

variants encountered without the need for confirmatory studies such as alkaline and acid electrophoresis. More importantly, identification of the common variants (i.e., HbC, HbD-Punjab, HbE, HbG-Philadelphia, HbHope, HbLepore, HbO-Arab, and HbS) that in combination with HbS leading to a clinically significant sickling disorder can be quickly and accurately accomplished by use of such algorithms without the need for further testing.

REFERENCES

1. Shimizu A, Nakanishi T, Miyazaki A. Detection and characterization of variant and modified structures of proteins in blood and tissues by mass spectrometry. *Mass Spectrom Rev* 2006; 25: 686-712.
2. Daniel YA, Turner C, Haynes RM, Hunt BJ, Dalton RN. Rapid and specific detection of clinically significant haemoglobinopathies using electrospray mass spectrometry-mass spectrometry. *Br J Haematol* 2005; 130: 635- 643.
3. Bain BJ. Hemoglobinopathy diagnosis 2001:260 Blackwell Science Ltd. Oxford, England.
4. Wild BJ, Stephens AD. The use of automated HPLC

- to detect and quantitate haemoglobins. *Clin Lab Haematol.* 1997; 19: 171-176.
5. Ou C-N, Rognerud CL. Diagnosis of hemoglobinopathies: electrophoresis vs. HPLC. *Clin Chim Acta* 2001; 313: 187-194
6. Riou J, Godart C, Didier H, Mathis M, Bimet C, Bardakjian-Michau J, et al. Cation-exchange HPLC evaluated for presumptive identification of hemoglobin variants. *Clin Chem* 1997; 43: 34-39
7. Hemoglobin and Clinical Microscopy Reference Committee. Hemoglobinopathy survey proficiency reports 1994-2003 College of American Pathologists Chicago, IL
Funding Support: None
Financial Disclosures: None.

From : Department of Biochemistry* and Pediatrics**, PGIMS, Rohtak, India

Address for Correspondence: Dr N D Vaswani, 9J-55 Medical Campus PGIMS ROHTAK. Email: dr_vaswani@yahoo.co.in

E-published: January 2010

EDUCATIONAL ARTICLE

THYROID MALIGNANCIES IN CHILDREN

S.N.Bhatnagar

Abstract

Thyroid malignancies in children are a known and distinct entity, though is less common than the thyroid malignancies in adults. The children tend to be treated in a manner similar to the adults with thyroid cancers, although there are striking differences in the presentation, clinical behavior, the differentiation pattern of the tumor and the outcome of management. Since the number of affected children are scarce and dispersed over wide regions, it is difficult to study these tumors in great detail. This article provides a review and comparative analysis between the adult and pediatric thyroid malignancies, thus guiding us in formulating appropriate approach for children.

Introduction

The Chernobyl tragedy in April 1986 in USSR showed the world the gruesome picture of occurrence of thyroid cancers in children which was otherwise seen very rarely (1) . According to the Chernobyl Forum, many years after the incident, about 4000 new cases of thyroid cancers occurred because the children consumed the cow's milk and the leafy vegetables contaminated with radioactive iodine, apart from the radiation effects of radioactive material on the thyroid (2).

In our clinical practice, albeit rarely, one does encounter nodules of the thyroid gland in children

which could be malignant. Since not much of research in terms of prospective randomized trials has been undertaken for the malignancies of thyroid gland in children, it is still a subject less well understood by clinicians.

Comparative Analysis

The salient features of malignancies of thyroid in children are that all children, especially those who are <10 years of age at presentation with thyroid nodules must be investigated thoroughly and a histopathological diagnosis established rapidly so that appropriate treatment is instituted at the earliest. An attempt is made here to provide a comparison between the adult and the pediatric thyroid malignancies with a view of improved understanding of the lesion (Table 1).

There are not many diagnostic modalities to differentiate between benign and malignant thyroid nodule (as depicted in Table 2). A baseline ultrasonography and a rapid histopathological evaluation by a Fine Needle Aspiration Biopsy (FNAB) or rarely open surgical biopsy (depending on the size of the lesion) is most essential.

The most widely accepted treatment modality is surgical excision of the lesion with excision of grossly involved lymphatic system, though a radical neck dissection is not recommended by all authors.

TABLE 1 : Comparison of features between adult and pediatric Thyroid malignancies

Features	Child	Adult
Age (most common)	Adolescent	3rd & 4th decades of life
Gender differentiation	Almost equal in younger children, but girls between 15-20 years are affected 3 times more than boys (3)	Women 4 times more likely (female hormones may be causative) (4)
Occurrence	Rare	Not as rare
Types	Papillary, follicular, medullary, anaplastic	Same
Most common type of malignancy	Papillary	Papillary
Most common presentation	Asymptomatic thyroid nodule	Usually asymptomatic , but malignant nodules often present with Pain, tenderness, compression of respiratory tract, dysphagia, inappropriate fixation of the neck
Incidence of malignancy in solitary thyroid nodule	20-73% (5,6,7)	5-10% (4)
Overall incidence of thyroid cancers	5%	95%
Risk of malignancy in thyroid nodule	4 times more i.e about 26%	Risk of malignancy in a thyroid nodule is less i.e. about 5%
Extent of disease at presentation	70% have extensive regional node involvement, 10-20% have distant metastases	30% have regional lymph node involvement 5-10% have distant metastases
Behavior of papillary nodule	More aggressive	Less aggressive
Prognosis	Better even with extensive disease, especially Papillary thyroid carcinoma (PTC)	Not good with extensive disease
Thyroid malignancy in infancy	Medullary Carcinoma, associated with Multiple Endocrine Neoplasia 2B (MEN 2B)	-
Most common site of Metastases	Lungs	Lungs and bone
Incidence of bone metastases	< 5% (3)	>40% (variable reports in different series) (4)
Mortality rates	< 10% (3)	Variable, increase significantly with extensive disease
Risk factors	<ul style="list-style-type: none"> • Exposure to radioactive iodine, • Follicular adenoma, • Autoimmune thyroiditis • Iodine deficiency • Radiation therapy for other cancers • Congenital hypothyroidism • Thyroglossal duct cyst (rare) 	<ul style="list-style-type: none"> • Radiation exposure • Low iodine diet (follicular and anaplastic carcinomas) • Age - <30 and >60 years • Nodule in a male • Familial adenomatous polyposis (Gardner's syndrome) • Hashimoto thyroiditis
Vocal cord paralysis	Rarely seen	More commonly seen
Family history of thyroid cancer	25%	Not ascertained, usually seen in Medullary carcinoma or in MEN 2B
Prognosis	NOT DEPENDANT ON Stage of disease, extensive lymph node involvement, degree of invasion,	DEPENDANT ON Age/sex of the patient, Size of the tumor > 4 cm, stage of the disease, extent of local invasion
Genetic influences	Ret and PTC3 oncogene - tumor more aggressive, faster growing, less differentiated Ret and PTC1 oncogene - tumor slower growing, and with more benign characteristics.	Similar for Medullary carcinoma of thyroid (MCT)

TABLE 2: Differentiating features between benign and malignant lesions on diagnostic tests.

Features	Benign	Malignant
Thyroid function tests	May be abnormal	Normal
Antithyroid antibodies	May be raised in thyroiditis	Normal
Calcitonin levels (pentagastrin stimulation)	High in Thyroid cell hyperplasia	Raised in Medullary carcinoma of thyroid
Serum Carcinogenic Embryonic Antigen (CEA)	Normal	High in MCT
Ultrasonography	multiple, solid isoechogenic or nonechogenic lesions and a uniform peripheral halo.	thick irregular halo
Colour doppler	No vascular flow in a cystic lesion	Increased vascularity in a cystic lesion or intranodular flow in solid lesion
Thyroid scintigraphy	Not proven worthwhile to distinguish benign from malignant disease Classic hot nodules have about 6% of malignancy Classic cold nodules have about 30% of malignancy	
Total body Radioactive Iodine Ablation (RIA) scans	Normal	Hot spots at metastatic sites, most commonly lungs.

Conclusion

Thyroid cancers in children usually occur in the age group of more than 10 years of age. If a child presents with a nodule in the thyroid, since the chances of it being malignant are high, it should be rapidly and thoroughly evaluated. In children, not many diagnostic tests will be able to confirm malignancy, except for histopathological examination of the biopsy from the nodule. In younger children, biopsy from needle aspiration is most often inadequate in which situation an open biopsy becomes mandatory. The prognosis of the children with thyroid malignancies does not correspond to the degree of invasion and the metastases, hence treatment should never be denied to these children, in spite of the higher risk of recurrence. The overall 20 year survival rate is in the range of 92-100%.

References

1. World Health Organization. Health effects of the Chernobyl accident. Available on URL http://www.who.int/ionizing_radiation/chernobyl/en/index.html. Accessed on 22nd December 2009.
2. Thyroid cancer effects in Children. Available at URL: <http://www.iaea.org/NewsCenter/Features/Chernobyl-15/thyroid.shtml>. Accessed on 22nd November 2009.

3. Gerber M, Reilly B. Thyroid cancer in children. Available on URL <http://emedicine.medscape.com/article/853737-overview>. Accessed on 22nd December 2009
4. Sharma PK, Johns MM. Thyroid cancer. Available on URL: <http://emedicine.medscape.com/article/851968-overview>. Accessed on 22nd December 2009
5. Bergholm U, Bergstrom R, Ekbohm A. Long-term follow-up of patients with medullary carcinoma of the thyroid. *Cancer*. 1997; 79: 132-138.
6. Chen H, Udelsman R. Papillary thyroid carcinoma: justification for total thyroidectomy and management of lymph node metastases. *Surg Oncol Clin N Am*. 1998; 7: 645-663.
7. Gharib H, Goellner JR. Fine-needle aspiration biopsy of the thyroid: an appraisal. *Ann Intern Med*. 1993; 118: 282-289.

From : Department of Pediatric Surgery, B.J.Wadia Hospital for Children, Parel, Mumbai, India.

Address for Correspondence: Dr Sushmita Bhatnagar, 56/B, Venus Apartments, Worli Sea Face, Worli, Mumbai 400018. E-mail - bhatnagar_s1206@yahoo.co.in

E-published: February 2010
