

A 72-Year Old Female with Neurologic Symptoms and an Abnormal Lymph Node

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History of the Present Illness

- 72 year-old, previously healthy, Hispanic female presents with acute worsening of multiple neurologic symptoms
 - Initially presented to OSH with acute weakness, numbness, and tingling in LLE in August 2013. Given IV steroids and followed up with outpatient neurology
 - Frustrated by lack of a diagnosis, stopped follow-up up in September 2013
- February 2014 - Presented to UCMC with progressive decline in neurologic status, notable for:
 - Worsening bilateral upper and lower extremity weakness
 - Incontinence of bowel and bladder
 - 2 weeks of progressively worsening bilateral vision
 - Sensory loss of the trunk, parts of the lower extremities, and facial numbness and tingling.

History of the Present Illness

- Extensive neurologic work-up, including FDG-PET/CT scan, reveals a hypermetabolic right supraclavicular lymph node. FNA of the LN reveals metastatic papillary cancer.
- The Endocrine service is consulted for assistance in further management.

Past Medical History

- Type 2 Diabetes (8 years)-controlled on **Metformin 500 mg bid**
- Neuropathy (etiology unclear) - **Gabapentin 300 mg tid**
- Hypertension - **Lisinopril 10 mg daily**
- Dyslipidemia – **Fenofibrate 48 mg daily**
- Depression – **Celexa 20 mg daily**
- Prior history for thyroid disease or exposure to irradiation is negative

Social and Family History

- Emigrated from Mexico 7 years ago, has not returned since then
- Previously worked as a farmer
- Lives with son and grand-daughter
- Does not speak English
- Never smoker, no etoh
- Previously independent for all ADLS/IADLs, but since August, wheel-chair bound due to weakness
- No family history of thyroid disease, cancers
- One son died of etoh-related cirrhosis

Review of Systems*

Constitutional: No fevers, chills, weight loss, night sweats. **Fatigue.**

HEENT: **Intermittent headaches. Worsening bilateral vision.**

Cardiovascular: No chest pain, palpitations, syncope, or edema.

Respiratory: No shortness of breath, wheezing, cough, or hemoptysis.

Gastrointestinal: No abdominal pain, nausea, vomiting, diarrhea.

Previously constipated, now with intermittent bowel incontinence.

Decreased appetite.

Genitourinary: **New intermittent loss of urinary continence.**

Skin: New sacral ulcer. No rashes.

Musculoskeletal: **Intermittent myalgias and diffuse arthralgias.**

Neurological: **Bilateral LE weakness, numbness, tingling. Progressive weakness, numbness, tingling, sensory loss in face, trunk, and legs.**

Psychiatric: **h/o depression**

*obtained by patient's family and chart review

Physical Examination

BP 144/65 P 92 T 36 (96.8) R 15 O2 95% RA BMI 18.56

General: Patient is in **mild acute distress**, alert, oriented, but unable to answer questions.

HEENT: EOMI. Oropharynx clear. **Left pupil non-reactive to light. Pupils equal.** Conjunctivae/sclerae normal.

Neck: Supple, thyroid is difficult to examine, but appears symmetric, with no palpable nodules or thyromegaly.

Cardiovascular: Regular rate and rhythm, without murmurs or gallops.

Pulmonary: Good respiratory effort. Clear to auscultation bilaterally.

Abdomen: Abdomen is soft, non-distended, non-tender.

Musculoskeletal: Moving all extremities. BLE without edema.

Neurological: A/O x 3. **Strength 1/5 Right and Left UE; 2/5 Right and Left LE,** 2+ biceps reflex

Skin: Warm, dry, 2x2 stage 1 sacral ulcer.

Psychiatric: Cooperative, behavior appropriate.

Diagnostic Evaluation

Glucose	225
Sodium	137
Potassium	3.8
Chloride	103
CO2	24
Anion Gap	10
BUN	8
Creatinine	0.5
GFR	>120
Calcium	9.5
Albumin	3.1
Total Protein	7.0
T bili	0.3
C bili	0.1
U bili	0.2
Alk Phos	102
AST	22
ALT	16

WBC	8.1
HGB	13.1
HCT	40.4
PLT	184

TSH	2.78
Free T4	1.20
T3	288

Diagnostic Evaluation

Neurologic

MRI Brain/Spine	T2/Flair abnormalities involving brain stem, cervical/thoracic cord, conus medularis, multiple cranial nerves and possible involvement of vestibular nerve/nuclei. T2 hyperintensities at C1-2, C4-6, T3-6, T12.
CSF Analysis (x2)	Negative cultures except CSF EBV + Negative for oligoclonal bands Cytology with no malignant cells Mostly T cells c/w an inflammatory process
NMO-IgG	Negative

Hematologic

SPEP	Unremarkable
Immunoglobulins	Normal
Flow Cytometry	Negative for lymphoma

Infectious Diseases

HIV	Negative
Quantiferon Gold	Negative
Blood, CSF Cultures all negative	

Rheumatologic

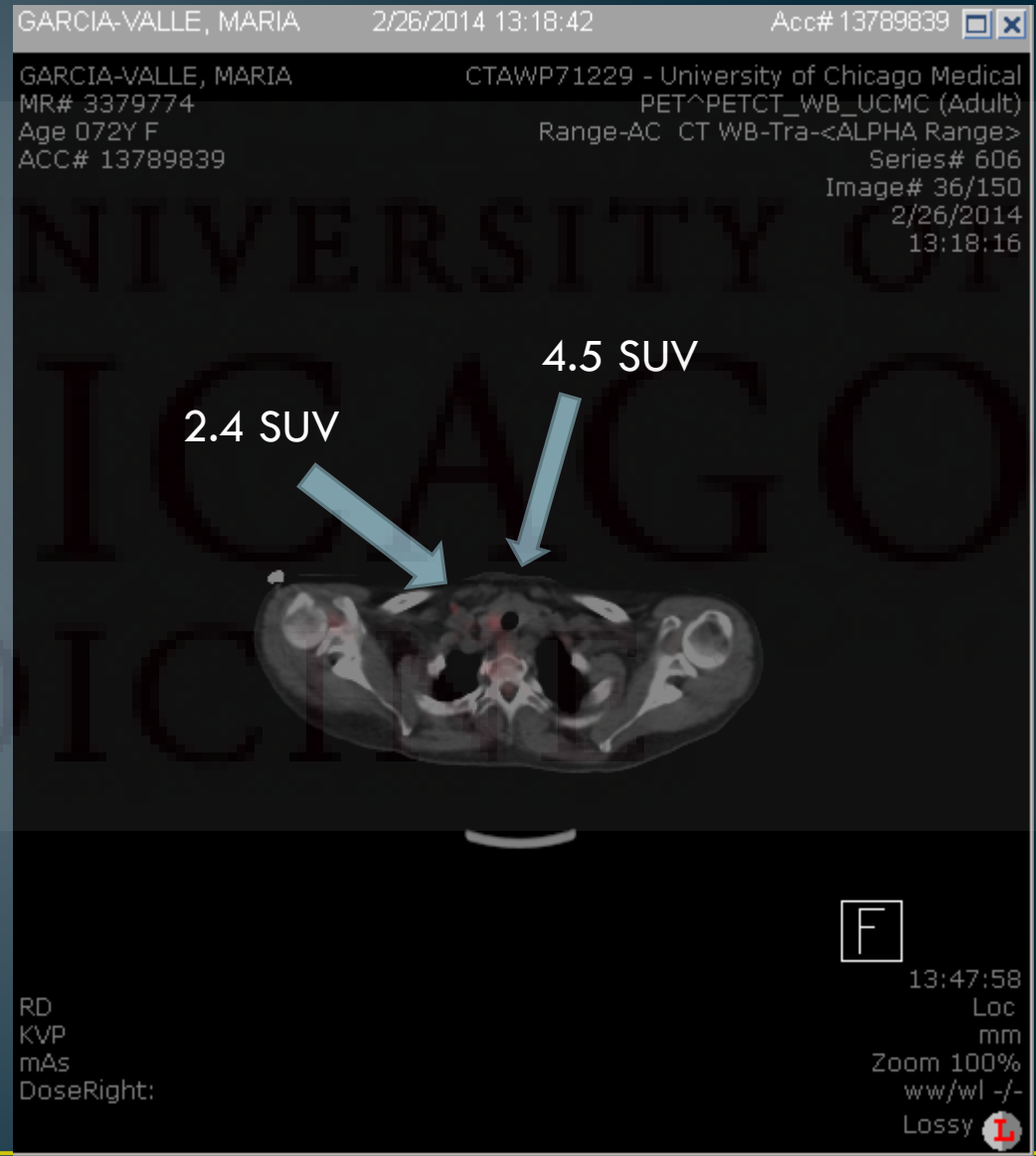
ESR	27
ANA Panel	ANA 160 (0-80) Panel otherwise negative
ACE	normal

PET Study

Multiple foci of hypermetabolic activity in the midbrain, brainstem, and spinal cord.

Right supraclavicular and multiple bilateral hilar lymph nodes demonstrating mildly hypermetabolic activity.

Increased activity in a nodule of the right lobe of the thyroid.



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CTAWP71229 - University of Chicago Medical
PET^PETCT_WB_UCMC (Adult)

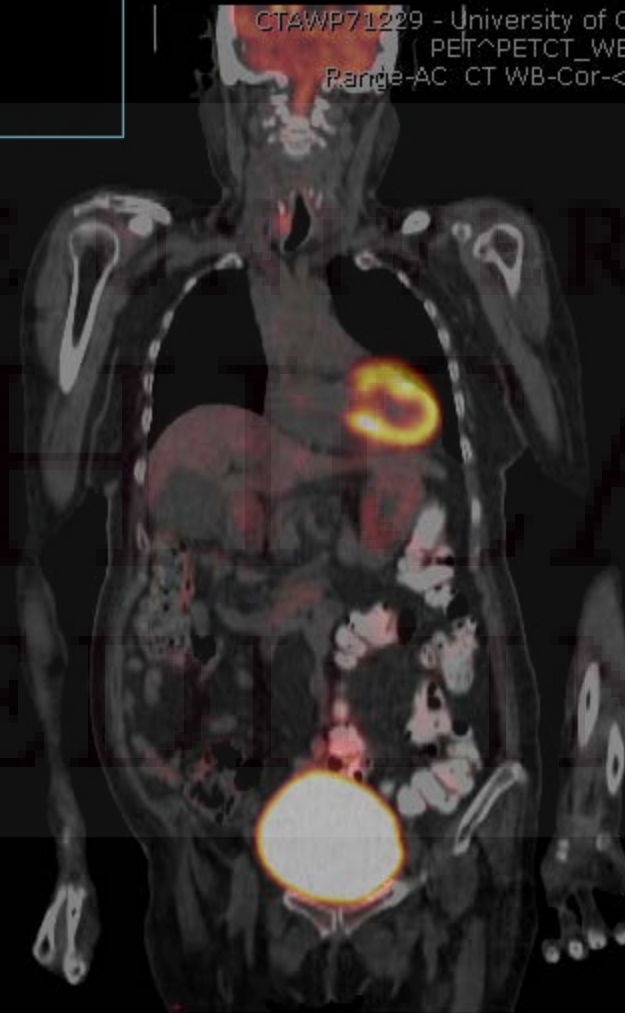
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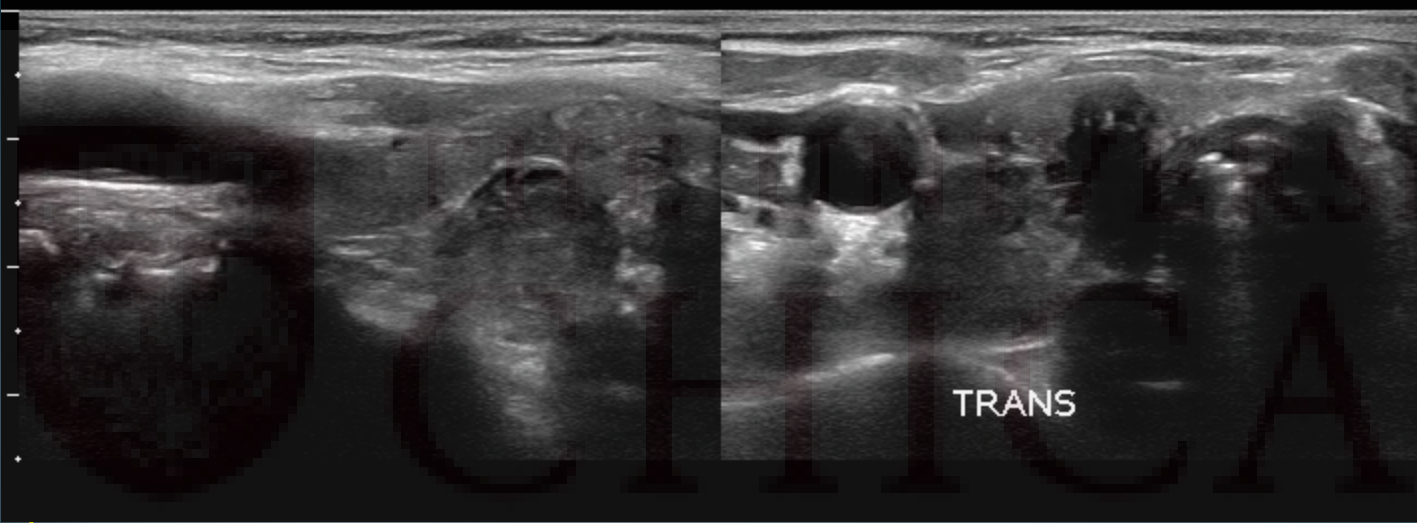
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CT PE PROTOCOL



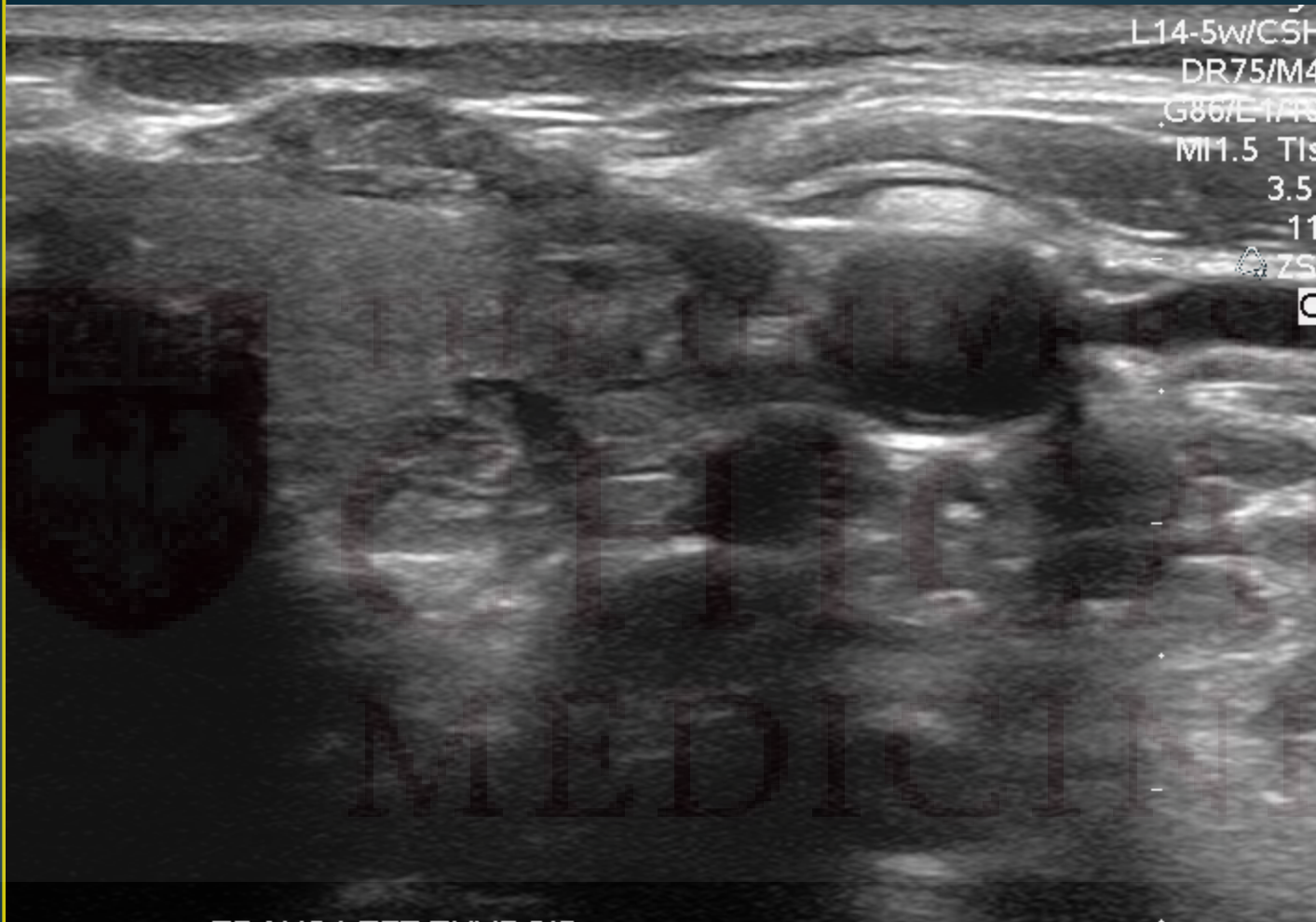
“Lobulated mass arising from the right thyroid gland partially obscured due to artifact on the current examination, proximally 1.5 x 2.5 cm in size and extending into the right of the cervical esophagus and terminally abutting in the spinal column. This was present on prior PET scan and may correlate to FDG avid lesion. The distal cervical trachea is deviated leftward by the mass.”

Thyroid Ultrasound



In the right mid pole, there is a markedly hypoechoic nodule with peripheral calcification and shadowing measures 1.6 x 1.4x 1.3 cm. Adjacent to this nodule, there is a solid nodule with peripheral calcification measuring 1.5x 1.4 x 1.5 cm.





TRANS LEFT THYROID

Image Time 15:
Zoom
www.fwl 22

In the left mid pole, there is a predominantly solid nodule with 1.0 x 0.6 x 0.8 cm. Adjacent to this nodule, there is an additional cystic nodule with colloid measuring 1.0 x 0.6 x 0.8 cm.

What are the clinical and pathologic characteristics of thyroid cancers incidentally diagnosed by PET Scans?

Are C, et al. Histological aggressiveness of fluorodeoxyglucose positron-emission tomogram (FDG-PET)-detected incidental thyroid carcinomas. *Ann Surg Oncol.* 2007;14(11):3210-15.

TABLE 2. *The histopathological features of the 22 patients*

SUV value	Patient number	Age/sex	Cell type	Size (cm)	ETE	Margins	Vascular invasion	Mitosis	Necrosis
7.2	1	67/M	PTC*	0.75	1	1	0	0	0
7	2	67/F	PTC*	1.3	0	0	1	0	0
2.9	3	58/M	PTC*	1.4	1	0	1	0	0
5.5	4	55/F	PTC*.,#@	0.38	0	0	0	0	0
2.3	5	35/F	PTC #.S	0.7	0	0	0	0	0
6.7	6	51/M	PTC #.S	0.9	0	0	0	0	0
4.2	7	71/F	FVPTC*	1.6	0	0	0	0	0
6.36	8	58/F	FVPTC*	2	1	0	0	0	0
14	9	38/2	FVPTC	4	0	0	0	0	0
NA	10	76/M	FVPTC	4.4	0	0	1	0	0
NA	11	56/F	TCVPTC	1.5	1	0	0	0	0
22.7	12	64/M	TCVPTC	1.8	1	0	0	0	0
27	13	78/M	TCVPTC	2.2	1	1	0	0	0
NA	14	61/F	TCVPTC@	1.6	1	0	0	0	0
3.2	15	28/M	TCVPTC	0.7	0	0	0	0	0
3.1	16	63/F	TCVPTC	0.6	1	1	0	0	0
4.5	17	53/M	TCVPTC	1.6	1	0	0	0	0
3.8	18	51/M	TCVPTC	1.1	1	0	0	0	0
3.4	19	67/F	TCVPTC	1.3	1	0	0	0	0
4.6	20	36/F	TCVPTC	0.85	1	1	0	0	0
5	21	55/F	TCVPTC	1.5	1	0	0	0	0
6.7	22	70/F	PDTC*	12	1	0	1	0	1

PTC: papillary thyroid carcinoma

FVPTC: follicular variant of papillary thyroid carcinoma

TCVPTC: tall-cell variant of papillary thyroid carcinoma

PDTC: poorly differentiated thyroid carcinoma

ETE: extra thyroidal extension

* with oncocytic features

microscopic

@ with Hashimoto's disease

S focal tall-cell features

Law TT, Lang BHH. Incidental thyroid carcinoma by FDG-PET/CT: A Study of clinicopathological characteristics. *Ann Surg Onc.* 2011;18:472-78.

TABLE 1 comparison of demographic data, history, and type of nonthyroidal malignancy as well as indication for imaging between the PET and USG groups

Variable	PET group (<i>n</i> = 22)	USG group (<i>n</i> = 11)	<i>P</i> -value
Age at diagnosis (years, range)	60 (37–79)	39 (23–83)	0.014
Gender (female:male)	16:06	8:03	0.653
History of nonthyroidal malignancy (%)	20 (90.9)	2 (18.2)	<0.001
Type of nonthyroidal malignancy (%)			0.298
Gastrointestinal malignancy	8 (36.4)	2 (18.2)	
Breast malignancy	6 (27.3)	0	
Gynecological malignancy	2 (9.1)	0	
Lung malignancy	1 (4.5)	0	
Hematological malignancy	2 (9.1)	0	
Indication for imaging (%)			<0.001
Evaluation for malignancy	20 (90.9)	2 (18.2)	
Evaluation for a medical condition	1 (4.5)	5 (45.5)	
Health check	1 (4.5)	4 (36.4)	

Bold values indicate *P* < 0.05

TABLE 2 Comparison of FDG-PET, ultrasonographic, FNA cytology (FNAC) findings, and treatment strategy between the PET and USG groups

Variable	PET group (<i>n</i> = 22)	USG group (<i>n</i> = 11)	<i>P</i> -value
Ultrasonographic findings			
Median size (mm) (range)	13.5 (5–28)	10 (5–15)	0.286
Suspicious features ^a (%)	13 (61.9)	7 (63.6)	0.784
FNAC of thyroid nodule (%)			
Benign	0 (0.0)	0 (0.0)	0.606
Inadequate for diagnosis	3 (13.6)	2 (18.2)	
Indeterminate	14 (63.6)	8 (72.7)	
Malignancy	5 (22.7)	1 (9.1)	
Type and extent of resection (%)			
Total thyroidectomy	20 (90.9)	10 (90.9)	1
Hemithyroidectomy	2 (9.1)	1 (9.1)	
Concomitant neck dissection (%)			
Central neck or level VI	9 (40.9)	0 (0.0)	0.062
Ipsilateral lateral neck	3 (13.6)	2 (18.2)	
Contralateral lateral neck	0 (0.0)	0 (0.0)	
Bilateral neck	1 (4.5)	0 (0.0)	
Radioiodine ablation (%)	15 (68.2)	5 (45.5)	0.223

^a Including taller-than-wide, macro- or microcalcifications, irregular margins, and marked hypoechogenicity

Law TT, Lang BHH. Incidental thyroid carcinoma by FDG-PET/CT: A Study of clinicopathological characteristics. *Ann Surg Onc.* 2011;18:472-78.

TABLE 3 Comparison of histological findings between the PET and USG groups

Histological finding	PET group (n = 22)	USG group (n = 11)	P-value
Histological type (%)			0.687
Papillary carcinoma	20 (90.9)	10 (90.9)	
Follicular carcinoma	1 (4.5)	1 (9.1)	
Undifferentiated carcinoma	0 (0.0)	0 (0.0)	
Hürthle cell carcinoma	1 (4.5)	0 (0.0)	
Median tumor size (mm) (range)			
Primary tumor	13 (3–30)	10 (1–18)	0.264
Contralateral lobe ^a	4 (1–10)	Not applicable	–
Tumor multifocality (%)	10 (45.5)	2 (18.2)	0.125
Tumor bilaterality ^a (%)	9 (45.0)	0 (0.0)	0.04
Extrathyroidal extension (%)	8 (36.4)	4 (36.4)	0.653
Capsular invasion (%)	8 (36.4)	2 (18.2)	0.284
Lymph node metastases (%)	7 (31.8)	2 (18.2)	0.407
Associated thyroiditis (%)	5 (22.7)	2 (18.2)	0.813
TNM tumor staging ^b (%)			0.021
I	5 (22.7)	8 (72.7)	
II	6 (27.3)	1 (9.1)	
III	11 (50.0)	2 (18.2)	
IV	0 (0.0)	0 (0.0)	

^a Only those who underwent total thyroidectomy were included

^b *AJCC Cancer Staging Manual*³⁸

Bold values indicate $P < 0.05$

Clinical Implications & Outcomes

- 2009 ATA guidelines on differentiated thyroid cancer cite additional pertinent studies:
 - “Patients with increasing volumes of 18-fluorodeoxyglucose (FDG)-avid disease seen on positron-emission tomography scans were less likely to respond to radioiodine and more likely to die during a 3-year follow-up compared with FDG-negative patients.”
 - “A study that retrospectively examined the clinical course of 400 thyroid cancer patients with distant metastases who had undergone 18FDG-PET... found [that] tumors that did not concentrate 18FDG had a significantly better prognosis after a median follow-up of about 8 years than did tumors that avidly concentrated 18FDG.”
 - “Radioiodine therapy of metastatic lesions that were positive on FDG-PET scanning was of no benefit.”

Wang W, et al. Prognostic value of [18F]fluorodeoxyglucose positron emission tomographic scanning in patients with thyroid cancer. *J Clin Endocrinol Metab.* 2000;85:1107–13.

Hooft L, et al. . Diagnostic accuracy of 18F- fluorodeoxyglucose positron emission tomography in the follow-up of papillary or follicular thyroid cancer. *J Clin Endocrinol Metab.* 2001;86:3779–86.

More on our patient...

TSH	2.78
Free T4	1.20
T3	288

Anti-TPO	<0.4
Anti-TG	<0.4

Thyroglobulin	24 ng/mL (Ref <29)

Urine Iodine	21889 (Ref 26-705 mcg/L)

Endocrine Surgery Consulted

“Definitive treatment for her papillary thyroid cancer would be total thyroidectomy with lymph node dissection. Based upon the CNS imaging and biopsy, it does not appear that the lesions in the CNS are metastatic thyroid cancer, thus treating her thyroid cancer at this time will not improve her neurologic status. If neurologic status stabilizes, I would then recommend total thyroidectomy with LN dissection followed by RAI when her urinary iodine levels are back to normal.”

Paraneoplastic Syndromes

- Our patient had unexplained neurological symptoms with no evidence of CNS metastases by CSF analysis or stereotactic brain biopsy of one of the lesions. Could her presentation represent a paraneoplastic syndrome?
- Are there paraneoplastic syndromes associated with thyroid cancer? Pub Med review shows rare case reports of various PN syndromes associated with papillary thyroid cancers:
 - Systemic lupus erythematosus (2013)
 - Adult-onset Still's disease (2012)
 - Acanthosis nigricans (2010)
 - SIADH (2010)
 - Polymyositis (2008)
 - Myoclonus (2007)

Study conclusion – use of PET-CT increased diagnostic yield for cancer by 18% in patients with suspected paraneoplastic neurologic disorders (for whom other standard oncologic evaluation was negative).

AChR Ganglionic Ab (High):

0.14

Reference range: ≤ 0.02

Unit: nmol/L

Test Performed or Referred by: Mayo Clinic Dept of Lab Med and Pathology, 200
First Street SW, Rochester, MN 55905

AntiGlial Nuc Ab Type 1:

Negative

Reference range: $< 1:240$

Unit: titer

Test Performed or Referred by: Mayo Clinic Dept of Lab Med and Pathology, 200
First Street SW, Rochester, MN 55905

Volt Gated K Chan Ab (High):

0.08

Reference range: ≤ 0.02

Unit: nmol/L

Test Performed or Referred by: Mayo Clinic Dept of Lab Med and Pathology, 200
First Street SW, Rochester, MN 55905

Interpretive Comments:

The following antibodies were identified: Neuronal AChR, Ganglionic (Alpha-3) and Neuronal (V-G) Potassium Channel.

* This profile is consistent with organ-specific neurological autoimmunity, and may be associated with multifocal neurological manifestations, including peripheral neuropathies, encephalopathies and limited forms of dysautonomia such as gastrointestinal dysmotility or orthostatic intolerance. A paraneoplastic basis should be considered. Investigation for neoplasia is warranted,

Acetylcholine-Receptor AB

Table 2. Neurological Associations in 155 α 3-AChR Ab-Seropositive Patients by Titer

Neurological Manifestation	No. (%)			
	Total	High (n=12 [8%])	Medium (n=85 [55%])	Low (n=58 [37%])
Peripheral nerve, autonomic	33 (21)	10 (84) ^a	17 (20) ^b	6 (18)
Limited dysautonomia	20	3	14	3
GI dysmotility	10 ^c	1	8	1
Orthostatism	5	1	3	1
Anhidrosis	3	1	1	1
Sicca syndrome	2	0	2	0
Pandysautonomia	13	7	3	3
Peripheral nerve, somatic	44 (28)	0	31 (36)	13 (37)
Sensorimotor polyneuropathy ^d	28	0	22	6
Small fiber sensory neuropathy	7	0	5	2
Polyradiculopathy	4	0	2	2
Cranial neuropathy	3	0	1	2
Sensory ganglionopathy	1	0	0	1
Multifocal motor neuropathy	1	0	1	0
Neuromuscular junction	4 (3)	0	1 (1)	3 (9)
Myasthenia gravis ^e	4 (3)	0	1	3
Central	26 (17)	1 (8)	20 (24)	5 (15)
Cortical and/or neuropsychiatric	15	1	11	3
Movement disorder ^f	5	0	5	0
Demyelinating CNS disorders	5	0	3	2
Stiff-man syndrome	1	0	1	0
Nonautoimmune disorder or none ^h	48 (31)	1 (8)	16 (19)	31 (54)

Table 1. Cancer Associations in 78 α 3-AChR Ab-Seropositive Patients Who Underwent Oncological Evaluation by Titer^a

	No. (%)			
	Total	High	Medium	Low
Patients	78	9	49	20
Cancers	30	2	20	8
Cancer type				
Adenocarcinoma	13 (43)	1	11	1
Breast	4	0	4 ^b	0
Prostate	3	0	2	1
Lung	2	1	1	0
GI tract	2	0	2 ^b	0
Thyroid, papillary	1	0	1	0
Renal cell carcinoma	2 (6)	0	1	1
Lymphoid	5 (17)	1	3	1
B cell lymphoma	3	0	2	1 ^c
CLL	1	1	0	0
Myeloma	1	0	1	0
Other	10 (34)	0	5	5
Melanoma	2	0	0	2 ^b
Bladder carcinoma	2	0	1	1
Small cell carcinoma, lung	1	0	0	1 ^{c,d}
Lung carcinoma ^d	1	0	1	0
Thymoma	1	0	1 ^b	0
Thyroid carcinoma ^e	1	0	0	1
Squamous	1	0	1	0
Ovarian carcinoma	1	0	1	0

Voltage-Gated K Channel Antibody

Table 2 Neurologic manifestations in 72 patients

Manifestation/level involved	No.	(%)
Cerebral cortex	54	(75)
Cognitive impairment	51	(71)
Seizures	42	(58)
Hallucinations	7	(10)
Frontosubcortical features	9	(13)
Depression/anxiety/agitation	9	(13)
Hypothalamic	27	(38)
Hyponatremia	26	(36)
Hyperphagia	5	(7)
Dyssomnia	19	(26)
Hypersomnia	9	(13)
Insomnia	10	(14)
Extrapyramidal*	15	(21)
Tremor	5	(7)
Parkinsonism*	8	(11)
Chorea	3	(4)
Cranial nerve/brainstem*	14	(19)
Cerebellum	6	(8)
Spinal cord	1	(1)
Myoclonus	21	(29)
Stiff-man phenomena	2	(3)

Autonomic*	24	(33)
Gastrointestinal*	12	(17)
Genitourinary*	8	(11)
Hyperhidrosis	7	(10)
Piloerection	3	(4)
Blood pressure	5	(7)
Cardiac arrhythmia	5	(7)
Somatic peripheral nerve	18	(25)
Hyperexcitability	12	(17)
Neuropathy	10	(14)
Morvan syndrome	2	(3)
Headache*	4	(6)
Gait disorder not otherwise specified	5	(7)

Occult Multifocal Papillary Thyroid Microcarcinoma Presenting as a Supraclavicular Mass Containing Anaplastic Thyroid Carcinoma

Michael Deutschmann, MD; Moosa Khalil, MBBCh, FRCPC; Shelly Bhayana, MD, MSc, FRCPC; Shamir Chandarana, MD, MSc, FRCSC

Importance: There are reports in the literature of anaplastic thyroid carcinoma in cervical lymph nodes with evidence of only papillary carcinoma in the thyroid gland. There have been no cases of this clinical scenario with only papillary microcarcinoma in the thyroid gland.

Observations: We describe the case of a 60-year-old man who initially presented with an enlarged right, level 5, supraclavicular lymph node. Initial fine-needle aspiration demonstrated evidence of papillary thyroid carcinoma. The final pathologic finding in the thyroid gland

showed only multiple foci of papillary thyroid microcarcinoma. The index neck mass showed evidence of anaplastic thyroid carcinoma.

Conclusions and Relevance: This is the first instance in the literature in which anaplastic thyroid carcinoma has appeared in metastatic cervical lymph nodes with only a focus of papillary microcarcinoma in the thyroid gland. With this case, we hope to build awareness of this rare finding.

JAMA Otolaryngol Head Neck Surg. 2013;139(4):415-418

Patient discharged home on 3/18 under home hospice care. Returns for Endocrine follow-up next week.

Conclusions

- Thyroid incidentalomas are identified in a small, but clinically significant percentage of FDG-PET studies.
- Those that are identified through this modality are more likely to be aggressive and less likely to be iodine avid.
- FDG-PET is useful in detecting recurrent and metastatic disease
 - Patients with elevated thyroglobulin but negative I-131 scan
- BUT, along with CT and MRI, FDG-PET is NOT:
 - Recommended for routine pre-operative use (Recommendation E)
- Although rare, papillary thyroid carcinomas may be associated with paraneoplastic syndromes and antibodies.

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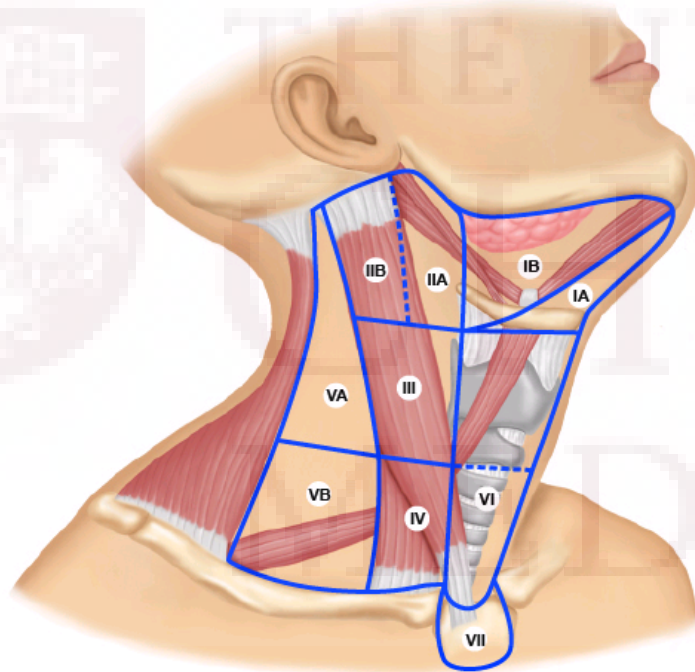
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Clinical Question:

Lymph node levels of the neck



Level I, submental (IA) and submandibular (IB); level II, upper internal jugular nodes; level III, middle jugular nodes; level IV, low jugular nodes; level V, posterior triangle nodes; level VI, central compartment; level VII, superior mediastinal nodes.

Adapted from: American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the AJCC Cancer Staging Manual, Seventh Edition (2010) published by Springer New York, Inc.