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Original contribution

Prevalence and prognostic significance of tall cell variant of papillary thyroid carcinoma

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Summary The aim of this study was to assess the prevalence, prognostic factors, and long-term outcome of tall cell variant (TCV) in comparison with the conventional forms of papillary thyroid carcinoma (PTC). A total of 945 patients with thyroid cancer were treated and followed up from 1960 to 1998. Pathologic review was performed in 778 patients (84%) of the cohort. Of these, 674 had PTC: 503 (74%) had conventional form (CF); 56 (8%), TCV; and 155 (17%), other variants of PTC. Tall cell variant was associated with tumors of larger size ($P < .001$), bilaterality ($P < .02$), multifocality ($P < .04$), and extrathyroidal invasion ($P < .001$). Treatment was similar in both groups, but neck dissection was performed more frequently in patients with TCV ($P < .04$). The 10-year overall and event-free survival rates were, respectively, 90% and 85% in the CF versus 79% and 67% in the TCV group ($P < .001$). Histologic subtype did not have an effect on clinical outcome after multivariate analysis, the most relevant factors being age, involved nodes, or the "Metastasis, Age, Completeness, Invasion, Size" classification after multivariate analysis. In this large cohort of patients, TCV represents 8.3% of PTC, and it is a more aggressive form of PTC than CF because of the higher stage and increased grade.

1. Introduction

Papillary carcinoma is the most frequent differentiated thyroid carcinoma, representing 60% to 80% of all malignant thyroid tumors. Papillary thyroid carcinomas (PTC) are characterized by an excellent overall prognosis with long-term survival close, in some series, to that of a normal population of similar age [1], with a 5% incidence of tumor deaths [1] and a survival rate of more than 98% for young patients [2].

Within papillary carcinomas, numerous variants have been described in the last decades: follicular [3]; macrofollicular [4,5], with lymphocytic stroma reaction [6]; pseudo-Warthin [7-9]; and clear cell [10,11], which are considered to have the same good prognosis as the classic PTC. The prognosis of the oncocytic [12,13] and solid or trabecular variants [11] is still subject to controversy. The diffuse sclerosing [14], diffuse follicular [15,16], tall cell (TCV), and columnar cell variants are associated with a less favorable outcome.

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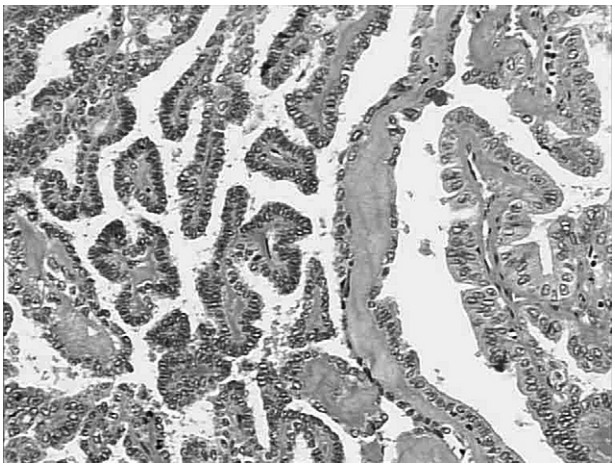

Fig. 1 Tall cell variant on the right hand, classic component on the left hand.

Although TCV was first described in 1976 by Hawk and Hazard [17]; it is still an underrecognized entity [18].The same applies for the seldom-occurring and recently described columnar cell carcinoma [19], which is sometimes difficult to differentiate from tall cell carcinoma with some mixed tall/columnar cell carcinomas [20,21]. There is a consensus in the literature that TCV and columnar cell carcinoma, in particular, the columnar cell variant, are clinically more aggressive. This poor prognosis has initially been ascribed to the histologic subtype, and hence, some authors emphasized the urgent need to properly diagnose these rarely occurring tumors to provide the most appropriate therapy [18].

The largest study published to date [22], challenged this prevailing opinion concerning the columnar cell variant, showing that the prognosis was related not to the histologic subtype but to the stage. Concerning the TCV, the literature is rather poor and confusing because some authors did not consider the stage, which is a prominent prognostic factor. Nonetheless, a recent study comparing different subtypes of PTC [23] concluded that not histologic subtype per se but histologic grade along with mitotic activity are the significant factors explaining the different prognosis.

The purpose of this retrospective study was to compare the clinicopathologic data, prevalence, and long-term outcome of patients with tall cell or columnar cell carcinomas with those of patients with conventional forms (CFs) of papillary carcinomas. Another aim was to consider the grade as described by Akslen [23] and the "Metasasis, Age, Completeness, Invasion, Size" (MACIS) classification, which is a prognostic scoring system coined at the Mayo Clinic [24].

2. Materials and methods

In 1996, both a prospective and retrospective study of all thyroid cancers originating from follicular cells was launched in the région de Basse Normandie, thanks to a computerized search of the files of the cancer registry and of the files of the pathology departments of the 2 hospitals involved in this study (University Hospital and the François Baclesse Comprehensive Cancer Center in Caen, Calvados, France), which allowed us to identify all patients with a diagnosis of thyroid carcinoma from January 1, 1960 to December 31, 1998. During this period, 945 patients with differentiated thyroid carcinoma were seen, and 875 (93%) were treated at either hospital. Information concerning demographic characteristics, medical history, clinical presentation, therapy administered, and outcome was available.

Patients originated from the 3 administrative areas (Calvados, Manche, and Orne) of the Basse-Normandie region. Women outnumbered men by a ratio of 5:1, and the mean age was 46 years (range, 7-87 years). Overall, 3% of the patients underwent previous cervical or mediastinal irradiation.

This study focused on carcinomas arising from follicular cells after exclusion of undifferentiated (anaplastic) carcinomas, thyroid lymphomas, medullary carcinomas, sarcomas, thyroid metastases, or thyroid invasion from another primary cancer located in the mediastinum or in adjacent organs.

After surgery, 68% of patients were given 1 to 16 therapeutic administrations of iodine 131 (^{131}I) for a median cumulative dose of 4.44 GBq. Cervical or mediastinal irradiation was administered to 54 (6%) of patients, 13 (5%) in the 281 patients with surgery only, and 41 (7%) after ^{131}I treatment.

Histologic review was performed by the same pathologist (M.J.J.) of all histologic slides, as follows:

1. Completion of a standardized form using the most recent nomenclature, with the aim to obtain the maximum histologic information, which was often missing in the initial pathologic report;
2. Updating and sometimes modifiying the original diagnosis, using immunohistochemistry whenever necessary, which allowed us to correct some ancient

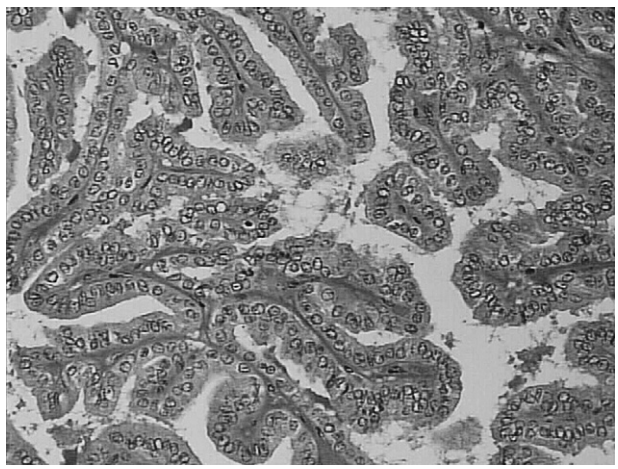

Fig. 2 Tall cell variant.