Columnar Cell Variant of Papillary Thyroid Carcinoma: Cytomorphological Characteristics of 11 Cases With Histological Correlation and Literature Review

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BACKGROUND: The columnar cell variant of papillary thyroid carcinoma (PTC-CCV) is a rare entity that demonstrates a more aggressive clinical course compared with the more common subtypes of PTC. On histology, it is defined by papillae or gland-like structures lined by columnar cells displaying prominent nuclear stratification. Because to the authors' knowledge no characteristic cytomorphological features have been identified to date and typical features of PTC often are absent on cytology, the diagnosis of PTC-CCV by fine-needle aspiration (FNA) is challenging. This prompted the authors to evaluate a series of PTC-CCV cases to identify features that could facilitate its diagnosis by FNA. **METHODS:** A total of 11 surgical specimens of PTC-CCV with corresponding preoperative cytology were identified over a 21-year period. The cytological features of the aspirated specimens, consisting mostly of Papanicolaou and Diff-Quick smears, were evaluated retrospectively. **RESULTS:** All cases demonstrated the presence of papillary structures. The most important features observed in PTC-CCV FNA specimens were hypercellularity with nuclear superposition and a paucity of nuclear pseudoinclusions and grooves. **CONCLUSIONS:** Although PTC-CCV may demonstrate features that overlap with those of the classic variant of PTC, hypercellular smears with papillary structures covered by cells with pseudostratified nuclei that show a paucity of nuclear pseudoinclusions and grooves should alert the cytopathologist to the possibility of this diagnosis. ***Cancer Cytopathol* 2017;125:389-97**. *© 2017 American Cancer Society.*

KEY WORDS: columnar cell variant; differential diagnosis; fine-needle aspiration (FNA); papillary thyroid carcinoma (PTC); thyroid cancer.

INTRODUCTION

The most common thyroid cancer is papillary thyroid carcinoma (PTC), which represents up to 80% of all thyroid cancers.[1] Although its global incidence has been increasing over the last decades, when its most common variants (ie, classic and follicular) are considered, the prognosis is very good and the mortality rate remains very low.[2,3] Conversely, so-called "aggressive variants of PTC" have been described, with a behavior that is intermediate between the common variants and poorly differentiated thyroid carcinomas. However, some experts have asserted that the prognosis of this group of tumors is related more to their clinical stage at the time of presentation than to the histological type itself, because circumscribed/encapsulated or small tumors demonstrate a better

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prognosis.[4-8] Thus, there still is debate concerning the inherent aggressiveness of these variants, which is complicated by the rarity of each individual subtype and of the group as a whole.

One common definition of "aggressive variants of PTC" encompasses the tall cell, diffuse sclerosing, solid, hobnail, and columnar cell variants.[9-14] Among these, the most misdiagnosed and underrecognized entity most likely is the columnar cell variant of PTC (PTC-CCV). Originally described by Evans et al in 1986, PTC-CCV is a rare entity that accounts for 0.15% to 0.4% of all PTC cases.[4,14-16] On histology, it is defined by the presence of papillae or gland-like structures lined by columnar cells demonstrating prominent nuclear stratification.[17] Because intranuclear pseudoinclusions and nuclear grooving often are absent, and to our knowledge no characteristic cytomorphological features have been identified to date, the diagnosis of PTC-CCV on fine-needle aspiration (FNA) represents a notable challenge for the cytopathologist.

However, considering that PTC-CCV represents an aggressive variant of PTC potentially portending an unfavorable prognosis, its correct preoperative identification on FNA cytology could be useful in guiding the initial surgical management.[14]

To our knowledge, to date only 8 cases with FNA findings of PTC-CCV have been described in 7 case reports.[18-24] The current study presents a cytological series of 11 cases of PTC-CCV from 10 patients, with the objective of defining the cytomorphological features of this entity that can help to suggest its diagnosis on FNA material.

MATERIALS AND METHODS

Case Identification

Pathology reports from the electronic archives of the study institutions were searched for cases of surgically resected PTC-CCV with corresponding preoperative cytology during the 21-year period from 1994 through 2015. Of the 14 cases identified, 2 were excluded because the columnar cell component represented <80% of the tumor volume. One additional case was excluded because cytological slides were not available for review. Histological diagnosis of the remaining cases that were retrieved was confirmed according to the current World Health Organization classification of tumors of endocrine organs.[3]

Thus, the study series was composed of 11 samples obtained from 10 patients: 6 cases from the Pathology Unit of the Arcispedale Santa Maria Nuova-IRCCS in Reggio Emilia, Italy; 2 cases from the Institute of Pathology in Locarno, Switzerland; 2 cases from the Department of Pathology at Haydarpasa Numune Education and Research Hospital in Turkey; and 1 case from the Department of Clinical Pathology at Geneva University Hospitals in Geneva, Switzerland. Clinicopathological information (including patient age, sex, prior medical history, imaging, and thyroid function tests) was retrieved for each patient, if available.

All cytological cases consisted of 5 to 15 alcohol-fixed, Papanicolaou-stained tests. In addition to the Papanicolaou-stained slides, 8 cases included air-dried, Diff-Quik-stained and May-Grunwald-Giemsa stained smears and 2 cases included liquid-based preparations. One of these cases (a primary tumor and its lymph node metastasis) has already been reported.[25]

Cytomorphologic Features

All cases were individually revised by 2 expert cytopathologists (M.B. and S.P.) who analyzed them for a series of architectural (cellularity, presence of papillae, microfollicles, colloid, necrosis, and psammoma bodies), cellular (cell size, presence of single cells, elongated cells, polygonal cells, and giant cells), and nuclear (chromatin appearance, presence of pseudostratified nuclei, nuclear atypia, nucleoli and mitosis, intranuclear pseudoinclusions, and nuclear grooves) features. For the majority of cytological features, only their presence or absence was recorded. For cellularity, cell size, chromatin appearance, nuclear atypia, and nucleoli, the predominant pattern was recorded: low versus high cellularity, small-to-medium versus medium-to-large cells, clear/ground glass versus dark/densely packed chromatin, absent/mild versus moderate/severe nuclear atypia, and conspicuous versus inconspicuous nucleoli. A more detailed score was used for intranuclear pseudoinclusions and grooves, which represent crucial findings in thyroid cytopathology. If these features were identified easily on each slide, then they were scored as present/abundant. If a thorough search was necessary to identify some nuclei with these features, then they were scored as present/scarce. If they were absent after a thorough search, then they were registered as such.

TABLE 1. Clinicopathologic Data

No. of cases		11
No. of patients		10[a]
Mean age (SD), y		49.4 (+/− 8.6)
Sex (female/male)		7/3
Average tumor diameter (range), mm		31.6 (9-100)
Histological diagnosis	PTC-CCV, pure	9
	Mixed: 90% PTC-CCV, 10% PDTC	1
	Metastatic PTC-CCV	1
Original cytological diagnosis	PTC, NOS	8
	PTC (suspicion of possible CCV)	1
	Suspicious for PTC (rule out MTC)	1
	Metastatic PTC, NOS	1

Abbreviations: MTC, medullary thyroid carcinoma; PDTC, poorly differentiated thyroid carcinoma; PTC-CCV, papillary thyroid carcinoma, columnar cell variant; PTC, NOS, papillary thyroid carcinoma, not otherwise specified; SD, standard deviation.
[a] One patient had undergone 2 fine-needle aspirations: one of the primary tumor and one of a lymph node metastasis.

RESULTS

Clinical Findings of PTC-CCV

The main clinical features are summarized in Table 1. The study series included 7 women and 3 men, with a mean age of 49.4 ± 8.6 years. One man underwent 2 FNAs: 1 from a thyroid nodule and the other from a metastatic lymph node that manifested 1 year later. The average size of the tumors was 31.6 ± 30.5 mm. It is interesting to note that none of the cases had been diagnosed cytologically as PTC-CCV (Table 1). On FNA, 9 cases, including the metastatic lymph node, were diagnosed as "PTC, not otherwise specified (NOS)"; 1 case was diagnosed as "PTC, NOS" but the possibility of the PTC-CCV variant was suggested in a note; and 1 case was diagnosed as "suspicious for PTC, rule out medullary thyroid carcinoma (MTC)."

Cytohistological Features

The cytological findings of the 11 cases are reported in Table 2. All cases were hypercellular (Fig. 1A). Papillary structures were observed in all cases (Fig. 1B); 3 cases had papillary architecture mixed with a syncytial/honeycomb pattern (Fig. 1C) and 3 cases had papillary architecture mixed with microfollicular structures. In one case, a cribriform pattern also was observed (Fig. 1D). Colloid deposits were evident in 6 cases (54.5%), whereas necrotic debris and psammoma bodies were never encountered.

TABLE 2. Cytomorphologic Features of 11 Thyroid FNA Specimens of PTC-CCV

Cytomorphologic Features		No. (%)
Architectural	Cellularity (high)	11 (100)
	Papillae	11 (100)
	Microfollicles (associated with papillary architecture)	3 (27.3)
	Colloid	6 (54.5)
	Necrosis	0 (0)
	Psammoma bodies	0 (0)
Cellular	Cell size (medium/large)	11 (100)
	Single cells	11 (100)
	Elongated cells	9 (82.0)
	Polygonal cells	4 (36.4)
	Giant cells	0 (0)
Nuclear	Chromatin appearance (dark/densely packed)	9 (82.0)
	Pseudostratified nuclei (nuclear crowding)	11 (100)
	Nuclear atypia (absent/mild)	10 (91.0)
	Nucleoli (Inconspicuous)	9 (82.0)
	Mitoses	1 (9.0)
	Intranuclear pseudoinclusions (absent)	8 (72.7)
	Intranuclear pseudoinclusions (present/scarce)	3 (27.3)
	Intranuclear pseudoinclusions (present/abundant)	0 (0)
	Nuclear grooves (absent)	4 (36.4)
	Nuclear grooves (present/scarce)	5 (45.5)
	Nuclear grooves (present/abundant)	2 (18.1)

Abbreviations: FNA, fine-needle aspiration; PTC-CCV, papillary thyroid carcinoma, columnar cell variant.

In all cases, medium/large cells and single cells (Fig. 2A) were noted; the cellular silhouette was mostly elongated (9 cases; 82%), with polygonal cells encountered in only 4 cases (36.4%). Giant cells were absent. Chromatin was predominantly dark/densely packed and granular in 9 of the 11 cases (82%) (Fig. 2B) and clear in the remaining 2 cases (18%). Nuclear pseudostratification (nuclear crowding) was observed in all cases (Figs. 2C and 2D); this aspect can give the cytopathologist the false impression of nuclear hyperchromasia. Absent/mild nuclear atypia was observed in nearly all cases (10 cases; 91%); the remaining case demonstrated enlarged nuclei and nuclear pleomorphism. Nucleoli were predominantly inconspicuous (9 cases; 82%) and only in 1 case did we observed 2 mitoses. Intranuclear pseudoinclusions were scarce despite the abundance of papillary structures; they were found in only 3 cases (27.3%) (Fig. 2E). Nuclear grooves were absent in 4 cases (36.4%), present in a low amount and after a thorough search in 5 cases (45.5%), and easily recognized in only 2 cases (18%) (Fig. 2F).

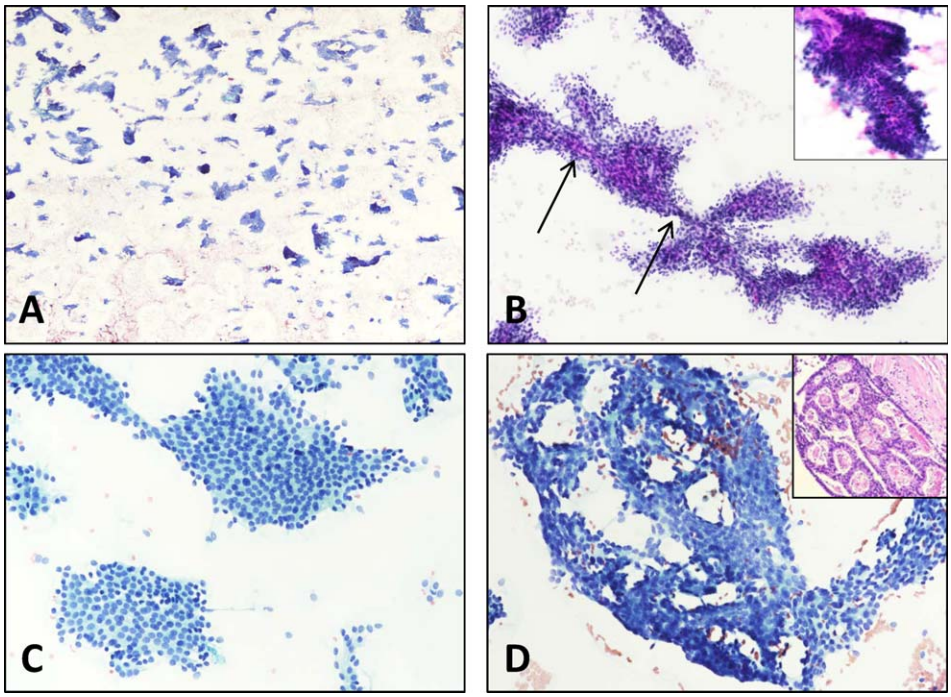

Figure 1. Architectural pattern of the columnar cell variant of papillary thyroid carcinoma. (A) A hypercellular smear composed of flat aggregates of cells (Papanicolaou stain, original magnification ×100). (B) Papillary structures with an inner fibrovascular core (arrows) and (*Inset*) peripheral cells with pseudostratified nuclei that gave the impression of a pseudohyperchromatic smear. The cytological diagnosis was that of papillary thyroid carcinoma, not otherwise specified. The histological diagnosis was that of the columnar cell variant of papillary thyroid carcinoma (Papanicolaou stain, original magnification ×200; *Inset*: Papanicolaou stain, original magnification ×400) (C) Flat sheet of cells in a honeycomb/syncytial arrangement (Papanicolaou stain, original magnification ×200). (D) In a different case, a cribriform pattern also was observed (Papanicolaou stain, original magnification ×100). *Inset*: corresponding histological specimen (H & E, original magnification ×400).

Based on these findings, the cytological features that are helpful in distinguishing a PTC-CCV variant are: 1) the presence of a hypercellular smear comprised of papillary structures and dispersed single cells and lacking necrosis; 2) the presence of cellular crowding and pseudostratified nuclei with dark chromatin without atypia, nucleoli, or mitosis; and 3) scarce/absent nuclear pseudoinclusions and predominantly scarce/absent nuclear grooves. The paucity of these last 2 features, which are the hallmarks of the classic variant of PTC, is a peculiar characteristic of PTC-CCV and should alert the cytopathologist to the possibility of this diagnosis.

On histology, all cases demonstrated papillary structures with branches covered by pseudostratified and elongated cells. Cribriform structures also were evident in 4 cases. Nuclei were hyperchromatic and centrally located with pseudostratification. Nuclear grooves and pseudoinclusions were present but in a lower amount compared with the classic variant of PTC; pseudoinclusions were completely absent in 5 cases (Figs. 3A-3D).

DISCUSSION

PTC-CCV has long been recognized as an independent entity.[15] It recently has come to the attention of pathologists due to the unexpected and controversial immunohistochemical finding of the expression of CDX2 (caudal type homeobox 2), which has been considered as a putative differentiation marker.[26-29]

Histologically, PTC-CCV differs from the conventional variant of PTC because of the presence of papillae or gland-like structures lined by pseudostratified columnar cells demonstrating prominent nuclear stratification. Occasional subnuclear or supranuclear cytoplasmic vacuoles, reminiscent of secretory endometrium, have been observed on histology. Because the nuclear features of PTC are not well represented in the CCV, these tumors may be mistaken for metastatic intestinal, endometrial, or pulmonary adenocarcinomas, from which they can be distinguished because of immunohistochemical positivity for both thyroglobulin and thyroid transcription factor 1 (TTF-1). To

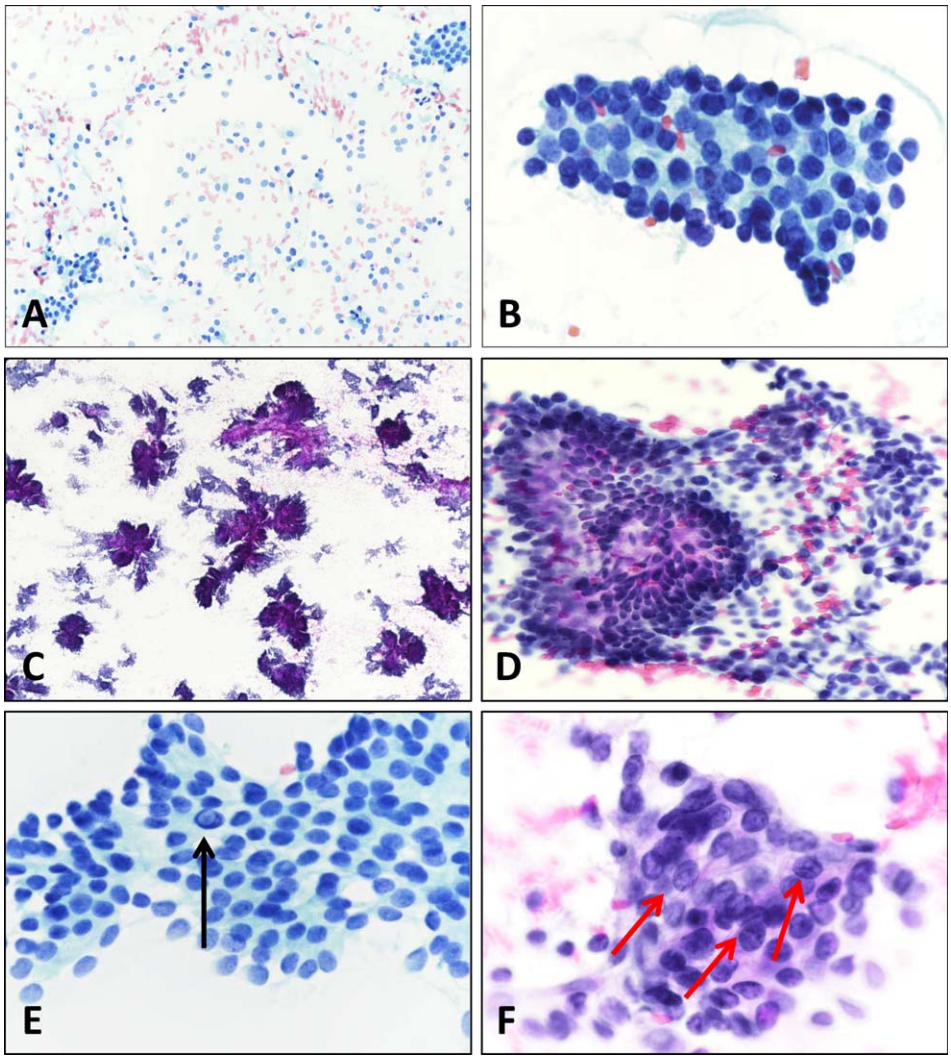

Figure 2. Cytologic features of the columnar cell variant of papillary thyroid carcinoma. (A) A hypercellular smear with a population of discohesive single cells (Papanicolaou stain, original magnification ×200). (B) Chromatin was predominantly densely packed and granular (Papanicolaou stain, original magnification ×400). (C) Crowded groups of cells with nuclear pseudohyperchromasia (Papanicolaou stain, original magnification ×100). (D) In the same patient, pseudostratified nuclei were observed at the periphery of the groups (Papanicolaou stain, original magnification ×200). (E) A different case showed flat sheets of cells with rare pseudoinclusions (arrows). In this case, the cytological diagnosis was papillary thyroid carcinoma, not otherwise specified; at histology, the columnar cell variant of papillary thyroid carcinoma was diagnosed (Papanicolaou stain, original magnification ×400). (F) A fragment containing follicular cells with clearer chromatin and easily identified nuclear grooves (arrow) and without nuclear pseudoinclusions. Nucleoli were inconspicuous (Papanicolaou stain, original magnification ×400).

the best of our knowledge, there is no clear consensus regarding the minimal percentage of columnar cells that confers a diagnosis of PTC-CCV, with reported cases varying from 30% to 80%[4,14,16]; all cases analyzed in the current study demonstrated a CCV component of ≥80% (cases with lower percentages were excluded).

Cytologically, PTC-CCV is far less characterized because it is rare and it has been believed to lack distinguishing cytomorphological features. Although these lesions sometimes can be diagnosed as PTC on FNA, they rarely are subcategorized as CCV. After the initial description of PTC-CCV by Evans et al,[15] a few case reports have attempted to define the cytomorphological features characterizing this entity. To our knowledge, to date only 8 cases of PTC-CCV and 2 cases of mixed PTC-CCV/tall cell variant (TCV) have been described in the cytological literature; the details of such cases are summarized in Table 3.[18-24] It is interesting to note that none of these cases was diagnosed as CCV on FNA cytology, and a diagnosis of PTC had been made in only 3 cases. This most likely is

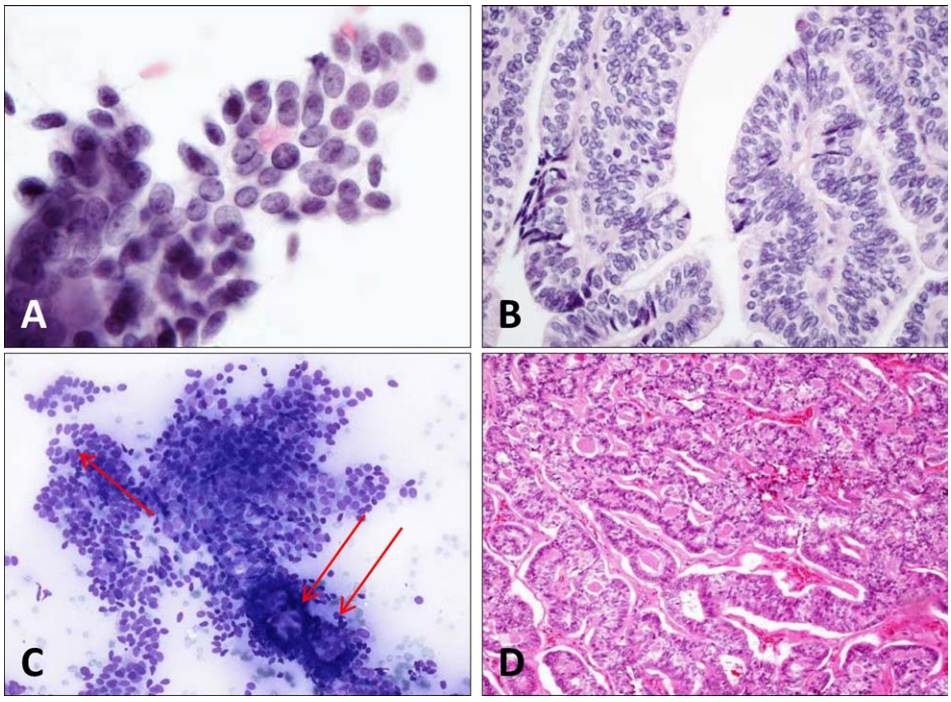

Figure 3. Cytohistological correlation in the columnar cell variant of papillary thyroid carcinoma. (A) A pseudopapillary structure composed of cells with clear chromatin and no nuclear pseudoinclusions (Papanicolaou stain, original magnification ×400). (B) The corresponding histological specimen showing papillary structures, clear nuclei, and nuclear stratification. Classic features of papillary thyroid carcinoma, namely nuclear pseudoinclusions and abundant grooves, were completely absent throughout the lesion (H & E, original magnification ×200). (C) In this case, the growth pattern on cytology was mostly solid and follicular (arrows) (May-Grunwald-Giemsa stain, original magnification ×200). (D) The corresponding histological specimen showed trabecular architecture with well-formed follicles (H & E, original magnification ×200).

because nuclear grooving and intranuclear pseudoinclusions (features that define the classic PTC variant) are present only rarely and in a minority of CCV cases; in fact, in the 8 published cases, they were reported as occasional findings in 4 and 2 cases, respectively.[18-24] As a case in point, one case of PTC-CCV was misdiagnosed as respiratory epithelium due to nuclear pseudostratification and the absence of nuclear grooves and intranuclear cytoplasmic inclusions; a case of PTC metastatic to a parotid gland was mistaken for a primary salivary gland neoplasm due to hypercellularity.[20,22]

From an architectural standpoint, papillary fragments were present in all 8 cases described to date (Table 3),[18-24] on either conventional smears or cell block preparations; other patterns that occasionally were identified included glandular/acinar structures (3 of 8 cases; 37.5%), monolayered sheets (3 of 8 cases; 37.5%), microfollicles (2 of 8 cases; 25%), and syncytial aggregates (2 of 8 cases; 25%). Only in 1 case were single cells found to be exclusively present. Columnar cells were observed in 7 cases, in 4 of which they demonstrated prominent pseudostratification; spindle morphology coexisted with the columnar one in 2 cases. The generally moderate-to-abundant cytoplasm sometimes was vacuolated (3 of 8 cases; 37.5%) and the nuclei were mostly oval to elongated (5 of 8 cases; 62.5%), with a chromatin described as stippled/granular (5 of 6 cases; 83%). Nucleoli, when described, most often were inconspicuous (3 of 5 cases; 60%).

The cytological features of both the TCV and CCV (ie, abundant nuclear grooving and intranuclear pseudoinclusions) associated with columnar cell and nuclear pseudostratification were described by Putti et al; Tranchida et al also observed frequent grooves and inclusions in the CCV component in a mixed (TCV and CCV) case.[30,31]

To the best of our knowledge, the current analysis of 11 samples (including 10 primary lesions and 1 metastatic lesion) exceeds the total number of isolated cases previously published, and it comprises PTC-CCV with an extensive columnar cell component (≥80%). In our practice, we have faced all the aforementioned diagnostic difficulties that hinder the correct identification of the CCV: indeed, 10 cases were diagnosed as "PTC, NOS" and the

TABLE 3. Clinicopathological and Cytomorphological Characteristics of Previously Reported PTC-CCV Cases

					Cytomorphological Features								
Patient No.	Study	Sex/Age, Years	Clinical Presentation	Lobe, Tumor Size, cm	Architecture	Colloid	Cell Shape	Cytoplasm	Nuclei	Chromatin	Nucleoli	Intranuclear Pseudoinclusions	Nuclear Grooving	Cytological Diagnosis
1	Hui 1990[18]	Female/21	Progressively enlarging nodule	Right, 1.5	Papillary, glandular	Absent	Pseudostratified columnar	Light-staining, tapering	Perpendicularly oriented, dark-staining, oval to elongated	Finely stippled	Indistinct	Absent	Occasional	Neoplastic/ carcinoma?
2	Perez 1998[19]	Male/77	Rapidly enlarging cervical mass, dyspnea, dysphagia, voice hoarseness	Right, 9.0	Scattered clusters, papillary fronds; cell block shows papillary and glandular formations	NR	Moderately large with sharp borders; cell block shows stratified columnar epithelial cells	Moderate to abundant, vacuolated; cell block shows subnuclear and supranuclear cytoplasmic vacuoles	Mostly round	Finely granular	Small, multiple	Absent	Occasional	PTC
3	Perez 1998[19]	Female/41	Asymptomatic cervical mass	Left, 3.6	Highly cellular monolayered sheets, syncytial-type cell aggregates; cell block shows papillary and microfollicular fragments	NR	Columnar cells with poorly defined cell borders; cell block shows columnar pseudostratified cells	Indistinct	Oval to elongated	Powdery	Inconspicuous	Absent	Absent	PTC
4	Jayaram 2000[20]	Female/27	Cervical nodule	Right, 4.0	Acinar pattern, occasional papillary fragments	Absent	Homogeneous population of tall columnar cells	Occasional vacuolation	Oval, elongated, pseudostratified	NR	NR	Absent	Absent	Contamination by respiratory epithelium
5	Ylagan 2004[21]	Female/24	Cervical nodule	Left, 3.0	Loosely cohesive papillary clusters, sheets, microfollicles	Absent	NR	NR	Oval, larger than in normal follicular cells	Evenly dispersed, granular	NR	Absent	Absent	MTC
6	Kini 2003[22]	Female/65	Slowly growing, painless left parotid mass	Left parotid, 7.0	Loosely cohesive sheets, groups, occasional papillary fragments, single cells	NR	Columnar to spindle-shaped	Moderate to abundant, cyanophilic	Eccentrical to central, oval to elongated, pleomorphic	NR	NR	Present	Present	Suspicion of primary parotid neoplasm
7	Sen 2014[23]	Fenmale/58	Progressively enlarging cervical nodule	Right, 3.5	Papillary fronds, rosettes, syncytial sheets	NR	Columnar cells showing prominent pseudostratification	Wispy	Nucleomegaly, anisonucleosis	Stippled	Occasional, inconspicuous	Rare	Frequent	PTC
8	Verma, 2016[24]	Female/21	Solitary cervical nodule	Isthmus, 2.0	Monolayered sheets, small clusters, few papillary fragments	Absent	Spindle to columnar	Vacuolated	Round	Stippled	Inconspicuous	Absent	Absent	MTC

Abbreviations: MTC, medullary thyroid carcinoma; NR, not reported; PTC, papillary thyroid carcinoma; PTC-CCV, papillary thyroid carcinoma, columnar cell variant.

remaining case was diagnosed as "PTC, rule out MTC." Surprisingly, none of the cases in the current study has been cytologically diagnosed as a metastatic tumor because only 1 patient had a previous history of colonic adenocarcinoma.[25] If relatively common malignancies such as colonic/endometrial adenocarcinoma are present in the patient's history, they might mislead the cytological diagnosis of PTC-CCV (discussed further below).

Similar to those reported so far, the cases in the current study demonstrated high cellularity and were composed mostly of papillary structures, monolayered fragments, syncytial aggregates, and microfollicular structures. Cells were medium to large in size and predominantly elongated. We noticed in the study cases of PTC-CCV a predominance of nuclei with densely packed chromatin and pseudostratified (crowded) nuclei, which confer to the smear a dark, pseudohyperchromatic appearance. In the reported cases (Table 3),[18-24] the appearance of the chromatin was quite different. Despite the presence of rare intranuclear pseudoinclusions (27.3%) and nuclear grooves (easily identified in 2 cases and visible only after a thorough search in another 5 cases), the diagnosis of PTC was not missed in any of the cases in the current study; this is in contrast to previously reported cases (Table 3)[18-24]: only 3 of the 8 cases were diagnosed as PTC. The presence of other diagnostic criteria for PTC in the current series, namely remarkable hypercellularity and papillary structures, most likely compensated for the lack of intranuclear pseudoinclusions and nuclear grooves. In one case, the diagnosis of PTC-CCV was suggested in a comment on the cytology report. Other cytological features typical of PTC, such as psammoma bodies and giant cells, were not observed in the current study cases.

The hyperchromatic nuclei and paucity of intranuclear pseudoinclusions could suggest MTC; in this instance, immunocytochemistry for thyroglobulin and calcitonin is mandatory.[24] In the cases in the current study, the diagnosis of MTC was suggested in only one case, yet immunocytochemistry was not performed to definitively rule out this possibility. Conversely, immunohistochemistry was performed on another case, the FNA specimen from the metastatic lymph node, because the patient had a previous history of colonic adenocarcinoma. In fact, the differential diagnosis with a metastatic process can be difficult, especially in patients with a known history of previous malignancies. Pseudostratified nuclei and CDX2 expression could raise suspicion of a metastatic colonic carcinoma.[10,26] However, true papillae are rare in the latter, whereas necrosis is more common.[18] The intense immunoreactivity for TTF-1 definitively helps to rule out a metastatic colon carcinoma.[25] In contrast to the other aggressive variants of PTC (TCV and the diffuse sclerosing variant) that demonstrate some particular ultrasonographic features (ie, microlobulated, markedly hypoechoic nodules with microcalcifications and extrathyroidal extension) and high [^{18}F]fluorodeoxyglucose uptake, PTC-CCV is not known to present with any specific radiologic characteristic.[32-34]

Conclusions

The cytological diagnosis of PTC-CCV is challenging because of its rarity and the consequent lack of relevant experience in the cytopathology community. However, some characteristic cytological features do exist: hypercellular smears composed almost exclusively of papillary structures with pseudostratified nuclei associated with rare nuclear grooves and intranuclear pseudoinclusions are highly suggestive of PTC-CCV.

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CONFLICT OF INTEREST DISCLOSURES

The authors made no disclosures.

AUTHOR CONTRIBUTIONS

Massimo Bongiovanni: Conceptualization, methodology, validation, investigation, writing–original draft, writing–review and editing, and supervision. **Maxime Mermod**: Methodology, formal analysis, investigation, writing–original draft, writing–review and editing, and visualization. **Sule Canberk**: Validation, resources, writing–original draft, and visualization. **Chiara Saglietti**: Writing–original draft and writing-review and editing. **Gerasimos P. Sykiotis**: Writing–review and editing and visualization. **Marc Pusztaszeri**: Investigation, resources, writing–review and editing, and visualization. **Moira Ragazzi**: Data curation and visualization. **Luca Mazzucchelli**: Resources and writing–review and editing. **Luca Giovanella**: Conceptualization, validation, formal analysis, investigation, resources, data curation, and writing–review and editing. **Simonetta Piana**: Writing–review and editing.

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