Quiz Case

Cytologic evaluation of solitary thyroid nodule in a child

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CLINICAL HISTORY

A 8-year-old boy with right sided thyroid lesion (1.5 × 1.5 cm firm, mobile, non-tender which moved with swallowing) since 1 year in addition to 1 × 0.5 cm lesion. Computed tomography scan lesion was heterogeneously enhancing with a few enlarged lymph nodes. Fine-needle aspiration (FNA) showed findings seen in Figure 1.

QUESTION

What is your interpretation?

a. Adenomatous nodule with oncocytic features
b. Hurthle cell neoplasm
c. Papillary thyroid carcinoma
d. Medullary thyroid carcinoma.

Figure 1: a through e: Aspirates revealed dispersed cells with finely granular cytoplasm showing some pink granules in MGG stained smears and with eccentric nuclei, inconspicuous nucleoli, and few binucleate and multinucleated cells (arrow) with loose aggregates showing nuclear pleomorphism. (a: MGG×200, b: PAP×400, c: MGG×400, d: MGG×400, e: PAP×400), with intranuclear cytoplasmic pseudo-inclusions (arrow in ‘c’). f and g: The H and E stained smear (×100) showed homogenous, eosinophilic material which demonstrated yellowish to apple green birefringence under polarizing microscopy. h and i: The cells were immunoreactive for calcitonin (h) and chromogranin (i).
Answer

The correct cytological interpretation is
d. Medullary thyroid carcinoma (MTC).

EXPLANATION

Cytology smears were cellular, comprising predominantly of
dispersed cells and few loose cellular aggregates [Figure 1a].
Cells were oval to polygonal in shape and showed
pleomorphism, with presence of anisokaryosis and some
binucleate to rare multinucleate cells [Figures 1d and e].
Nuclei were round and placed eccentrically and the simultaneous
presence of moderately abundant, and fairly dense cytoplasm
with well-defined borders imparted a distinct plasmacytoid
aspect [Figures 1b-e]. Intranuclear cytoplasmic inclusions
were also noted [Figure 1c]. Nucleoli were inconspicuous.
Few of the cells showed pink cytoplasmic granules
[Figure 1d]. These appearances were fairly characteristic of
MTC. Additional confirmation was forthcoming by way of
few dense amorphous clumps of eosinophilic material
evident on hematoxylin and eosin staining [Figure 1f], which
was verified to be amyloid by virtue of yellow birefringence
under the polarizing microscope subsequent to Congo red
staining [Figure 1g]. Finally, intense cytoplasmic positivity
for calcitonin [Figure 1h] and chromogranin [Figure 1i] was
demonstrable on immunocytochemistry.

ADDITIONAL QUESTIONS

1. Regarding MTC which of the following features is not true -
   a. It can occur in sporadic or hereditary forms
   b. In hereditary form, pattern of inheritance is
      autosomal dominant
   c. It is generally unilateral
   d. Lymph node metastasis may be seen at the time of
diagnosis.

2. Which of the following statements is true regarding MTC -
   a. It is a tumor of parafollicular C-cells
   b. It secretes calcitonin
   c. Amyloid is found in 80–85% of cases
   d. All of the above.

3. Which of the following is/are cytological feature of MTC?
   a. Dispersed cellular aspirate with anisocytosis
   b. Eccentric nuclei with binucleate and multinucleate
      forms
   c. Cytoplasmic granularity
   d. All of the above.

4. Which of the following immunocytochemical stains
   yield negative results in MTC-
   a. Thyroglobulin
   b. Calcitonin
   c. Chromogranin
   d. Synaptophysin.

Figure 2: A 8-year-old boy presenting with the right sided thyroid
swelling and a separate swelling in the neck (arrows).
BRIEF REVIEW OF THE TOPIC

Thyroid swellings are uncommon in the pediatric age group and the reported incidence, in the age group of 8–18 years, is estimated to be 0.05–1.8%, whereas, in adults, the reported incidence ranges between 3.2% and 8%. Most thyroid nodules developing in childhood are benign and are examples of either follicular adenoma or nodular hyperplasia. However, the proportion of carcinomas is much higher (5–50%) than that seen in adults (5–15%), to the point of surpassing the benign processes in some series. Papillary thyroid carcinoma accounts for 90% of all pediatric thyroid cancers followed by medullary carcinoma (about 5%) and Hurthle cell neoplasms. Follicular carcinoma, poorly differentiated carcinoma, and anaplastic thyroid carcinoma are extremely rare. The most frequent cause of goiter in children is autoimmune thyroid disease; although a benign colloid goiter is also a common cause. MTC is a rare tumor arising from parafollicular C-cells. It accounts for <5% of all thyroid cancers. The incidence of pediatric MTC is estimated to be 0.03 cases/100,000 population/year. Due to extremely low incidence of pediatric MTC, we should have awareness of this entity. MTC occurs either sporadically or in an inherited autosomal dominant manner. In adults, sporadic MTC accounts for 65–75% of MTC, but in children, sporadic MTC is very rare; the vast majority of MTC diagnosed in the childhood are hereditary. Hereditary, MTC occurs as familial MTC or as a part of multiple endocrine neoplasia Type 2A and 2B syndromes. MTC diagnosed during childhood almost always results from activating mutations in the RET proto-oncogene, which encodes the RET receptor tyrosine kinase. The prognosis of pediatric MTC is extremely satisfactory, with a 5-year overall survival (OS) of 95% and 15 year OS of 86%.

The aspirates of MTC are cellular, comprising dispersed cells to loosely cohesive groups of plasmacytoid, spindle, and/or epithelioid cells. The characteristic nuclear features include variable nuclear pleomorphism, bi or multinucleated tumor cells, and granular chromatin pattern. The presence of intranuclear inclusions in MTC has been described. These are not diagnostic of MTC, as they are also observed in papillary thyroid carcinoma as well as some benign lesions of the thyroid. The cells have variable amount of cytoplasm ranging from scant to abundant. The cytoplasm is gray or gray-reddish with fine granules, which represents neurosecretory granules. Bose et al. have reported the presence of cytoplasmic granules in 85% of their cases. Amyloid has been demonstrated in 43–81% of MTC cases. Congo red staining has been used to highlight the presence of amyloid. The use of immunocytochemistry for calcitonin is sufficient for the diagnosis of MTC, since it is expressed in 80% of the tumors. There is also coexpression of keratin, vimentin, and CEA. Thyroglobulin expression is negative in MTC and is used as negative control marker. If calcitonin expression is negative in suspected MTC, then positive immunostaining using antibodies against chromogranin A or synaptophysin should be sought.

The common cytological differential diagnoses of MTC include Hurthle cell neoplasm, papillary thyroid carcinoma and metastatic tumor, particularly melanoma. Hurthle cell neoplasm is a frequent consideration, as it also features dispersed to loosely cohesive cells with moderate to abundant cytoplasm. However, in MTC, chromatin is coarse and macronucleoli are rarely seen. Furthermore, red cytoplasmic granules are observed in MTC with Romanowsky stain. The extremely eccentrically placed nucleus and presence of amyloid can also assist in proper identification of MTC. In both papillary thyroid carcinoma and MTC, intranuclear inclusions are seen, but other nuclear and architectural features help in distinguishing the two. MTC and metastatic melanoma are difficult to distinguish by cytomorphology alone. Immunocytochemistry is helpful in these cases. Furthermore, serum calcitonin levels are elevated in virtually all patients with MTC. In our patient, serum calcitonin level was elevated. He was further investigated and operated at some other center. Hence, the results of genetic studies, and thus, the type of MTC (sporadic vs. familial) is not known. However, none of his family (parents and one elder sibling) gave a prior history of the disease. The patient’s relatives were contacted and the child was well and disease free at 16 months after the surgery. The cytomorphological features of MTC are quite distinctive and in most of the cases, definitive diagnosis on FNA can be achieved, which can be confirmed with immunocytochemistry.

COMPETING INTERESTS STATEMENT BY ALL AUTHORS

The authors declare no conflicts of interest.

AUTHORSHIP STATEMENT BY ALL AUTHORS

This manuscript has been read and approved by all the authors and represents honest work.

ETHICS STATEMENT BY ALL AUTHORS

As this is a quiz case without identifiers, our institution does not require approval from Institutional Review Board (IRB) (or its equivalent).

LIST OF ABBREVIATIONS (in alphabetic order)

FNA – Fine-needle aspiration
MTC – Medullary thyroid carcinoma.

EDITORIAL/PEER-REVIEW STATEMENT

To ensure the integrity and highest quality of CytoJournal publications, the review process of this manuscript was conducted under a double-blind model (the authors are blinded for reviewers and vice versa) through automatic online system.
REFERENCES

1. Chan JK. Tumors of the thyroid and parathyroid glands. In: Fletcher CD, editor. Diagnostic Histopathology of Tumors. 4th ed. Philadelphia, PA: Elsevier; 2013. p. 1177-272.
2. Buley ID. Thyroid gland. In: Gray W, Kocjan G, editors. Diagnostic Cytopathology. 3rd ed. London, England: Elsevier; 2010. p. 487-512.
3. Huang SA. Thyromegaly. In: Lifshitz F, editor. Pediatric Endocrinology. 5th ed. New York: Informa Healthcare; 2007. p. 443-53.
4. Rosai J, Tallini G. Thyroid gland. In: Rosai J, editor. Rosai and Ackerman's Surgical Pathology. 10th ed. London, England: Elsevier; 2011. p. 487-564.
5. Niedziela M. Pathogenesis, diagnosis and management of thyroid nodules in children. Endocr Relat Cancer 2006;13:427-53.
6. Rossi ED, Martini M, Cenci T, Capodimonti S, Larocca LM. The role of thyroid FNA cytology in pediatric malignant lesions: An overview of the literature. Cancer Cytopathol 2017;125:594-603.
7. Muirhead S. Diagnostic approach to goitre in children. Paediatr Child Health 2001;6:195-9.
8. Vinciguerra GL, Noccioli N, Cippitelli C, Minucci A, Capoluongo E, Bartolazzi A. Oncocytic variant of medullary thyroid carcinoma: A rare case of sporadic multifocal and bilateral RET wild-type neoplasm with revision of the literature. Rare Tumors 2016;8:6537.
9. Watkinson JC. The British thyroid association guidelines for the management of thyroid cancer in adults. Nucl Med Commun 2004;25:897-900.
10. Hogan AR, Zhuge Y, Perez EA, Koniaris LG, Lew JJ, Sola JE. Pediatric thyroid carcinoma: Incidence and outcomes in 1753 patients. J Surg Res 2009;156:167-72.
11. Mulligan LM, Kwok JB, Healey CS, Elsdon MJ, Eng C, Gardner E, et al. Germ-line mutations of the RET proto-oncogene in multiple endocrine neoplasia type 2A. Nature 1993;363:458-60.
12. Bose S, Kapila K, Verma K. Medullary carcinoma of the thyroid: A cytological, immunocytochemical, and ultrastructural study. Diagn Cytopathol 1992;8:28-32.
13. Zeppa P, Vetrani A, Marino M, Fulciniti F, Boschi R, DeRosa G, et al. Fine needle aspiration cytology of medullary thyroid carcinoma: A review of 18 cases. Cytopathology 1990;1:35-44.
14. Bhanot P, Yang J, Schnadig VJ, Lograno R. Role of FNA cytology and immunohistochemistry in the diagnosis and management of medullary thyroid carcinoma: Report of six cases and review of literature. Diagn Cytopathol 2007;35:285-92.
15. Saad MF, Ordonez NG, Guido JJ, Samaan NA. The prognostic value of calcitonin immunostaining in medullary carcinoma of the thyroid. J Clin Endocrinol Metab 1984;59:850-6.
16. Papapaskeva K, Nagel H, Droese M. Cytologic diagnosis of medullary carcinoma of the thyroid gland. Diagn Cytopathol 2000;22:351-8.
17. Cibas ES. Thyroid. In: Cibas ES, Ducatman BS, editors. Cytology. 4th ed. Philadelphia, PA: Elsevier; 2014. p. 267-97.

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