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A Thyroid Thriller: Acute Transient and Symmetric Goiter after Fine-Needle Aspiration of a Solitary Thyroid Nodule

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Objective: To report a case of a patient who developed an acute and transient, tender, and bilateral swelling of the thyroid that occurred during fine-needle aspiration (FNA) of a solitary nodule in the left thyroid lobe; to add accurate ultrasound measurements to support our clinical observation; and to analyze a possible underlying mechanism of this rare condition.

Results and clinical follow-up: The calculated thyroid volume increased from 23 to 57 mL before and at 4 minutes, respectively, after the needle aspiration, but the thyroid volume returned to prediagnostic level after 4 hours. Cytology, serum calcitonin, and histology were concordant, and the nodule was diagnosed as a medullary thyroid carcinoma. Immunohistochemistry was positive for calcitonin, chromogranin, and the very potent vasodilator calcitonin gene-related peptide (CGRP).

Conclusion: This is a rare case of acute and transient thyroid swelling during a common procedure as FNA of a thyroid nodule. This is the first case with documented acute volume expansion quantified by ultrasound measurements supporting our clinical observation, which is in accordance with two historical case reports. The clinical and ultrasound data support the hypothesis of vasodilation as the underlying mechanism, possibly evoked by the release of the vasodilator CGRP.

Introduction

Fine-needle aspiration (FNA) of thyroid nodules is a common practice since thyroid nodules are highly prevalent (1) and FNA is the first-line, cost-effective examination in nonfunctional thyroid nodules (2–4). It generally results in highly valuable information on the nature of the thyroid nodule, and—except from local pain and mild discomfort—complications of this diagnostic technique are extremely rare (5).

In this study we describe a patient with a rare complication of FNA, and provide ultrasound and immunohistochemical data supporting acute vasodilation as the underlying mechanism.

Case Report

A 56-year-old man was referred to the hospital because of a nodule in his left thyroid lobe. He presented with a visible and palpable thyroid nodule in the left thyroid lobe. The nodule was firm, mobile, and measured 20×20 mm on clinical examination. There was no relevant personal or family medical history, no sweating or diarrhea, and no use of medication. The thyroid function tests were normal. Ultrasound showed a normal-sized homogeneous right thyroid lobe (16×11×57 mm) (Fig. 1A) and a single hypoechoic hypervascular nodule (20×20×33 mm) in the left thyroid lobe (25×24×60 mm) (Fig. 1B).

Subsequently, FNA of the nodule was performed using a 24-gauge needle and a capillary sampling technique [without aspiration (device)]. Immediately after the second needle pass, the patient suffered from acute pain and a visible swelling of the entire thyroid gland. On clinical examination, there was an acute tender and diffuse goiter. No local swelling or ecchymosis was observed at the needle-insertion place. An intrathyroidal bleeding was suspected. However, signs of airway obstruction were absent. Repetition of the ultrasound revealed a striking increase of the thyroid volume with a significant increase in all dimensions. The anteroposterior diameter of the isthmus increased nearly threefold (8.6 mm, Fig. 2C) compared to a normal value of 3 mm before the procedure (Fig. 1C). The transverse diameters of the right thyroid lobe increased nearly twofold (22×24 mm, com-

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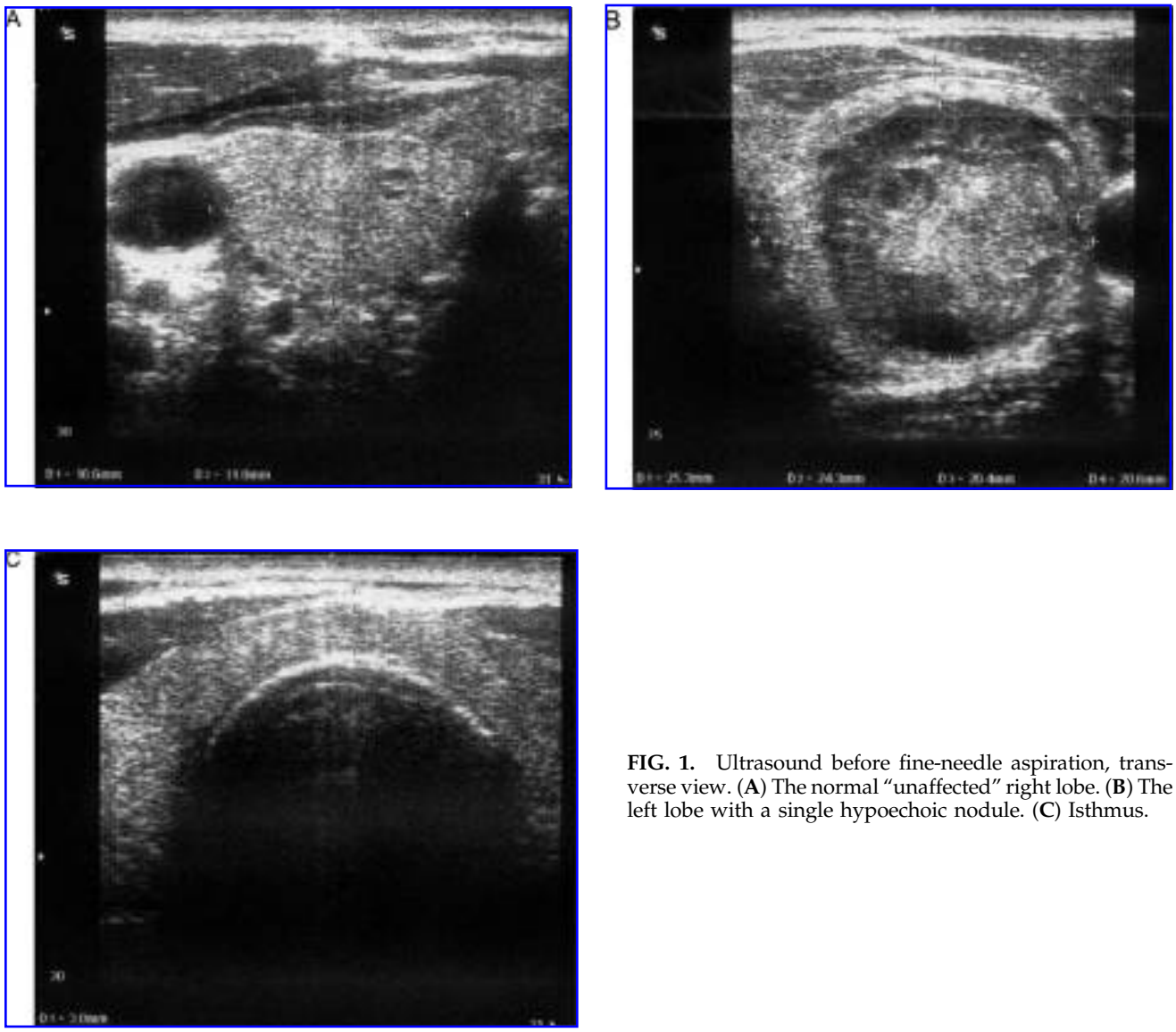

FIG. 1. Ultrasound before fine-needle aspiration, transverse view. (**A**) The normal "unaffected" right lobe. (**B**) The left lobe with a single hypoechoic nodule. (**C**) Isthmus.

pared to 16×11 mm) approximately 3 minutes after the FNA, and threefold (27×29 mm) approximately 4 minutes after the procedure (Fig. 2A). The transverse diameters of the left thyroid lobe increased to 32×33 mm, which represented a nearly 1.5-fold increase compared to the initial measurements (Fig. 2B).

The ultrasound pattern of the right lobe was patchy with hypoechoic areas, which contrasted to the homogeneous pattern before the FNA. Adjacent to the nodule in the left thyroid lobe, intrathyroidal vessels were also enlarged. No signs of hemorrhage were noted along the way of the needle passage (Fig. 2B).

At that point the pain decreased and the ultrasound measurements remained stable over the next 10 minutes. Later on, the swelling gradually disappeared within 1 hour. After 4 hours, the ultrasound examination was repeated. The volume and aspect of the thyroid gland were identical to the status before the aspiration.

Cytology showed findings concordant with a diagnosis of medullary carcinoma. Accordingly, the serum calcitonin level measured after the procedure was clearly elevated (4,220 pg/mL; normal <8.3 pg/mL).

A total thyroidectomy and bilateral central neck dissection was performed 8 weeks later. The perioperative clinical course was uneventful, especially no blood pressure problems were present. Postoperative serum calcitonin levels normalized. Gross examination of the thyroidectomy specimen revealed the presence of a nodule in the left lobe with dimensions of 20×20×25 mm. Histology and immunohistochemical staining (positive for calcitonin and chromogranin) confirmed the diagnosis of medullary thyroid carcinoma, $n = 5$ lymph nodes that were negative. Immunohistochemistry for calcitonin gene-related peptide (CGRP) was positive in the cytoplasm of some of the tumor cells, and in the extracellular area.

Discussion

A PubMed search from 1980 up to 2006 revealed two reports of acute and transient thyroid swelling after FNA (6,7).

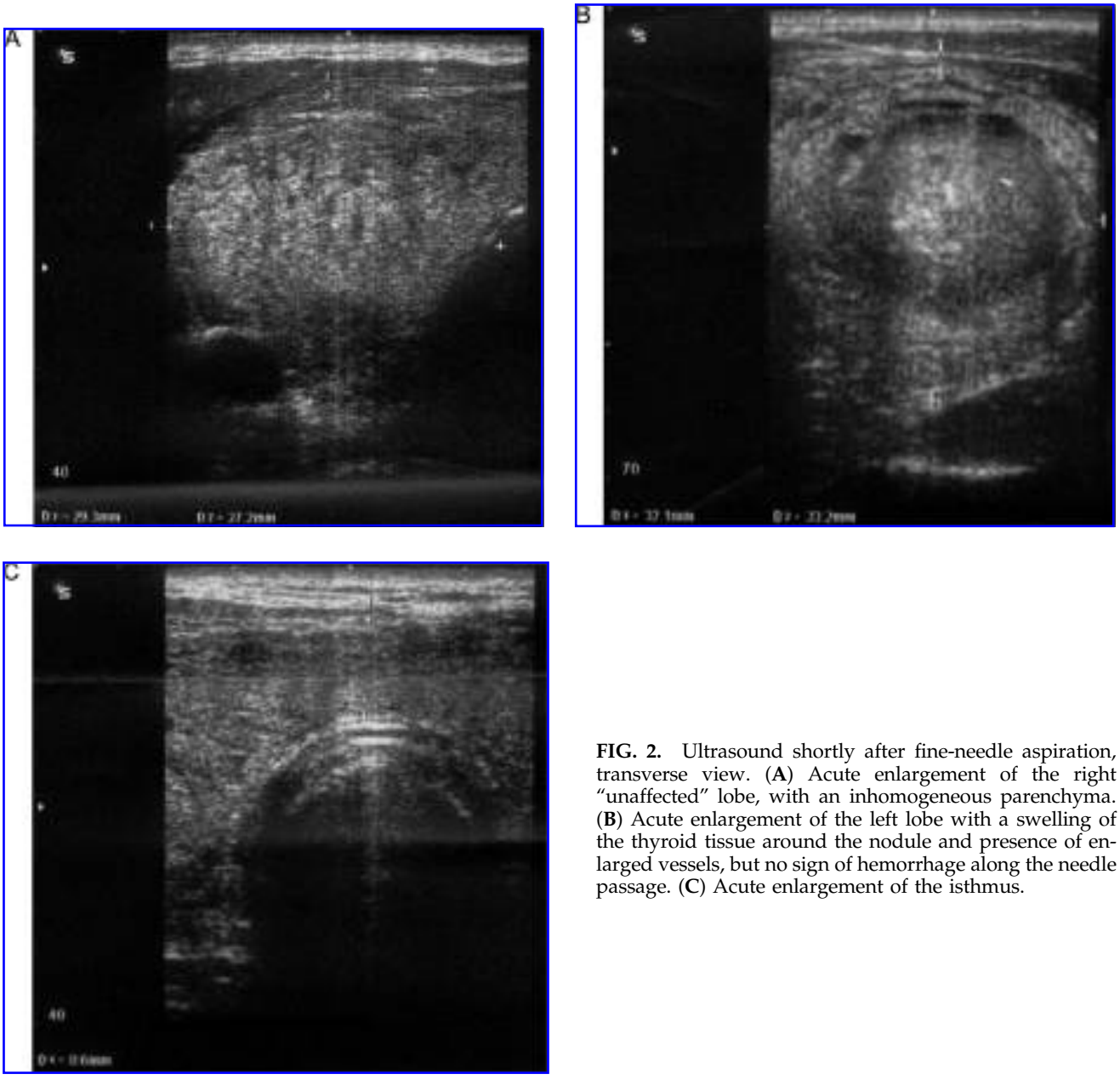

FIG. 2. Ultrasound shortly after fine-needle aspiration, transverse view. (**A**) Acute enlargement of the right "unaffected" lobe, with an inhomogeneous parenchyma. (**B**) Acute enlargement of the left lobe with a swelling of the thyroid tissue around the nodule and presence of enlarged vessels, but no sign of hemorrhage along the needle passage. (**C**) Acute enlargement of the isthmus.

Haas (6) reported a nearly 2.5-fold increase of the thyroid volume following fine-needle biopsy of a 20×30 mm nodule in the right thyroid lobe, appearing 2 to 3 minutes after completion of the procedure (six needle passes with a 22-gauge needle, with aspiration of a small amount of dark, brownish fluid on two of the passes). Cytology was reported as class I negative. Dal Fabbro *et al.* (7) reported a case of acute swelling immediately after the withdrawal of the needle with a threefold-enlarged thyroid gland, subsequently returning to normal size in a few hours. The final histologic diagnosis was a follicular carcinoma.

The present case represents the first case mentioned with accurate measurements documented by ultrasound. The calculated volume increase (from 23 mL to 57 mL within a time span of 10 minutes) corresponds very well to the previous clinical observations.

As reported by Haas and Dal Fabbro *et al.*, the episode was acute and "frightening." The unexpected course on the one hand and the absence of problematic vital signs on the other hand obviated accurate Doppler documentation in our patient. An intrathyroidal bleeding was first suspected, but was hardly probable on retrospect due to the hyperacute swelling, which had a reversible nature within 1 hour. In the literature, two cases of hemorrhage with airway compression have been reported; these cases could be referred to as *delayed* swelling after FNA since these patients developed symptoms (pain, swelling, dysphagia) 2 hours after the procedure with gradual progression and presentation with airway obstruction at the emergency department 4 to 5 hours after the FNA (5,8). These patients needed to undergo intubation and surgery: in the first patient, a well-circumscribed hematoma was evacuated and an actively bleeding site on the thyroid capsule was located

(5); in the second patient, the thyroid showed a huge, edematous, nonfluctuant, firm swelling and easy bleeding on touch, no obvious actively bleeding vessel was present, and thyroidectomy showed massive parenchymal hemorrhage (8). In our case and in the cases described by Haas and Dal Fabbro *et al*., the clinical course with an acute and transient swelling suggested vasodilation and capillary leak. This hypothesis is supported by our ultrasound data, showing large vessels adjacent to the aspirated nodule and a temporary inhomogeneous pattern of the extranodular thyroid parenchyma. A medullary thyroid carcinoma was present with positive immunostaining for calcitonin and chromogranin. Due the hyperacute local vasodilation, suggestive for the release of a potent, locally produced vasodilator substance, we hypothesized that CGRP could be responsible for the observed phenomenon, since it is known as the most potent endogenous vasodilator. Indeed, immunostaining for CGRP was clearly positive. CGRP is a 37 amino acid neuropeptide closely related to calcitonin. Normally, it is mainly produced in the central and peripheral nervous system, and is suggested to play an important role in blood pressure modulation. Although our case is highly suggestive for a local iatrogenic release of a vasodilator substance, it should be mentioned that CGRP is almost universally expressed by medullary thyroid cancer (9,10), and that other potential vasoactive substances, such as somatostatin, serotonin, catecholamines, histaminase, and the like, released by the medullary carcinoma cells might have been responsible for the observed phenomenon. Also, CGRP cannot explain the phenomenon in the two cases of the literature.

Altogether, we report a rare case of acute, painful, and transient swelling of the entire thyroid gland after FNA of a solitary thyroid nodule, with accurate measurements of the volume increase documented by ultrasound. We suggest that vasodilation and capillary leakage constitute the underlying pathophysiological mechanisms, provoked by the release of a potent vasodilator substance, probably CGRP. Although such an episode is frightening, the acute swelling is self-limiting and transient, contrary to a delayed swelling caused by hemorrhage, which may progress and cause airway obstruction necessitating thyroidectomy.

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