Thyroid Hemiagenesis associated with Oncocytic Type Follicular Adenoma with KRAS mutation - A Case Report

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Introduction

Thyroid hemiagenesis is a rare congenital disorder characterized by an absence of one thyroid lobe. It is found more frequently in females. Left thyroid hemiagenesis is more common. It is usually incidentally diagnosed during imaging of the neck region. Ultrasonography can visualize lobe absence and the presence or absence of an isthmus and often demonstrates underlying pathology of the gland. The appearance of thyroid hemiagenesis with an associated isthmus has been described as having the appearance of a hockey stick ("hockey stick" abnormality)[1]. The prevalence of this condition is reported to vary from 0.05% to 0.5%, although the true frequency is uncertain[2-5]. Most of the reported thyroid hemiagenesis cases have been sporadic, but familial clustering has also been reported [6]. Structural and functional thyroid disorders are documented in thyroid hemiagenesis. We report a case of follicular adenoma of Oncocytic type with associated KRAS mutation in a patient with thyroid hemiagenesis.

Case Presentation

A 59-year-old female with past medical history of hyperlipidemia, asthma and seasonal allergies was evaluated for chronic hoarseness of voice which was present for 10 years. She underwent laryngoscopy and was noted to have asymmetry of vocal wave and right vocal cord stiffness. She was planned to undergo transnasal vocal fold augmentation, and preoperative CT scan of the head and neck showed a large multinodular right thyroid lobe with a dominant nodule of approximately 1.5 cm. The patient had a subsequent thyroid ultrasound which showed an absent left thyroid lobe and a multinodular remaining right lobe with a solid, isoechoic dominant nodule of 1.7 x 1.2 x 1 cm. Fine needle aspiration cytology showed Atypia of Undetermined Significance (AUS) with some Hurthle cells with uniform to variable, small to enlarged nuclei, small to inconspicuous nucleoli and scant to abundant granular cytoplasm dispersed singly, as strips, monolayered sheets, clusters and micro follicles. Molecular testing with Thyroseq V3 indicated a 50 - 60% probability of cancer or NIFTP with KRAS mutation (15% variant allele frequency). Patient was referred to endocrine surgery and underwent total thyroidectomy. Surgical pathology showed follicular adenoma, oncocytic type without malignancy.

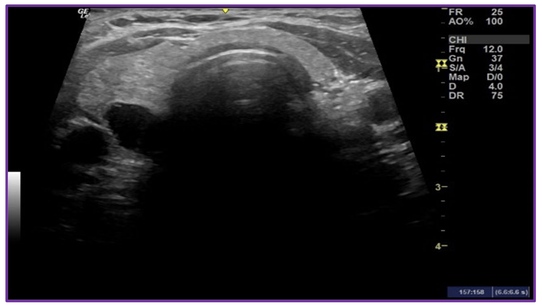

Fig 1. Ultrasound image of left thyroid hemiagenesis

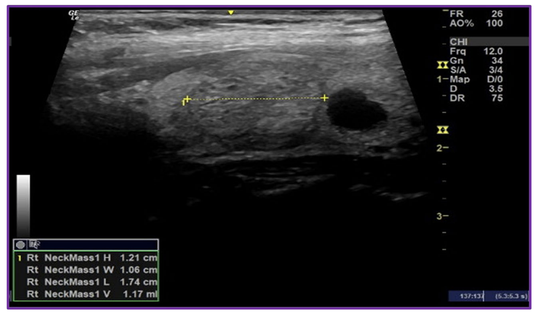

Fig 2. Ultrasound image of right isoechoic dominant nodule

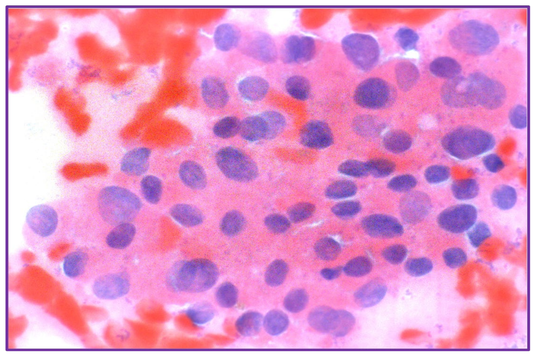

Fig 3 . Hurthle cell nodule showing a sheet of Hurthle cells with enlarged and irregular nuclei with granular eosinophilic cytoplasm (Papaniolaou (Pap) stain. direct smear x40

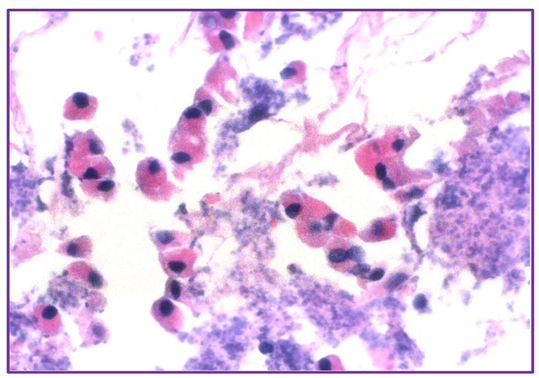

Fig 4. Hurthle cell nodule showing single and strips of Hurthle cells with eccentrically-placed nuclei and granular eosinophilic cytoplasm - Hematoxylin and eosin (H&E) stain. Cell block x40

Discussion

Thyroid hemiagenesis is a developmental disorder of the thyroid characterized by the absence of one thyroid lobes. It is often associated with functional and morphological abnormalities of the thyroid gland including autoimmune thyroid disease or thyroiditis, multinodular goiter, differentiated thyroid cancer, and/or other developmental disorders including thyroglossal duct cyst, ectopic thyroid [6]. The diagnosis is usually in the form of incidental finding of absent thyroid lobe on neck imaging. Thyroid ultrasonography is the preferred diagnostic tool due to it being cost effective, easily accessible, and without radiation exposure. Thyroid uptake scan, Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) can also be used to diagnose thyroid hemiagenesis, but they are seldom used as the first modality for diagnosis. Hemiagenesis can be associated with multinodular goiter. Our case had a solid, isoechoic dominant nodule in the right lobe which showed Atypia of Undetermined Significance - Bethesda category III with Hurthle cell predominance. The use of molecular testing is beneficial in proper diagnosis and risk stratification of thyroid nodule with indeterminate FNA cytology. The primary benefit of a negative molecular test result is the reduction in diagnostic thyroid surgeries for benign nodules. In a recent retrospective analysis of consecutive FNA samples from primary thyroid nodules clinically tested by ThyroSeq V3 from Winter 2018 to Spring 2021 was performed following the approved University of Pittsburgh Institutional Review Board protocol, out of 40622 samples of AUS/FLUS - Bethesda category III cytology nodules, 71% had a benign (negative) call rate after molecular testing [7]. Our patient had a 50-60% probability of cancer or NIFTP with KRAS mutation on ThyroSeq V3 gene testing and decided to undergo total thyroidectomy. The surgical pathology however showed follicular adenoma, oncocytic type without malignancy. In a study of 204 thyroid fine-needle aspiration cases positive for RAS mutations with corresponding surgical pathology resection specimens, KRAS12/13 mutation was associated with a significantly lower carcinoma outcome (41.7%) when compared with HRAS61 (95.5%) and NRAS61 (86.8%) mutations [8]. Further studies need to be done to risk stratify and determine the value of conservative management of indeterminate thyroid nodules with KRAS mutations.

References

1. Melnick JC, Stemkowski PE. Thyroid hemiagenesis (hockey stick sign): a review of the world literature and a report of four cases. J Clin Endocrinol Metab. 1981;52(2):247–251.

2. Maiorana R, Carta A, Floriddia G, Leonardi D, Buscema M, Sava L, Calaciura F, Vigneri R. Thyroid hemiagenesis: prevalence in normal children and effect on thyroid function. J Clin Endocrinol Metab. 2003;88(4):1534–1536.

3. Korpal-Szczyrska M, Kosiak W, Swieton D. Prevalence of thyroid hemiagenesis in an asymptomatic schoolchildren population. Thyroid. 2008;18(6):637–639.

4. Shabana W, Delange F, Freson M, Osteaux M, De Schepper J. Prevalence of thyroid hemiagenesis: ultrasound screening in normal children. Eur J Pediatr. 2000;159(6):456–458.

5. Gursoy A, Anil C, Unal AD, Demirer AN, Tutuncu NB, Erdogan MF. Clinical and epidemiological characteristics of thyroid hemiagenesis: ultrasound screening in patients with thyroid disease and normal population. Endocrine. 2008;33(3):338–341.

6. Ewelina Szczepanek-Parulska, Ariadna Zybek-Kocik, Leonard Wartofsky, Marek Ruchala, Thyroid Hemiagenesis: Incidence, Clinical Significance, and Genetic Background, The Journal of Clinical Endocrinology & Metabolism, Volume 102, Issue 9, 1 September 2017, Pages 3124–3137, https://doi.org/10.1210/jc.2017-00784

7. Simon Chiosea, Steven P Hodak, Linwah Yip, Devaprabu Abraham, Chelsey Baldwin, Zubair Baloch, Seza A Gulec, Zeina C Hannoush, Bryan R Haugen, Lija Joseph, Atil Y Kargi, Elham Khanafshar, Masha J Livhits, Bryan McIver, Kepal Patel, Snehal G Patel, Gregory W Randolph, Ashok R Shaha, Jyotirmay Sharma, Nikolaos Stathatos, Annemieke van Zante, Sally E Carty, Yuri E Nikiforov, Marina N Nikiforova, Molecular Profiling of 50 734 Bethesda III-VI Thyroid Nodules by ThyroSeq v3: Implications for Personalized Management, The Journal of Clinical Endocrinology & Metabolism, Volume 108, Issue 11, November 2023, Pages 2999–3008, https://doi.org/10.1210/clinem/dgad220

8. Radkay LA, Chiosea SI, Seethala RR, Hodak SP, LeBeau SO, Yip L, McCoy KL, Carty SE, Schoedel KE, Nikiforova MN, Nikiforov YE, Ohori NP. Thyroid nodules with KRAS mutations are different from nodules with NRAS and HRAS mutations with regard to cytopathologic and histopathologic outcome characteristics. Cancer Cytopathol. 2014 Dec;122(12):873-82. doi: 10.1002/cncy.21474. Epub 2014 Aug 12. PMID: 25132659.

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