

**Mini-Review****Acute transient thyroid swelling following needle biopsy:  
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**INTRODUCTION**

Fine needle biopsy (FNB) is regarded as the method of choice in the management of thyroid nodules because of its simplicity, reliability, accuracy and cost-effectiveness.<sup>1</sup> Indeed, the use of FNB has halved the number of patients undergoing thyroidectomy and has doubled the yield of malignancy in patients who finally have undergone surgery, thereby reducing the cost of medical care.<sup>2</sup> Clinical complications following thyroid FNB have been previously summarized;<sup>3</sup> the most common are local pain or discomfort and minor hematomas, while the other adverse events, including acute transient thyroid swelling, seem to be rare. In 2009, there were only three cases of post-FNB acute transient thyroid swelling in the literature.<sup>4,6</sup> Recently, Norrenberg et al,<sup>7</sup> Nakatake et al<sup>8</sup> and

Nakagawa et al<sup>9</sup> have reported two, three and one new cases, respectively, of acute transient swelling. Considering these six new cases and one more after subclavian vein catheterization reported by Bowman et al,<sup>10</sup> the number of reported cases has more than tripled since 2009. However, acute transient swelling remains a complication of unknown origin. Even the nature of the fluid which fills the gaps of the transiently “cracked” thyroid is as yet undetermined. We hereby summarize the existing cases with the aim of elucidating potential common conditions, if any, predisposing to acute transient thyroid swelling.

**LITERATURE SEARCH**

An advanced computerized search for primary evidence was performed in the PubMed (Public/Publisher MEDLINE) electronic database, as reported in detail elsewhere.<sup>3</sup> In brief, relevant journal articles were initially retrieved by using a combination of terminological (MeSH terms) and methodological search filters. The bibliographic search was extended to the ‘Related Articles’ link next to each selected article in PubMed and its references. More specifically, we repeated the previously described method,<sup>3</sup> with the time limited to between 1 July 2008 and 31 December 2011, as the same search had been previously performed up to 30 June 2008.<sup>3</sup> All articles found were of level 3 of evidence, leading to grade C recommendations, since they were case reports or case series.<sup>11</sup>

**Key words:** Acute transient swelling, Adverse events, Complications, Fine needle aspiration biopsy, Fine needle biopsy, Fine needle capillary biopsy, Thyroid nodule, Thyroid volume

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Received 10-01-12, Revised 13-03-12, Accepted 29-03-12

**Table 1.** Published cases of acute transient thyroid swelling following thyroid FNB or other diagnostic modalities

First author, year*	Case(s)/ Gender	Age (years)	Goiter	Thyroid function tests (TSH/antibody)	Biopsied nodule's characteristics	Technique/ Needle's gauge (G)
Haas SN, 1982 <sup>5</sup>	1/F	47	No	Normal/NA	3.0 max diameter; R lobe	P-FNA/22
Dal Fabbro, 1987 <sup>4</sup>	1/F	63	No	Normal/NA	3.8 cm max diameter, solid, hypoechoic; R lobe	P-FNA/22
Van den Bruel, 2008 <sup>6</sup>	1/M	56	No	NA/NA	3.3 max diameter, hypoechoic, hypervascular; L lobe	US-FNC/24
Bowmann, 2009 <sup>10</sup>	1/M	69	Yes	NA/NA	-	Subclavian vein catheterization
Norrenberg, 2011 <sup>7</sup>	2/F/F	27/46	No/ No	Case #1: low/positive Case #2: normal/ normal	Case #1: 1cm max diameter, hypoechoic, marked vascularization; L lobe/ Case #2: 1.5 cm max diameter, hypoechoic, heterogenous, capsular calcification; R lobe	US-FNA/21
Nakatake, 2011 <sup>8</sup>	3/F/M/F	58/31/45	Yes/ Yes/ Yes	Case #1: normal/ normal Case #2: normal/ normal Case #3: normal/ normal	Case #1: 0.9 cm max diameter, solid, heterogenous; L lobe / Case #2: 1.5 cm max diameter, solid, heterogenous, irregular margin; R lobe/ Case #3: 2.4 cm max diameter, solid, heterogenous; L lobe	NA-FNA/22
Nakagawa, 2011 <sup>9</sup>	1/F	67	Yes	Normal/NA	4.1 cm max diameter, isoechoic with cystic degeneration; L lobe	NA-FNA/22

## REVIEW OF THE EXISTING CASES

The reported cases of acute transient thyroid swelling are summarized in Table 1. All the patients experienced acute 1.5 to 3-fold volume increase in both thyroid lobes, although FNB was performed unilaterally. Importantly, there was no neck ecchymosis or airway obstruction in any of the cases. Acute swelling was ultrasonographically verified in seven of the described cases and the ultrasonographic pattern was fairly similar: a patchy and heterogenous appearance, so that the entire thyroid appeared “cracked”. On application of Doppler ultrasound, no blood flow was observed in the “cracks”.<sup>8</sup> The complication resolved spontaneously in all cases within 1-20 hours. The empirical use of cold packs, paracetamol, diclofenac or hydrocortisone in some cases did not seem to affect the duration of the swelling. Notably, repeat FNB in one case a week later did not reproduce the complication.<sup>6</sup>

Acute transient thyroid swelling is characterized by acute onset, quick recovery, absence of ecchymosis or airway obstruction unlike massive hemorrhage.<sup>12</sup> Moreover, contrary to the syndrome of delayed swelling of prethyroid soft tissues,<sup>3,13</sup> acute transient thyroid swelling is characterized by an increase of the thyroid volume per se rather than a swelling of the prethyroid tissues.

Interestingly, the patients reported were not of the same gender or of a similar age. No patient had a reported history of allergy nor did they share concomitant disease or medication. Thyroid function tests and anti-thyroid antibodies, when available, were normal in all but one female patient with postpartum thyroiditis. Five patients had increased thyroid volume (goiter) pre-FNB, while the biopsied nodules had different ultrasonographic characteristics. Cytological (or histological) diagnosis also varied. Regarding the FNB method, ultrasound-guidance

**Table 1.** (continued)

Number of passes	Pain	Start of swelling	Volume increase (approximately)	Cytological diagnosis	Duration of swelling	Additional information
6	Anesthesia with lidocaine	3 min after FNA	2.5-fold (clinically)	Benign	1 h	Cold packs application
2	Mild pain/ the patient swallowed while the needle was in situ	During FNA	3-fold (clinically)	Non-diagnostic (repeat FNA: follicular neoplasm)	Within a few hours	Cold packs application/ Thyroidectomy/ Histologically follicular carcinoma
2	Acute pain	During FNC	1.5 to 3-fold (US)	Medullary carcinoma	1 h	Thyroidectomy/ Histologically medullary carcinoma
Several unsuccessful attempts	NA	15 min post-procedure	N/A	-	4 h	
2/1	Acute pain/ Acute pain	Both during FNA	2-fold (US)/ 3-fold (US)	Non-diagnostic/ Benign	3 h / 1 h	Case #1: History of post-partum thyroiditis/ Diclofenac administration Case #2: Concomitant diabetes mellitus/ Paracetamol administration
1/2/2	Mild pain/ Acute pain/ NA	1 h/1.5 h/2h after FNA	3-fold (US)/ 2-fold (US)/ 2.5-fold (US)	All benign	All within a few hours	Case #1: - Case #2: On warfarin and aspirin/ acute pain Case #3: -
NA	NA	1h after FNA	2-fold (US)	NA	20 h	Hydrocortisone (200 mg) intravenously

(\*) References are presented in publication date order

F: female; FNA: fine needle aspiration; NA: not available; L: left; M: male; max, maximum; P-FNA: palpation-guided FNA; TSH: thyroid stimulating hormone; US-FNA: ultrasound-guided FNA; R: right; US: ultrasound; US-FNA: ultrasound-guided fine-needle aspiration; US-FNC: ultrasound-guided fine-needle capillary.

does not seem to prevent the complication, given that most of the described patients were subjected to ultrasound-guided FNB. In all but one patient, fine needle aspiration (FNA) technique was performed using 21- to 22-G fine-needles. In only one case<sup>6</sup> was fine-needle capillary (FNC) technique carried out, using a smaller caliber needle (24-G). Most patients experienced acute or mild pain during or shortly after the procedure (Table 1). In cases wherein pain was not described, there was previous anesthesia with lidocaine (one case) or several unsuccessful attempts at subclavian catheterization (one case), in whom pain was expected. In another case, the patient swallowed while the fine-needle was in situ.

## CLOSING REMARKS

Regarding the fluid filling the “cracks” during acute transient swelling, it is not likely to be bloody, this estimation mainly based on the quick reversibility of the complication since parenchymal hemorrhage or hematoma usually needs several days to resolve.<sup>3,12</sup> Furthermore, extranodular hemorrhage would have resulted in a homogeneous pattern of the thyroid parenchyma in ultrasonography, which is not described in any of the cases reported. Although the fluid is probably exudate, this has not as yet been proved. Magnetic resonance imaging (MRI) during the acute phase, best followed by repeat imaging on recession, could provide strong indications as to the aqueous nature of the fluid.

Regarding the pathogenesis of acute transient swelling, there is currently no solid explanation. Anaphylactic reaction does not seem to be a convincing hypothesis since no history of allergy was reported and no other signs or symptoms of allergy (i.e., erythema, itching etc) were described. In the case of medullary thyroid carcinoma, calcitonin gene-related peptide, which is a potent vasodilator, could explain vasodilation and capillary leakage.<sup>6</sup> However, this hypothesis cannot explain the remaining eight cases.

We believe that an acute onset of pain followed by the appearance of short-lasting thyroid edema point to a neurohumoral basis of the phenomenon, analogous in some aspects to the well known triple response of Lewis elicited after minor skin injury. Lowered pain threshold in the involved area, action of inflammatory-vasoactive substances and vasodilation are the key-elements of this reaction.<sup>14</sup> Increased density of mast cells, a known source of vasoactive mediators, has been reported in human thyroid cancer,<sup>15</sup> although their abundance has not been explored in benign thyroid nodules. In support of this hypothesis, ultrasonographically enlarged intrathyroidal vessels with no sign of hemorrhage was described in one of the cases.<sup>6</sup>

Regarding the management of this complication, a post-FNB ultrasound is usually advised when the patient experiences acute pain or swelling. In the event of acute swelling, the patient should not be discharged and should be placed under close monitoring until swelling subsides. Furthermore, if sudden swelling or persistent pain occurs after discharge from the hospital, the patient should be advised to communicate regularly with her/his physician.

In conclusion, acute thyroid swelling may be frightening, but it is transient and self-limited and requires no specific treatment. Considering that the three cases of Nakatake et al<sup>8</sup> were observed within the space of only six weeks, acute transient swelling may possibly not be as rare as is currently believed, but rather under-diagnosed and under-reported. Awareness helps to avoid unnecessary interventions, while publishing such cases will eventually help to elucidate its pathogenetic basis. The benign nature of acute transient swelling does not render the overall safety of thyroid FNB questionable.

*Conflict of interest: No conflict of interest related to this manuscript*

*Grants or fellowship supports: None*

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