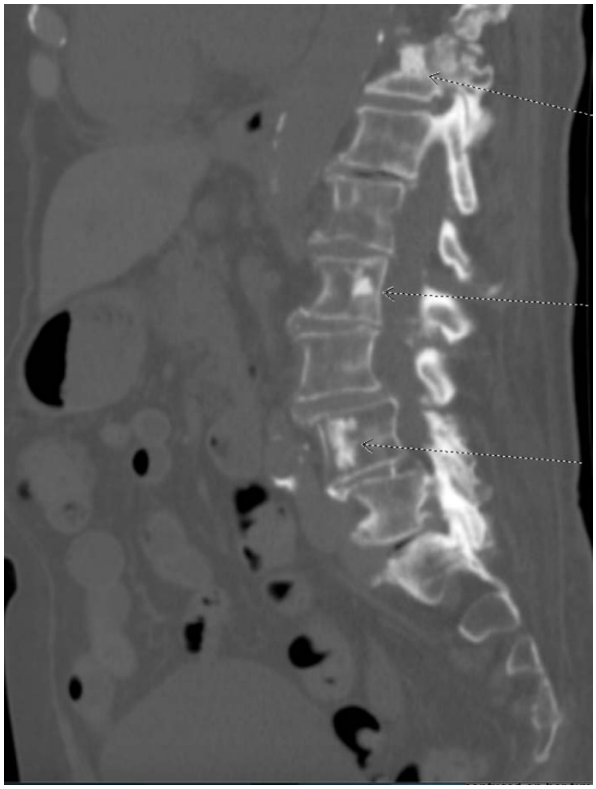

Figure 14: June 2023 CT abdomen pelvis without contrast. Sagittal view. Findings: Diffuse osseous metastatic disease. Several of the metastases are sclerotic and unchanged from prior. However, there are new and/or increased lytic metastases, for example at L1 inferior endplate with associated osseous erosion. Increased size of expansile metastasis in the lateral right sixth rib. Relatively unchanged expansile metastasis in the left inferior pubic ramus.

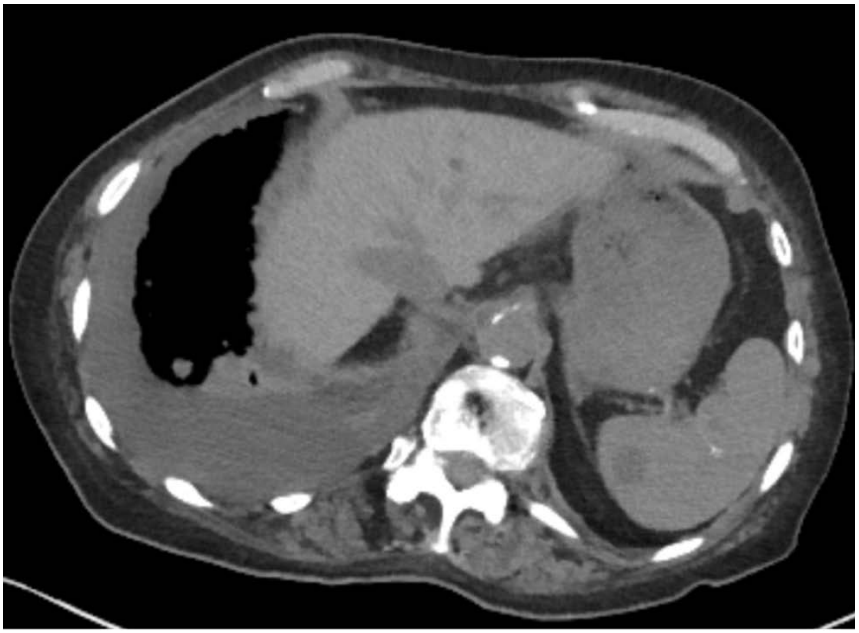

Figure 15: June 2023 CT chest. Axial view. Nodularity of the right pleura with small right pleural effusion, presumably malignant. Thoracentesis performed.

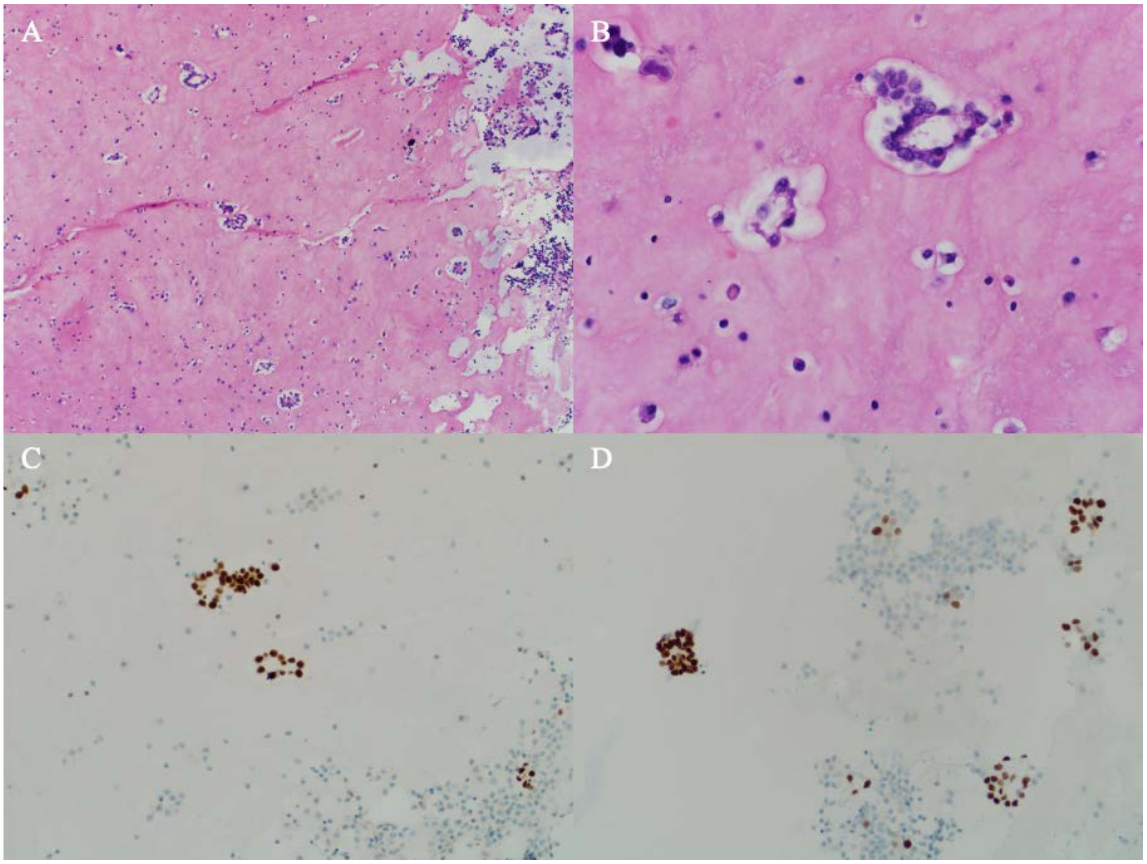

Figure 16: June 2023 Right pleural fluid histopathology and histochemical images.
A, B. Small tumor cell clusters present at low and high power in pleural fluid cell block A. 10X H and E cell block B. 40X H and E cell block
C. 20X Positive nuclear immunohistochemical staining for PAX-8
D. 20X Positive nuclear immunohistochemical staining for TTF-1

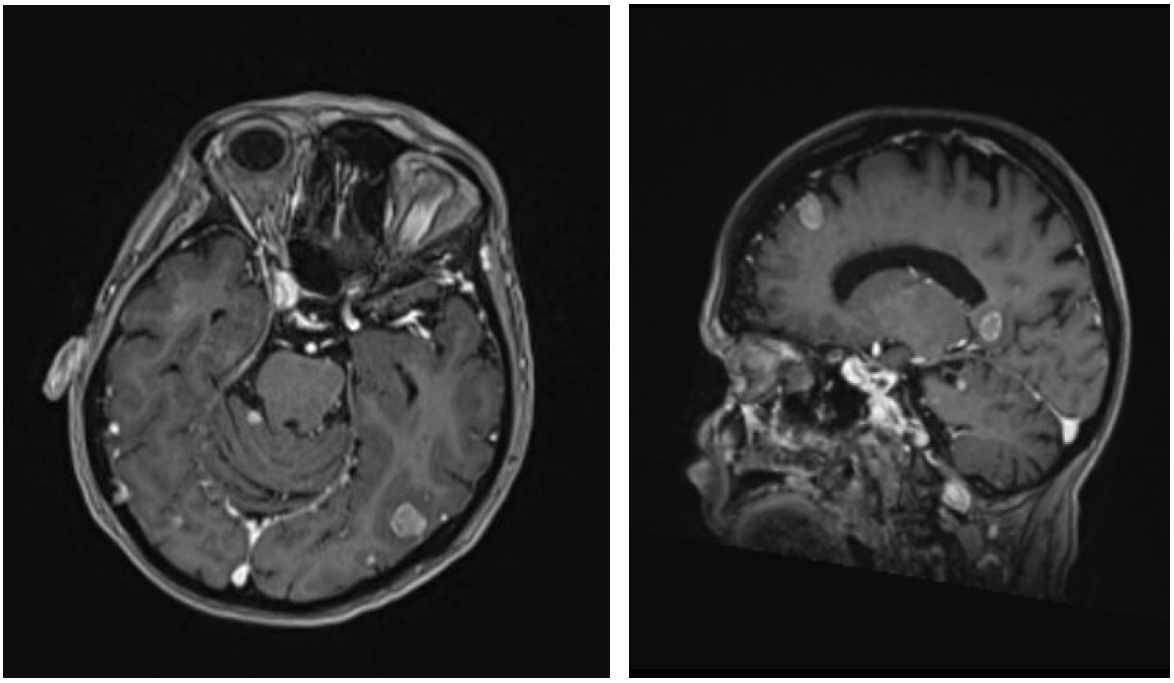

Figure 17: August 2023. MRI brain with and without contrast. Multiplanar, multisequential imaging of the brain. Multiple heterogeneously enhancing metastases throughout the bilateral cerebral and cerebellar hemispheres with associated vasogenic edema. The largest measure 1.3 cm in the left occipital lobe, 1.1 cm in the left medial cerebellar hemisphere, and 1.4 cm in the right anterior frontal lobe.

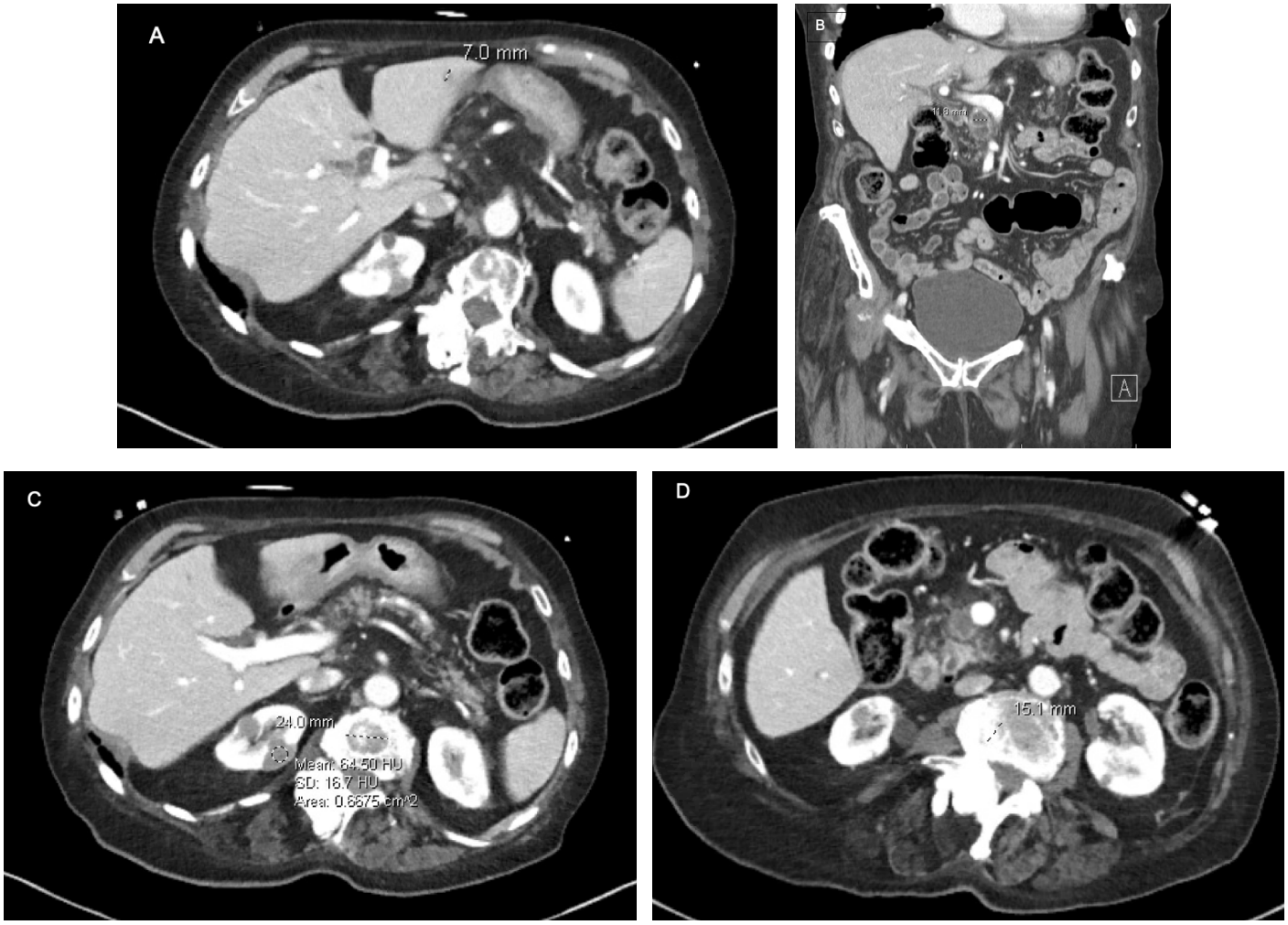

Figure 18: September 2023. CT chest abdomen pelvis with contrast. Axial and coronal views. A. New hypoenhancing hepatic lesions suspicious for metastasis. Stable presumed splenic metastatic lesions. Increasing indeterminate hypoenhancing renal lesions. Grossly unchanged metastatic sclerotic and lytic lesions of the axial and appendicular skeleton. Similar appearance of numerous metastatic pulmonary nodules.

A. Multiple hypoenhancing hepatic lesions with the largest measuring 7 mm.
B. Homogenous enhancement of the pancreas. Main pancreatic duct is enlarged measuring up to 7 mm with a bilobed cystic lesion or 2 adjacent cystic lesions in the pancreatic head measuring up to 12 and 11 mm respectively. Differential includes IPMN, metastasis, and peripancreatic fluid collection.
C. Increased L1 vertebral body lytic lesion along inferior endplate measuring 2.4 cm.
D. Stable lytic and sclerotic lesion on superior endplate of L3 measuring up to 1.5 cm.

KEYWORDS

Thyroid cancer; Papillary thyroid cancer; Cutaneous metastasis; Rare metastasis; Skin metastasis

Consent: Did the author obtain written informed consent from the patient for submission of this manuscript for publication? Yes.

Human and animal rights: IRB approval was obtained from UND and CHI St. Alexis Hospital.