

AGGRESSIVE VARIANTS OF PAPILLARY THYROID CARCINOMA

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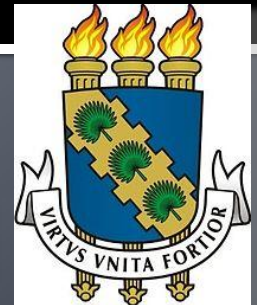
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Introdução

- Variantes histológicas agressivas de tumores bem diferenciados
- Células altas, colunares, esclerosante difusa e variáveis insulares
- Oncocítica, sólida e trabecular

Introdução

- Idade, sexo, invasão extracapsular, invasão intravascular e metástase
- Fator prognóstico tipo histológico ou apenas aumento de fatores de risco?

Variante de Células Altas

- Células colunares, grande quantidade de citoplasma granular
- Prevalência – 4 a 19%

Table 1. Tall cell variant of papillary thyroid carcinoma.

Report	No. cases or % of PTC	Pathology	Genetic	Comparative mortality
Hawk and Hazzard ⁷ 1976	18/197 (9%)	30% of cells 2× as long as they are wide, large cell size, granular cytoplasm, eccentric nuclei, pleomorphism		PTC 17/197 (8.6%) TCV 4/18 (22.2%)
Ostrowski et al ¹² 1996	11/92 (12%)	Leu M1 and ZC-23 positive in TCV but not in CPTC		At 43 months 33% LRR 36% DM 29% mortality At mean 16 years 0 mortality
Sywak et al ¹³ 2004	209 cases	67% ECS 57% nodes		At 5 years 25% LRR 22% DM 16% mortality
Machens et al ¹⁴ 2004	16/332 (5%)	50% nodes 31% DM		10 years CPTC 10% TCV 21%
Michels et al ¹⁵ 2007	56/503 (11%)			
DeLellis et al ⁸ 2004		"Composed predominately of cells whose heights are at least 3× their width"		
World Health Organization definition of TCV				
Ghossein and LiVolsi ¹⁷ 2008			High prevalence of <i>BRAF</i> somatic mutation	
Sheu et al ²⁰ 2009			High prevalence of <i>BRAF</i> mutation	

Abbreviations: PTC, papillary thyroid carcinoma; TCV, tall cell variant; CPTC, conventional papillary thyroid carcinoma; ECS, extracapsular spread; LRR, locoregional recurrence; DM, distant metastases.

Variante de Células Altas

- Leu M1 e ZC-23
- BRAF?
- Células Altas x Fatores de Risco

Variante de Células Colunares

- Prevalência de 0,15 a 0,2%
- Células altas com núcleo alongado hipercromático e pseudoestratificado
- Diferente histologicamente
- Clínica similar
- Tratamento cirúrgico agressivo

Table 2. Other variants of papillary thyroid carcinoma.

Series	Variant No. (%)	Pathology	Clinical	Prognosis
Evans ²² 1986	CCV 0.15% to 2% of all PTC	Tall cells with elongated hyperchromatic pseudostratified nuclei -- lack the cytologic nuclear features of TCV 30% of cells are columnar		
Sywak et al ¹³ 2004	CCV 41 cases	27% ECS, 50% nodes		At 43 months 33% LRR 36% DM 29% mortality

Variante Esclerosante Difusa

- Esclerose Difusa, infiltração linfocítica e corpos psammoma abundantes
- RET/PTC x BRAF
- Natureza infiltrante e tendência a metástase linfonodal – tratamento agressivo

Table 2. Other variants of papillary thyroid carcinoma.

Series	Variant No. (%)	Pathology	Clinical	Prognosis
Fujimoto et al ²⁴ 1990	DSPTC	Dense sclerosis, patchy lymphocytic infiltration, and abundant psammoma bodies		At mean 16 years, 0 mortality
Carcangiu and Bianchi ²⁹ 1989	DSPTC 15 cases		Greater incidence of cervical metastases, lung metastases	Decreased disease-free survival
Albareda et al ³⁰ 1998	7 DSPTC vs 76 CPTC			No difference in outcome
Falvo et al ³¹ 2006	83 DSPTC vs 183 CPTC		Higher aggressiveness, diffuse intrathyroid growth, and high incidence of nodes and DM	
Thompson et al ³² 2005	DSPTC 22 cases		Diagnosis of this entity should lead the clinician to aggressively manage these patients	

Variante Sólida / Trabecular

- Arranjo arquitetural, características citológicas usuais
- 37% dos tumores Chernobyl

Table 2. Other variants of papillary thyroid carcinoma.

Series	Variant No. (%)	Pathology	Clinical	Prognosis
Sywak et al ¹³ 2004	Solid trabecular	Cord-like architectural arrangement of typical PTC cells	37% of the radiation induced thyroid tumors among survivors of Chernobyl	High ECS 83% nodes More aggressive than CPTC Only 15 deaths
Nikiforov ³⁴ 2006	Solid trabecular 4000 reviewed		15 x increase preponderance among Chernobyl survivors	

Carcinoma Insular de Tireóide

- Ilhas de tumor em núcleos monomórficos, escurecidos, arredondados e citoplasma escasso
- Freqüentemente >4cm, expansão extracapsular, componente Papilífero/Folicular
- Predominante x Focal – pior prognóstico

Table 2. Other variants of papillary thyroid carcinoma.

Series	Variant No. (%)	Pathology	Clinical	Prognosis
Carcangiu et al ³⁵ 1984	Insular	nests or insulae of tumor cells uniformity, hypercellularity, and scant colloid	Often large tumors May be focal	
Akslen & LiVolsi ³⁸ 2000	Insular 16 focal 17 pre-dominant			Higher number of tumor-related deaths and DM with the predominantly insular vs focal group
Sywak et al ¹³ 2004	Insular 213 cases	44% ECS, 51% nodes	Tumor	Mean 72 months LRR or DM 64% Tumor mortality 32%

Abbreviations: CCV, columnar cell variant; PTC, papillary thyroid carcinoma; TCV, tall cell variant; ECS, extracapsular spread; LRR, locoregional recurrence; DM, distant metastases; DSPTC, diffuse sclerosing variant of papillary thyroid cancer, CPTC, conventional papillary thyroid carcinoma.

Câncer de Tireóide Pouco Diferenciado

- Presença de células malignas foliculares, presença de padrões sólido, trabecular e insular
- Mutação RAS

Table 3. Poorly differentiated thyroid carcinoma.

Report	Pathology	Genetic	Comparative mortality
Volante et al ³ 2007	Presence of malignant thyroid follicular cells, solid, trabecular and/or insular patterns, absence of typical PTC nuclei throughout, and the presence of either convoluted nuclei, necrosis, or mitoses.	PDTC are genetically homogeneous, <i>RAS</i> mutations being the almost exclusive genetic event.	A significant difference in survival was observed between the PDTC group and the well-differentiated group.

Abbreviations: PDTC, poorly differentiated thyroid carcinoma; PTC, papillary thyroid carcinoma; PDTC, poorly differentiated thyroid carcinoma.

Gradação x Variante Histológica

- Variante histológica – análise univariável
- Volume do tumor e gradação – sobrevida
- Grau 2 – atipia nuclear, necrose tumoral ou invasão vascular
- Fatores de risco = pior prognóstico – freqüente em variáveis agressivas

Tratamento

- Fatores de risco, estágio, gradação, tipo histológico
- Tireoidectomia, esvaziamento cervical, RIT, procura por metástase, RT

Conclusão

- Variantes potencialmente mais agressivas
- Fator preditivo independente baixo
- Fatores de risco e gradação
- Tratamento agressivo e procura de metástases
- RIT
- RT