

Management of Thyroid Nodules in Children

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Estimates of the prevalence of thyroid nodules in children depend on the method of detection, ranging from 1 to 1.5% for detection by palpation to 3% for detection on ultrasound scans. Several risk factors are associated with a higher risk of developing thyroid nodules. These factors include puberty, iodine insufficiency, family history of thyroid disease, thyroid diseases, whether autoimmune (Hashimoto thyroiditis, Grave's disease) or congenital (congenital hypothyroidism with organification defects), genetic syndromes (such as familial adenomatous polyposis, Carney's complex or Cowden disease) and a history of exposure to radiation after medical treatment (before bone marrow transplantation or in patients with Hodgkin's lymphoma) or through the environment [1]. Thyroid nodules occur in a broad range of thyroid disorders, including solitary nodule formation, multinodular goiter, chronic lymphocytic thyroiditis (Hashimoto disease) and Graves' disease. They may also reflect the formation of cysts in the thyroglossal duct.

The goal in thyroid nodule (TN) evaluation is to distinguish between those patients with thyroid cancer who require thyroid surgery and those with benign disease. Thyroid nodules are less common in children than in adults, but the risk of malignancy is much higher in children (an estimated 10 to 25% of TNs are malignant in children, versus only 5% in adults). TNs are more frequent in female than in male subjects, but this sex bias is less marked in children than in adults (F/M sex ratio of 1.5/1). Male subjects, children under the age of 10 years and children with a history of irradiation are at the highest risk of cancer. Children exposed to irradiation early in their lives are more likely to develop thyroid cancer than those exposed at a later stage [1, 2].

The initial management of TN includes taking the patient's history and a physical examination, thyroid function tests, thyroid ultrasound scan, fine-needle aspiration biopsy and, in some more recent cases, molecular studies.

History and clinical evaluation

Patients with suspect nodules include those previously exposed to radiation, those with a family history of thyroid cancer, younger patients, those with thyroid nodules that have recently grown rapidly, those with persistent pain over a period of several weeks and those with cervical lymphadenopathy.

Most patients with TN are asymptomatic at the time of diagnosis, but the physical examination includes an evaluation of nodule size, consistency (hard/firm nodule), fixation to adjacent tissue, cervical lymphadenopathy and vocal cord paralysis. Children with differentiated thyroid cancers have a higher risk of having regional lymph node and lung metastases at the time of presentation [3].

Laboratory tests

All patients with a thyroid nodule should undergo thyroid function tests, including the determination of serum TSH, FT4, thyroid antibody and calcitonin concentrations. In cases of hyper- or hypothyroidism, thyroid hormone concentrations should be normalized before any surgical intervention.

Imaging

Thyroid scintigraphy (TS) should be performed in patients with TSH suppression. However, TS is not particularly useful for distinguishing between benign and malignant lesions, because few functional nodules are found to be malignant, despite the reassurance classically associated with the discovery of a "hot" nodule. Most hot nodules are toxic follicular adenomas.

Thyroid ultrasound is a non invasive method for the accurate evaluation of thyroid nodules. It should be the first-choice evaluation test in all children with thyroid nodules and should also be systematically used in screening for asymptomatic thyroid nodules in children who have had radiotherapy of the head and neck or total body irradiation. It provides information about the size, shape, echogenicity, location, and number of nodules and about the potential involvement of regional lymph nodes. It also provides information about the characteristics of

nodules associated with a higher risk of thyroid cancer, such as hypoechogenicity, irregular margins of the lesion, high levels of intranodular vascularity and microcalcifications. The tumor is likely to be benign if the margin is well defined, if there is a peripheral halo or if the lesion is entirely cystic in composition. The ultrasound features of small nodules (no greater than 10 mm across on ultrasound scan) are sensitive for the selection of lesions for fine needle aspiration and cytological testing. Ultrasound scans can also provide more accurate serial assessments of growth. They can be used to guide fine needle aspiration and to identify coexisting nodules [1, 4]. However, the patterns of nodule growth, in the presence or absence of L-thyroxine treatment, cannot be used to distinguish between benign and malignant.

Fine needle aspiration (FNA) and cytology is the most efficient way to evaluate the etiology of a thyroid nodule. Sedation of the patient and ultrasound guidance improve tolerance and the likelihood of obtaining an appropriate sample. The accuracy of FNA depends on the operator performing the FNA and the cytopathologist responsible for cytological analysis. FNA should be carried out in a center with extensive experience of this technique. The false negative rate for malignancy is very low (less than 5 %) and most false negative results concern nodules less than 1 cm [5, 6]. Recent advances in molecular genetics have increased the accuracy of cytological analysis, through the detection of BRAF or RET/PTC mutations [7].

The risk of malignancy is similar for solitary nodules and multinodular goiters. Thus, in patients with multiple nodules, FNA should be performed on as many nodules as possible, including, in particular, nodules identified as suspect on ultrasound scan and the largest nodules.

Most childhood thyroid carcinomas are derived from follicular cells and the vast majority (>90%) are papillary [2].

Treatment

Thyroid nodules in children often require surgical treatment, which should be performed by a surgeon with expertise in neck surgery in children. Total thyroidectomy and lymphadenectomy are recommended, when indicated, for the initial management of most thyroid cancers. These procedures are commonly followed by ablative radioiodine treatment to destroy residual thyroid tissue, decreasing the risk of relapse [1, 8, 9]. Long-term L-thyroxine suppression is also required. Surgery is also recommended for thyroid nodules with

an undetermined cytology. For nodules with benign cytological features, lobectomy or medical surveillance are recommended, depending on the size of the nodules and the symptoms of the patient.

Follow-up

- In cases of thyroid follicular cancer, post-surgical evaluation after initial treatment should include evaluations at regular intervals (serum thyroglobulin concentration determinations and ultrasound scans), and ^{131}I ablation of residual thyroid tissue, if necessary.
- In cases of benign thyroid nodules, repeated ultrasound scans should be used to monitor the nodule after conservative treatment or to screen for nodule recurrence in the contralateral lobe after lobectomy. FNA should be repeated if the nodule increases in size. L-thyroxine treatment should not be routinely administered, as there are insufficient data to demonstrate that this treatment decreases the size of benign thyroid nodules in euthyroid patients and concerning the potentially adverse effect of the decrease in bone mineral density this treatment provokes.

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