Diffuse Sclerosing Variant of Papillary Thyroid Carcinoma

Sonography and Specimen Radiography

Hyun Kyung Jung, MD, Soon Won Hong, MD, Eun-Kyung Kim, MD, Jung Hyun Yoon, MD, Jin Young Kwak, MD

The purpose of this pictorial essay is to show the limitations of sonography and complementary usefulness of specimen radiography in detecting microcalcifications of the diffuse sclerosing variant of papillary thyroid carcinoma, which mostly manifests as diffusely scattered microcalcifications in the thyroid gland.

Key Words—diffuse sclerosing variant of papillary thyroid carcinoma; sonography; specimen radiography; thyroid gland

Received June 21, 2012, from the Departments of Diagnostic Radiology (H.K.J., E-.Y.K., J.Y.K.) and Pathology (S.W.H.), Research Institute of Radiological Science, Yonsei University College of Medicine, Seoul, Korea; Department of Diagnostic Radiology, Inje University College of Medicine, Haeundae Paik Hospital, Busan, Korea (H.K.J.); and Department of Diagnostic Radiology, Bundang CHA Medical Center, CHA University, School of Medicine, Seongnam, Korea (J.H.Y.). Revision requested July 16, 2012. Revised manuscript accepted for publication August 20, 2012.

Address correspondence to Corresponding author: Jin Young Kwak, MD, Department of Radiology, Yonsei University College of Medicine, 50 Yonsei-ro, Seodaemun-gu, Seoul 120-752, Korea.

E-mail: docjin@yuhs.ac

Among various imaging modalities, sonography is generally considered the most accurate imaging modality for the evaluation and characterization of thyroid nodules[1] and preoperative or intraoperative staging.[2] Although sonography is widely used in the management of thyroid nodules, this proven efficient modality has its limitations in detecting microcalcifications.[3,4]

The diffuse sclerosing variant of papillary thyroid carcinoma is a rare variant of papillary thyroid carcinoma, which is mostly characterized by the presence of diffusely scattered microcalcifications with or without the presence of an associated mass, diffuse heterogeneous hypoechogenicity of the background thyroid parenchyma on sonography, and a higher incidence of cervical lymph node metastases.[5–7] In cases of the diffuse sclerosing variant, which manifests as microcalcifications only, sonography may have its limitations in detecting microcalcifications and assessing the disease extent. Several recent articles reported that specimen radiography could show microcalcifications more easily and the additional cancer foci that contained microcalcifications, which were not detected on sonography in patients with thyroid carcinoma.[4,8]

Sonographic and Specimen Radiographic Technique

Sonography was performed with a 7–15-MHz linear array transducer (HDI 3000 or 5000; Philips Healthcare, Bothell, WA) or a 5–12-MHz linear array transducer (iU22; Philips Healthcare). When using both machines, compound imaging was performed in all cases. Preoperative real-time sonography was performed by 1 of 2 board-certified radiologists with 7 or 11 years of experience in thyroid imaging. After surgery, specimen radiographs were obtained with a Selenia full-field digital mammography system (Lorad/Hologic, Danbury, CT), which is a dedicated mammography unit. The system, based on a detector with amorphous selenium, uses a direct capture 70-μm pixel device and yields a 2560 × 3328 matrix image with an 18 × 24-cm paddle. The system was set to allocate 16-bit images and store them at 12 bits. Routine views of thyroid specimens were obtained (focal spot size, 0.3 mm). These images were displayed on a pair of high-resolution 5-megapixel liquid crystal display monitors (MFGD 5621HD; Barco NV, Kortrijk, Belgium) that were part of the review workstation (Selenia Softcopy; Lorad/Hologic) with soft copy reading software (MeVis BreastCare; MeVis Medical Solutions, Bremen, Germany).

Clinical Features and Importance

Previous studies reported the prevalence of the diffuse sclerosing variant of papillary thyroid carcinoma to range from 0.3% to 5.3%.[6,9] It occurs more frequently in young patients (mean age, 19.5–34.7 years) and in women.[10] Serum thyroid antibodies were more frequently increased in patients with a diagnosis of the diffuse sclerosing variant.[9] In addition, it has been known to have a high incidence of cervical lymph node metastases, which frequently are bilateral, and lung metastasis and, therefore, a more unfavorable prognosis than conventional papillary thyroid carcinoma.[5,7,11] However, some recent studies reported that its prognosis was similar to that conventional papillary thyroid carcinoma because it usually occurs in young women, and these patients undergo aggressive treatment.[9,10,12]

Sonographic and Specimen Radiographic Findings

The characteristic sonographic features of the diffuse sclerosing variant of papillary thyroid carcinoma are diffuse enlargement of the thyroid gland with heterogeneous hypoechogenicity, diffuse scattered microcalcifications with or without an associated suspicious mass, and the presence of cervical lymph nodes that are suspicious for metastases (Figures 1–5).[13] Although the prominent sonographic "snowstorm appearance" has been well known for the diffuse sclerosing variant, cases presenting as localized microcalcifications were also reported.[14] Histopathologically, these microcalcifications are known to correlate with psammoma bodies, extensive fibrosis, and lymphocytic infiltrations.[13] The diffuse sclerosing variant has unique pathologic features, which are characterized by diffuse involvement of one or both thyroid lobes, dense fibrosis, extensive squamous metaplasia, patchy lymphocytic infiltration with germinal centers, and numerous psammoma bodies with characteristic nuclear features of papillary thyroid carcinoma (Figures 1–5).[6] The diffuse sclerosing variant tends to invade lymphatic vessels in the early stages of the disease and disseminate within the thyroid gland without making mass lesions. The extensive lymphocytic infiltrations correlate with a high incidence of lymph node metastasis and post-therapy disease persistence.[7]

Because of its appearance of diffuse enlargement of the thyroid gland, heterogeneous hypoechogenicity on sonography, and increased serum thyroid antibodies, the diffuse sclerosing variant of papillary thyroid carcinoma can be confused with chronic thyroiditis, and correct diagnosis is often delayed.[15] However, the abundant psammoma bodies on histopathologic examination are typical for the diffuse sclerosing variant only, not in patients with chronic thyroiditis.

Specimen radiography can show microcalcifications more easily than sonography (Figures 1–5), along with additional cancer foci that contain microcalcifications in patients with a diagnosis of thyroid carcinoma.[4,8] A recent article reported that specimen radiography is useful for accurate diagnosis and predicting the extent of thyroid carcinoma.[4] This article showed that among a total of 122 patients, the microcalcifications within the thyroid were only detected by specimen radiography in 27 patients (18.5%), which were not detected by sonography. Sixteen of the 27 specimens were associated with the presence of cancer foci. In addition, after specimen radiographs were reviewed, the diagnosis was changed to the diffuse sclerosing variant in 2 of the 16 patients, the cancer extent 13 of the 16 patients, and both in 1 of the 16 patients.

Value of Specimen Radiography

Although preoperative specimen radiography of the thyroid gland cannot be performed like mammography because compression cannot be applied to the thyroid glands with the current technique, our pictorial essay

Figure 1. Diffuse sclerosing variant of papillary thyroid carcinoma in a 39-year-old woman. **A** and **B**, Transverse and longitudinal sonograms of the right thyroid gland showing a poorly defined, markedly hypoechoic mass (white arrows) containing microcalcifications (black arrows). **C** and **D**, Transverse and longitudinal sonograms of the left thyroid gland showing no abnormal lesion. **E**, Specimen radiograph showing scattered faint amorphous microcalcifications in both lobes of the thyroid gland (white arrows). Microcalcifications located in the left thyroid gland were proven as additional cancer foci in this patient, and the diagnosis was confirmed as the diffuse sclerosing variant. **F** and **G**, Pathologic specimens showing a main mass (**F**, black arrows) in the right thyroid gland and additional cancer foci with psammoma bodies (**G**, black arrows) in the left thyroid gland (hematoxylin-eosin, original magnification ×100).

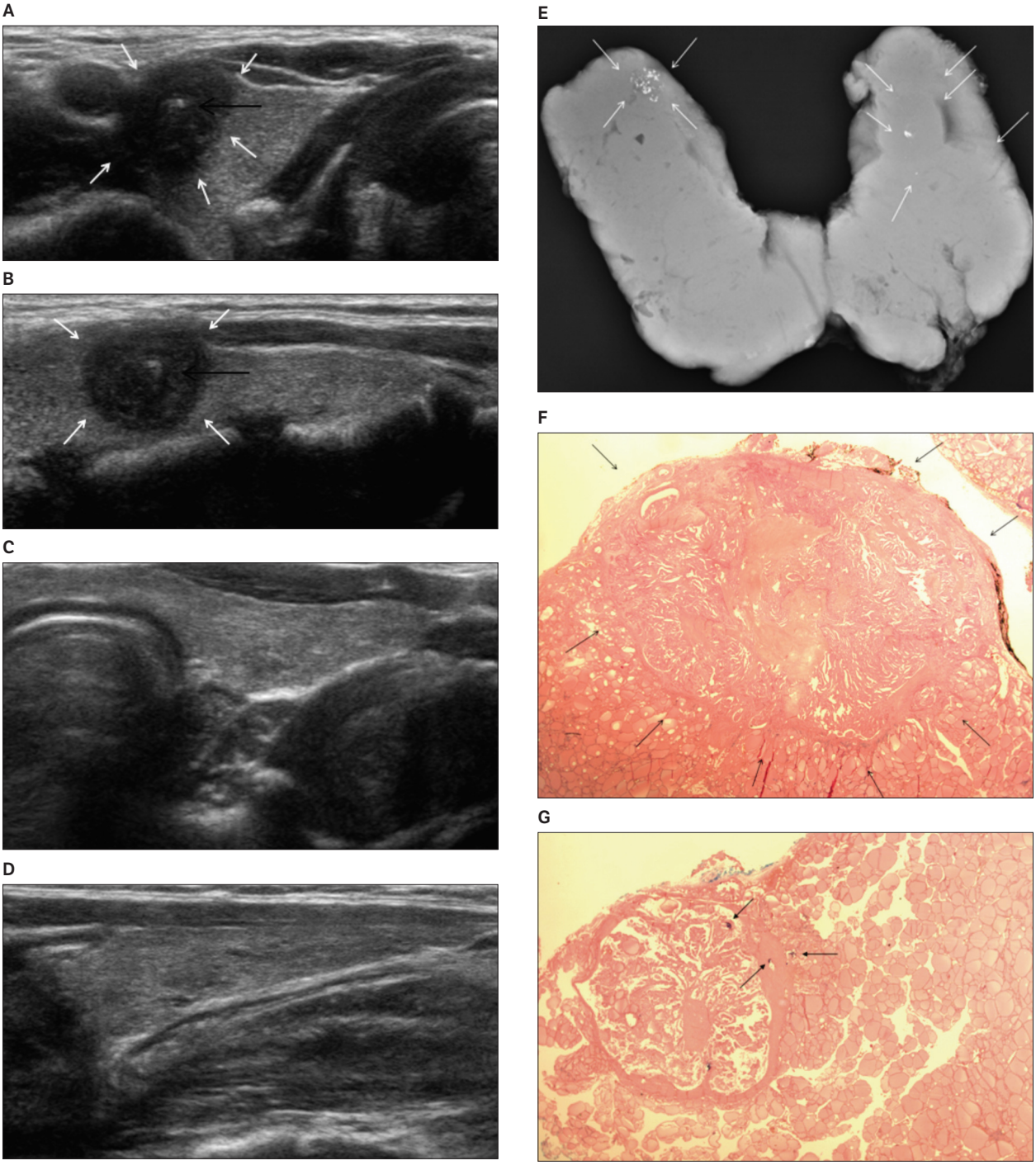
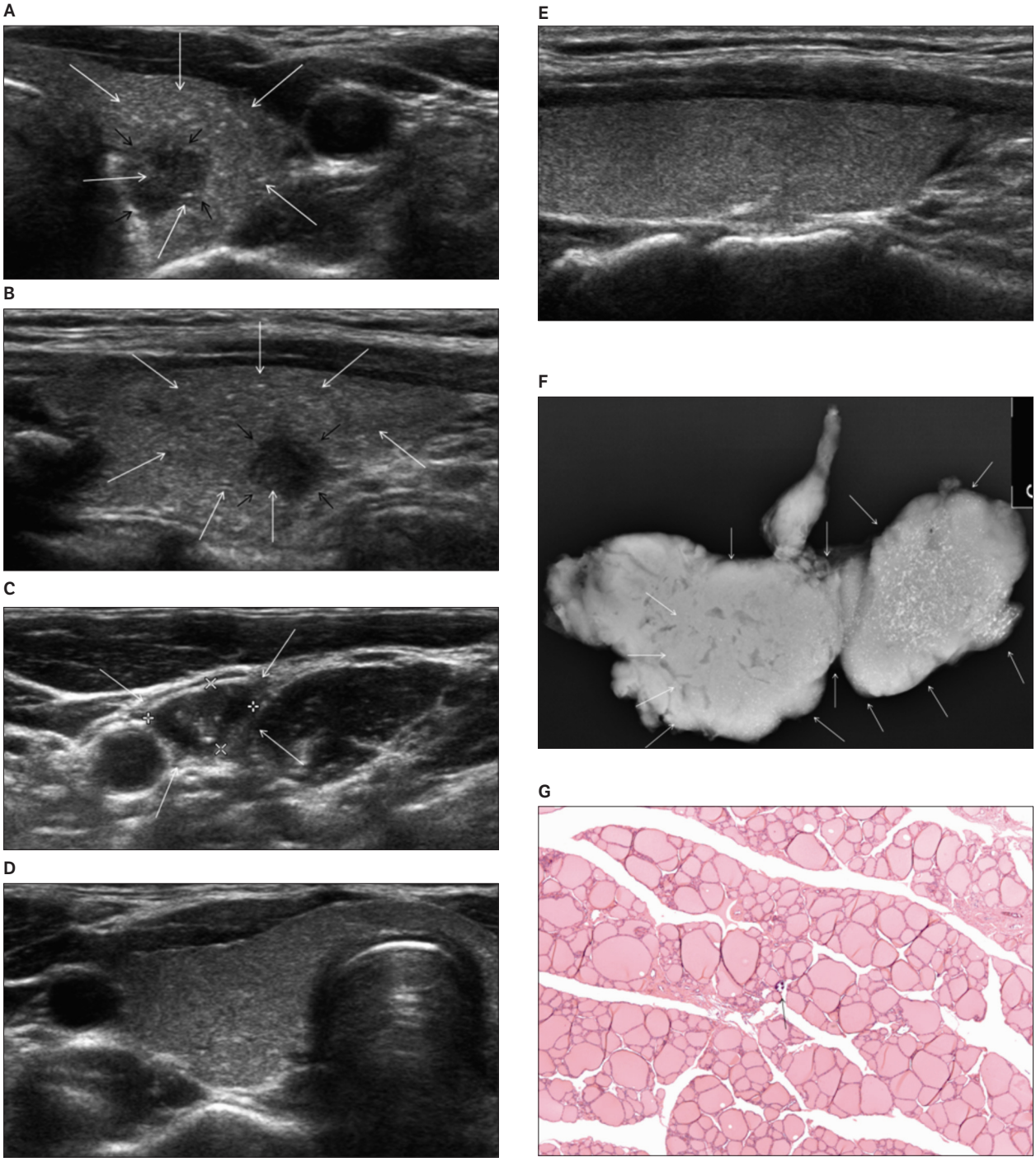


Figure 2. Diffuse sclerosing variant of papillary thyroid carcinoma in a 29-year-old woman. **A** and **B**, Transverse and longitudinal sonograms of the left thyroid gland showing a poorly defined hypoechoic mass (black arrows) and microcalcifications (white arrows) both within and outside the mass. **C**, Transverse sonogram of the left neck at level IV showing a 1-cm lymph node containing echogenic microcalcifications (white arrows). **D** and **E**, Transverse and longitudinal sonograms of the right thyroid gland showing no abnormal findings. **F**, Specimen radiograph showing diffusely scattered microcalcifications (white arrows) in both thyroid glands. Microcalcifications of the right thyroid gland were detected only on specimen radiography, which showed additional cancer foci in this patient. **G**, Pathologic specimen of the right lobe showing psammoma bodies (black arrows), which correlated with the findings on specimen radiography (hematoxylin-eosin, original magnification ×100).



shows that specimen radiography can potentially contribute in 3 ways: (1) by showing that the diffuse sclerosing variant of papillary thyroid carcinoma should be considered when sonography shows microcalcifications that are not associated with a nodule; (2) by encouraging ultrasound system manufacturers to make changes to their equipment to improve microcalcification detection rates; and (3) by encouraging pathologists to use specimen radiography, assuming that any improvement in sensitivity can be shown to be beneficial in some way, such as by detecting microcalcifications that might not be found with routine specimen processing.

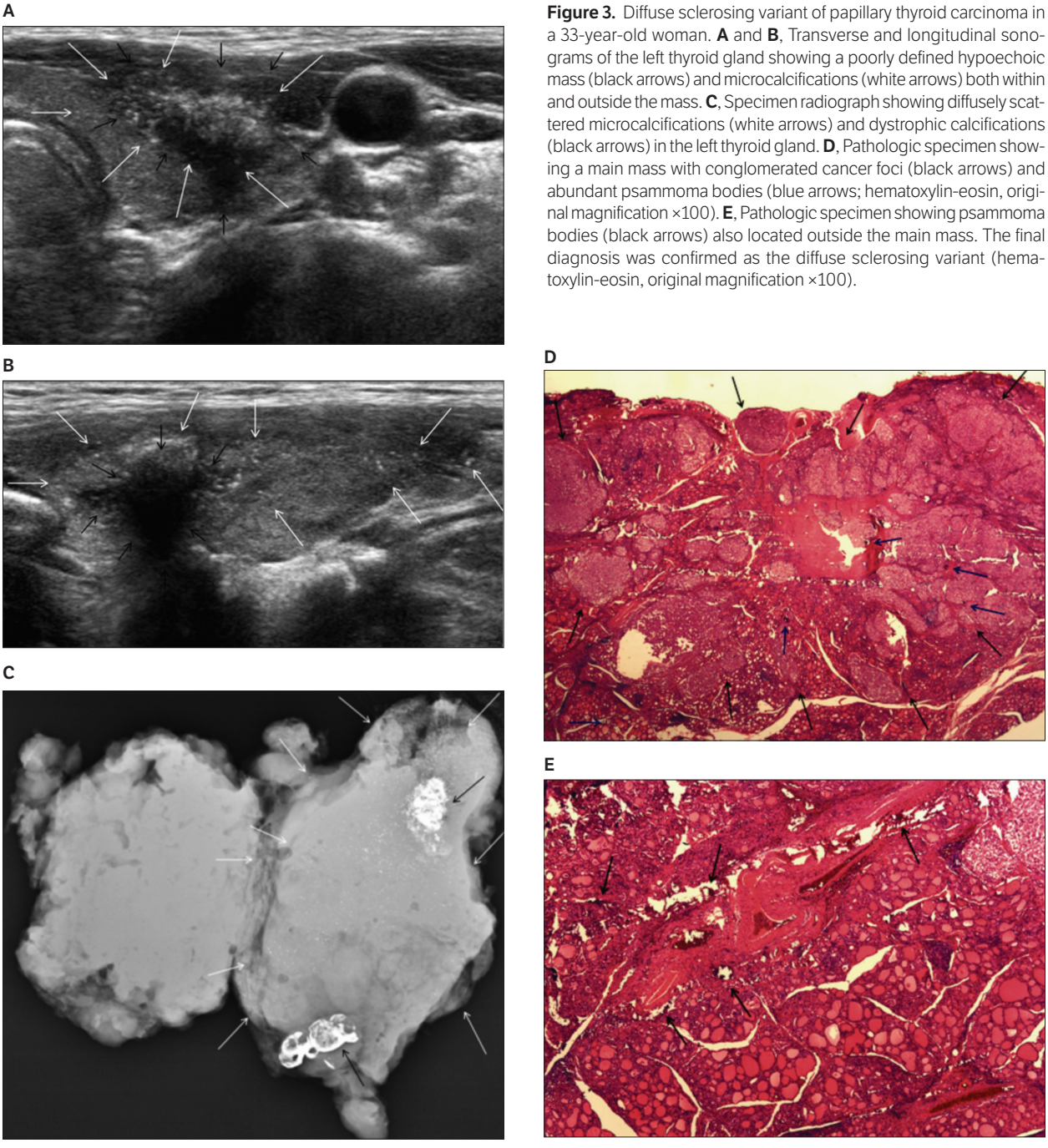
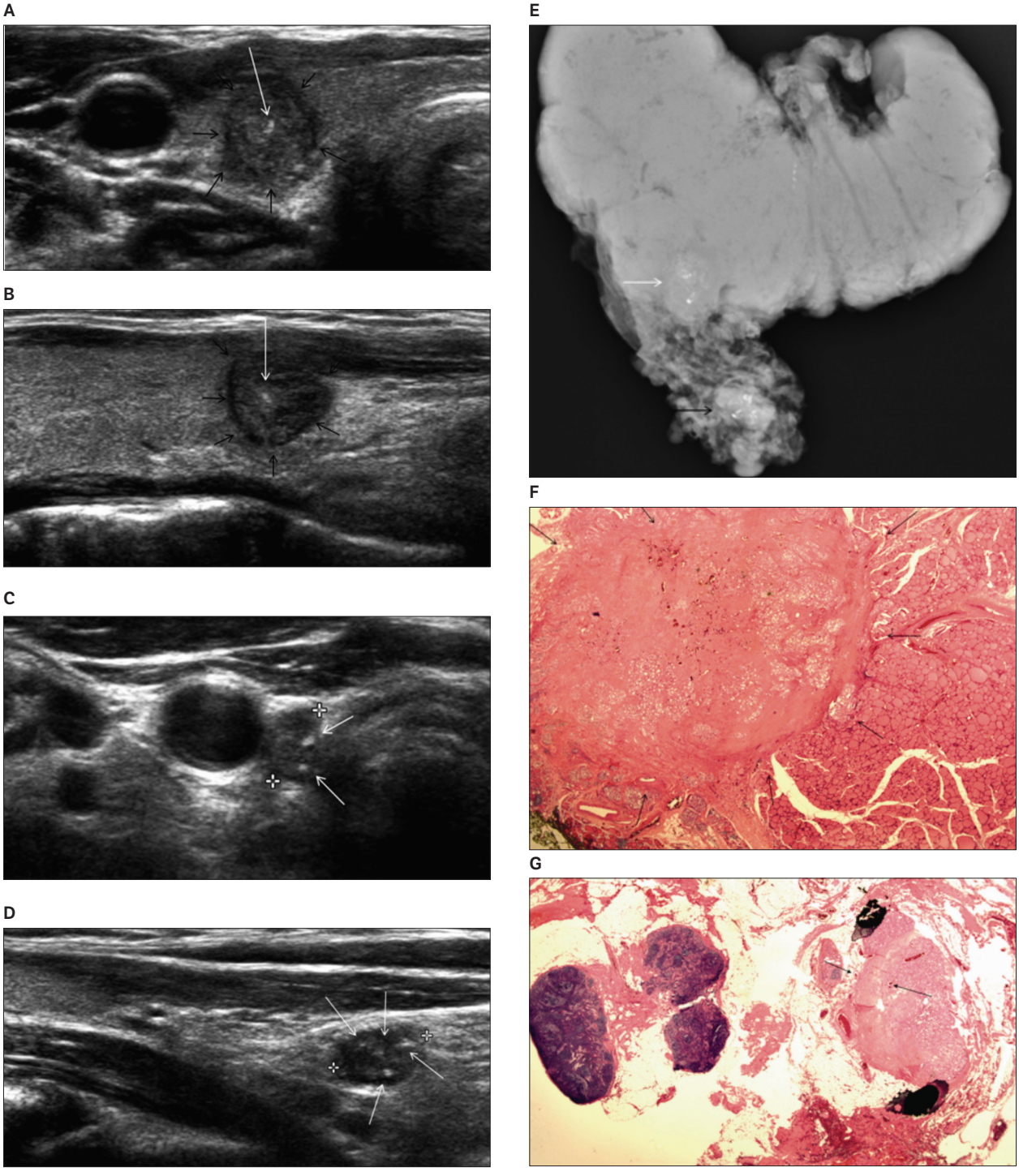
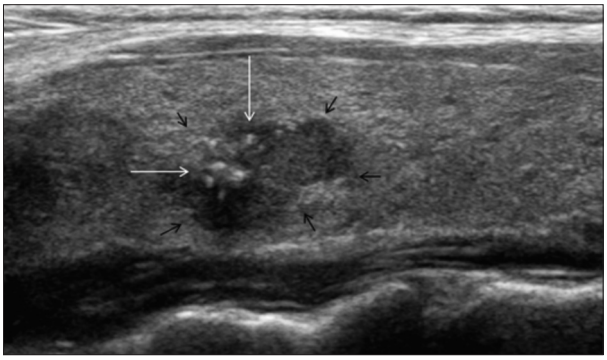


Figure 3. Diffuse sclerosing variant of papillary thyroid carcinoma in a 33-year-old woman. **A** and **B**, Transverse and longitudinal sonograms of the left thyroid gland showing a poorly defined hypoechoic mass (black arrows) and microcalcifications (white arrows) both within and outside the mass. **C**, Specimen radiograph showing diffusely scattered microcalcifications (white arrows) and dystrophic calcifications (black arrows) in the left thyroid gland. **D**, Pathologic specimen showing a main mass with conglomerated cancer foci (black arrows) and abundant psammoma bodies (blue arrows; hematoxylin-eosin, original magnification ×100). **E**, Pathologic specimen showing psammoma bodies (black arrows) also located outside the main mass. The final diagnosis was confirmed as the diffuse sclerosing variant (hematoxylin-eosin, original magnification ×100).

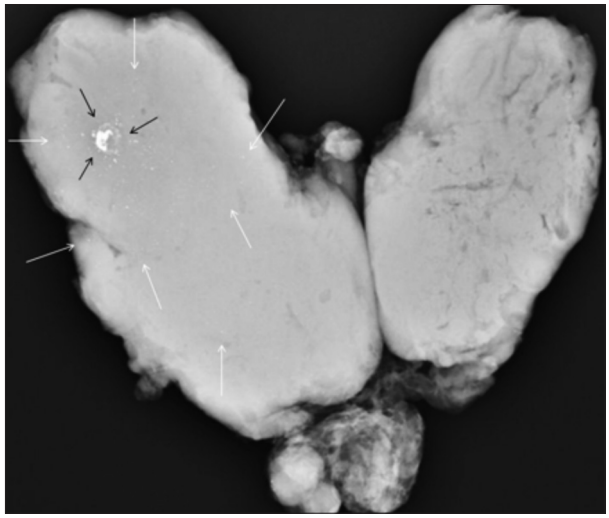
Figure 4. Diffuse sclerosing variant of papillary thyroid carcinoma in a 46-year-old woman. **A** and **B**, Transverse and longitudinal sonograms of the right thyroid gland showing a poorly defined hypoechoic mass (black arrows) with internal microcalcifications (white arrows). **C** and **D**, Transverse and longitudinal sonograms of the right central neck showing a suspicious lymph node containing internal microcalcifications (white arrows). **E**, Specimen radiograph showing amorphous microcalcifications in the right thyroid gland (white arrow) and the right central neck (black arrow). **F**, Pathologic specimen showing a mass within the thyroid gland (black arrows; hematoxylin-eosin, original magnification ×100). **G**, Pathologic specimen showing psammoma bodies (black arrows) in the right central neck lymph node, suggesting metastasis (hematoxylin-eosin, original magnification ×100).



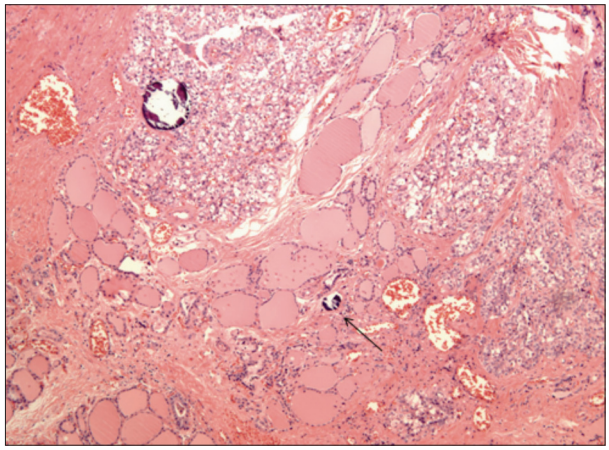
A



B



C



D

Figure 5. Diffuse sclerosing variant of papillary thyroid carcinoma in a 35-year-old woman. **A** and **B**, Transverse and longitudinal sonograms of the right thyroid gland showing a poorly defined hypoechoic mass (black arrows) with internal microcalcifications (white arrows). **C**, Specimen radiograph showing dystrophic calcifications (black arrows) and additional areas of scattered microcalcifications (white arrows) consisting of a broader extent of the right thyroid gland compared to the sonograms. **D**, Pathologic specimen showing psammoma bodies (black arrow), which are located outside the main mass (hematoxylin-eosin, original magnification ×100).

Conclusions

Although sonography is an essential modality in the evaluation of thyroid nodules, specimen radiography is more sensitive than sonography for detection of microcalcifications of thyroid carcinoma, especially in the diagnosis of the diffuse sclerosing variant of papillary thyroid carcinoma. However, new diagnostic techniques that can detect microcalcifications in the thyroid along with the disease extent and that can be performed preoperatively have not yet been established. This new technique is expected to be of further use in the future, thus helping management for patients with thyroid carcinoma.

References

1. Pacini F, Schlumberger M, Dralle H, Elisei R, Smit JW, Wiersinga W; European Thyroid Cancer Taskforce. European consensus for the management of patients with differentiated thyroid carcinoma of the follicular epithelium. *Eur J Endocrinol* 2006; 154:787–803.
2. Lew JI, Solorzano CC. Use of ultrasound in the management of thyroid cancer. *Oncologist* 2010; 15:253–258.
3. Kim EK, Park CS, Chung WY, et al. New sonographic criteria for recommending fine-needle aspiration biopsy of nonpalpable solid nodules of the thyroid. *AJR Am J Roentgenol* 2002; 178:687–691.
4. Kwak JY, Kim EK, Hong SW, Kim MJ, Moon HJ, Park CS. Value of specimen radiographs in diagnosing multifocality of thyroid cancer. *Br J Surg* 2010; 97:517–524.

5. Zhang Y, Xia D, Lin P, Gao L, Li G, Zhang W. Sonographic findings of the diffuse sclerosing variant of papillary carcinoma of the thyroid. *J Ultrasound Med* 2010; 29:1223–1226.
6. Kwak JY, Kim EK, Hong SW, et al. Diffuse sclerosing variant of papillary carcinoma of the thyroid: ultrasound features with histopathological correlation. *Clin Radiol* 2007; 62:382–386.
7. Lee JY, Shin JH, Han BK, et al. Diffuse sclerosing variant of papillary carcinoma of the thyroid: imaging and cytologic findings. *Thyroid* 2007; 17:567-573.
8. Kwak JY, Kim EK, Hong SW, et al. Diffuse slcerosing variant of papillary carcinoma of the thyroid gland: specimen radiographic features with histopathological correlation. *J Clin Endocrinol Metab* 2009; 94:1491–1492.
9. Chow SM, Chan JK, Law SC, et al. Diffuse sclerosing variant of papillary thyroid carcinoma: clinical features and outcome. *Eur J Surg Oncol* 2003; 29:446–449.
10. Lam AK, Lo CY. Diffuse sclerosing variant of papillary carcinoma of the thyroid: a 35-year comparative study at a single institution. *Ann Surg Oncol* 2006; 12:176–181.
11. Caplan RH, Wester S, Kisken AW. Diffuse sclerosing variant of papillary thyroid carcinoma: case report and review of the literature. *Endocr Pract* 1997; 3:287–292.
12. Fujimoto Y, Obara T, Ito Y, Kodama T, Aiba M, Yamaguchi K. Diffuse sclerosing variant of papillary carcinoma of the thyroid: clinical importance, surgical treatment and follow-up study. *Cancer* 1990; 66:2306–2312.
13. Kobayashi K, Fukata S, Amino N, Miyauchi A. A case with diffuse sclerosing variant of papillary carcinoma of the thyroid: characteristic features on ultrasonography. *J Med Ultrasonics* 2006; 33:159–161.
14. Kwak JY, Kim EK, Son EJ, et al. Papillary thyroid carcinoma manifested solely as microcalcifications on sonography. *AJR Am J Roentgenol* 2007; 189:227-–231.
15. Martin-Pérez E, Larrañaga E, Serrano P. Diffuse sclerosing variant of papillary carcinoma of the thyroid. *Eur J Surg* 1998; 164:713–715.