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Poorly Differentiated Thyroid Carcinoma: A Case Report

Carcinoma de tiroides pobremente diferenciado: reporte de un caso

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SUMMARY

Poorly differentiated thyroid carcinoma (PDTC) is a follicular cells neoplasm that shows limited follicular cell differentiation which is morphologically and behaviorally intermediate between differentiated carcinoma (follicular or papillary) and anaplastic carcinoma. Poorly differentiated thyroid carcinoma is rare ranging from 0.3 % to 6.7 % of all thyroid cancers. These tumors are aggressive and often lethal and have a rapid and fatal outcome despite appropriate treatment. This paper reports a case of poorly differentiated thyroid carcinoma in a 76-year-old male patient. Macroscopic examination showed thyroid tissue in the form of nodules of 1.5 cm diameter with areas of infiltrative solid nodules. Histopathologic examination showed proliferation of neoplastic cells with oval round nuclei, ground glass, cleaved or convoluted nuclei features not found, irregular nuclear membrane, hyperchromatic, mild nuclear pleomorphism, mitotic activity >20/10 HPF, and necrotic area. These tumors form an insular and solid pattern infiltrating into connective tissue, fat, and skeletal muscle. In accordance with the criteria in the Turin consensus, these tumors were concluded as poorly differentiated thyroid carcinomas, infiltrated into skeletal muscle and fat tissue (stage pT3b).

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RESUMEN

El carcinoma de tiroides pobremente diferenciado (PDTC) es una neoplasia de células foliculares que muestra una diferenciación limitada de células foliculares que es morfológica y conductualmente intermedia entre el carcinoma diferenciado (folicular o papilar) y el carcinoma anaplásico. El carcinoma de tiroides pobremente diferenciado es raro y oscila entre el 0,3 % y el 6,7 % de todos los cánceres de tiroides. Estos tumores son agresivos ya menudo letales y tienen un desenlace rápido y fatal a pesar del tratamiento adecuado. Este artículo reporta un caso de carcinoma pobremente diferenciado de tiroides en un paciente masculino de 76 años. El examen macroscópico mostró tejido tiroideo en forma de nódulos de 1,5 cm de diámetro con áreas de nódulos sólidos infiltrantes. El examen histopatológico mostró proliferación de células neoplásicas con núcleos redondos ovalados, vidrio esmerilado, características de núcleo hendido o contorneado no encontradas, membrana nuclear irregular, hipercromática, plemorfismo nuclear leve, actividad mitótica> 20/10 HPF y área necrótica. Estos

tumores forman un patrón insular y sólido que se infiltra en el tejido conectivo, la grasa y el músculo esquelético. De acuerdo con los criterios del consenso de Turín, estos tumores se concluyeron como carcinomas de tiroides pobremente diferenciados, infiltrados en músculo esquelético y tejido graso (estadio pT3b).

Palabras clave: *Carcinoma pobremente diferenciado, tiroides, consenso de Turín.*

INTRODUCTION

Poorly differentiated thyroid carcinoma (PDTC) is a follicular cell neoplasm (1) that shows limited evidence of follicular cell differentiation and is morphologically and behaviorally intermediate between differentiated (follicular and papillary) carcinomas and anaplastic carcinoma (2-4).

Poorly differentiated thyroid carcinoma (PDTC) is rare. If the Turin consensus criteria represent a small fraction of thyroid carcinomas, less than 2 % in the United States and less than 1 % in Japan are PDTC, although a prevalence of approximately 5 % has been reported in the area of Turin in Italy and some regions of France.

One case of poorly differentiated thyroid carcinoma is reported, in a man aged 74 years with a high stage. Determining the diagnosis clinically requires careful observation and morphological observation to distinguish it from other thyroid carcinomas, thus meeting the criteria according to the Turin consensus.

CASE DESCRIPTION

A patient from Karangasem hospital was referred on December 8, 2017, with a diagnosis of tumor colli and suspected multiple nodule thyroid. The patient came to the Polyclinic of Surgery Oncology Sanglah Hospital with complaints of lumps in the neck that had been there for a long time and becoming enlarged for 3 weeks; the patient also complained of breathlessness and difficulty swallowing but had no complaints of hoarseness. The patient was scheduled for surgery on December 11, 2017. On physical examination, local status found lumps or mass in the right colli region of 8x5 cm and the left colli of 5x5 cm in size. Vital sign examination found blood pressure 140/90 mmHg, pulse 86x/minute, respiration rate 28x / minute, and temperature axilla 37 ºC.

Results of the Fine-needle aspiration biopsy (FNAB) cytology examination at Karangasem hospital, on November 4, 2017, showed follicular neoplasm. Ultrasound examination on October 26, 2017, showed an enlarged size, solid nodule appearance, well-circumscribed with a size of 7x4x6 cm, a single nodule thyroid (SNT) impression of a lethal suspicious malignant lobe, and an impression of multiple thyroid nodules of the left lobe.

The CT Scan examination at **Sanglah Central General Hospital,** on 9 November 2017, showed a size of 6.3x6,7x7,5 cm for the nodule, impressed of the right thyroid mass, with macro calcification urging trachea and thyroid to the left (Figure 1).

Figure I. Multi-slice CT. (A) Midface. (B) Colli axial slices indication of the mass of the right thyroid, with urgent calcification of the trachea and the left thyroid to the left.

Previous laboratory results at Karangasem hospital on October 25, 2017, showed the result of thyroid function to be FT4 1,66 ng/dL (Normal = 0,93-1,70) and TSH 2,49 μIU / mL (Normal = 0,27-4, 20).

The patient underwent isthmolobectomy surgery at Sanglah Hospital on December 11, 2017, then was sent to the Anatomical Pathology Laboratory **Sanglah Central General Hospital** for histopathology examination. The macroscopic examination showed pieces of thyroid tissue, the largest with a size of 7.5x 5x 1.5 cm, the smallest PAPILARY with a size of 1.5x1x0.8 cm. Most of these tissues appeared to have necrosis. On the largest tissue slices, one nodule with a diameter of 1.5 cm in appearance, was seen as an area of infiltrative solid nodules in some parenchyma (Figure 2A). Other tissues are not visibly mass, on partially hard, partially fragile fragments, with blackish-colored areas (Figure 2B).

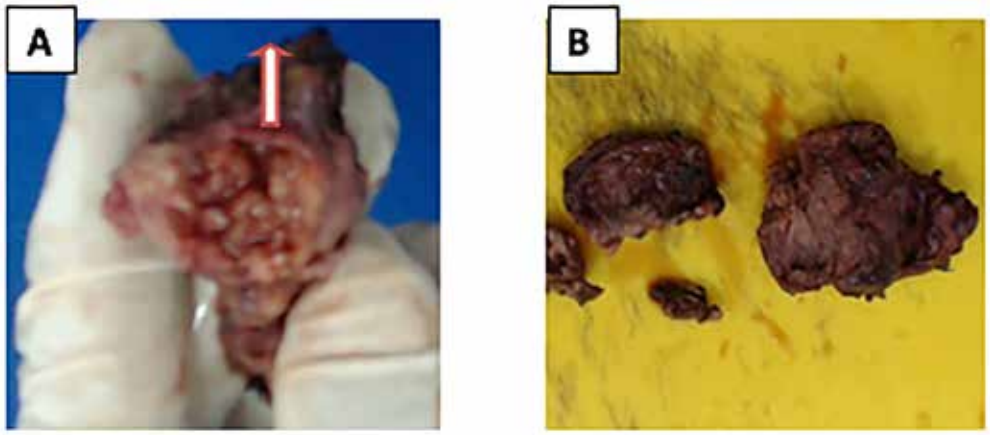

Figure 2. Macroscopic. (A) Solid infiltrative nodule appearance. (B) Necrosis with blackish color

The histopathological examination (5) showed pieces of thyroid tissue containing mass consisting of the neoplastic cells composed proliferated of insular and solid patterns (Figure 3).

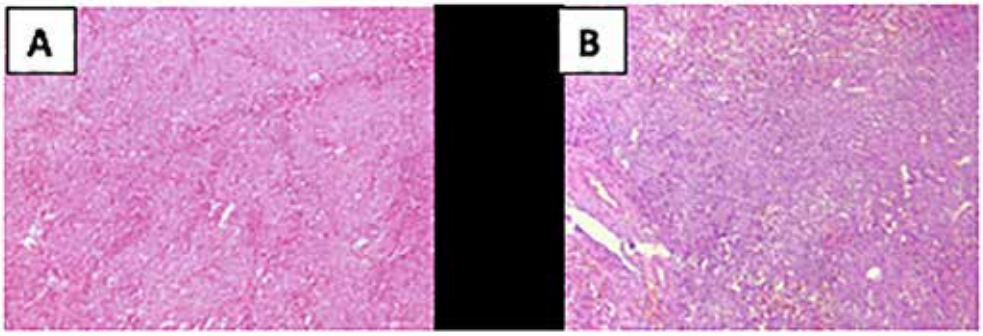

Figure 3. (A) Insular pattern separated fibrovascular stroma (HE, 100X). (B) Solid (HE, 100X).

The morphology of these cells is oval round, eosinophilic cytoplasm, with an oval round nucleus, absence of ground glass nuclear and cleaved or convoluted nuclear features, irregular nuclear membrane, hyperchromatic, mild nuclear pleomorphism, mitotic activity >20/10 LPB, and area of necrosis (Figure 4).

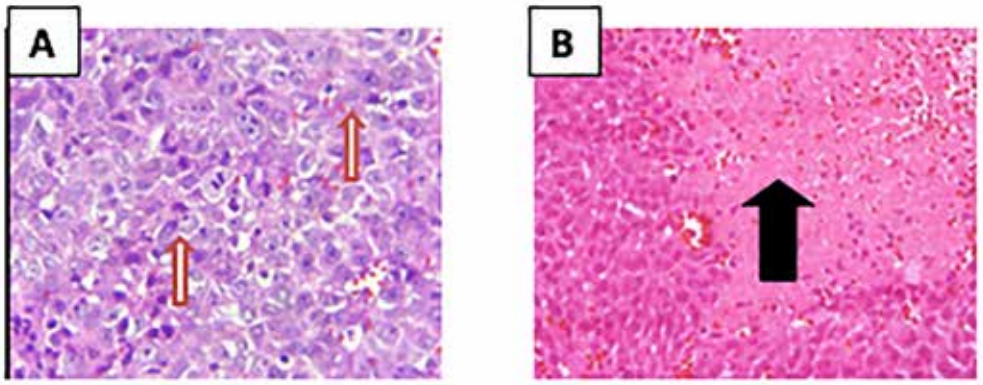

Figure 4. Poorly differentiated thyroid carcinoma. (A) Mitosis (HE, 400X). (B) Necrosis (HE, 400X).

The appearance of the neoplastic cells was infiltrative between the connective tissue stroma, skeletal muscle, and fat tissue (Figure 5).

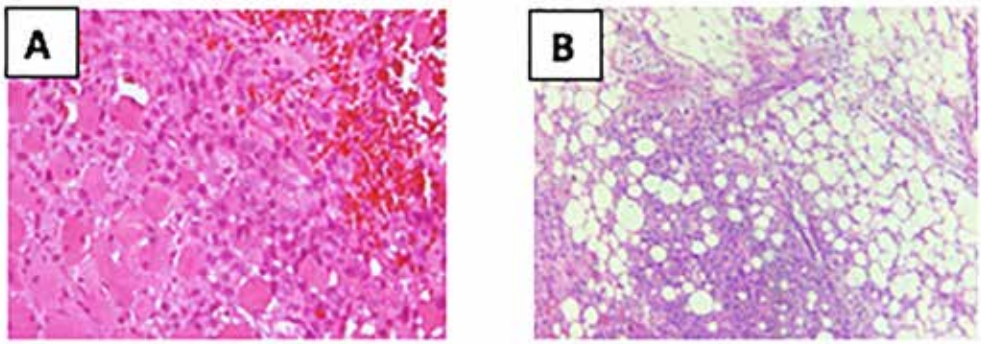

Figure 5. A. Infiltrative tumors between skeletal muscle tissue (HE, 40X). B. Infiltrative to fat tissue (HE, 100X).

DISCUSSION

From the routine histopathologic examination above, this case meets the diagnostic criteria for the Turin consensus to be concluded as a poorly differentiated thyroid carcinoma (PDTC), which infiltrated the skeletal muscle and fat tissue. The patient returned on December 18, 2018, to Surgical Oncology Polyclinics with a diagnosis of multiple nodule thyroid (MNT) post isthmolobectomy with a radiotherapy plan in Mangusada hospital, Badung.

Thyroid carcinoma with poor differentiation is a rare and different case because the characteristics of the cells are uniform and sometimes the architectural patterns are insular. These tumors are aggressive and often fatal and cause rapid death despite appropriate treatment. These tumors represent the intermediate entities of well-differentiated thyroid carcinomas to the anaplastic thyroid carcinoma (6,7).

Poorly differentiated thyroid carcinoma accounts for a small proportion of all thyroid cancers at 0.3 % in Japan and 1.8 % in the USA, the proportions somewhat higher in some geographic regions of Latin America and Europe with reported prevalence rates of 4-6.7 %. The mean patient age at diagnosis is 55-63 years, with rare cases diagnosed in a young patient (2). In this case, it occurred in a man of 74 years with a high stage.

The cause of this tumor is probably a deficiency of iodine that contributes to environmental factors, given the poorly differentiated carcinoma relationship with long-standing goiter. Enlargement of the thyroid, or goiter impaired synthesis caused by thyroid hormone, which is most often the result of dietary iodine deficiency. Impairment of thyroid hormone synthesis leads to a compensatory rise in the serum TSH level, which, in turn, causes hypertrophy and hyperplasia (8–10). Recurrent hyperplasia may lead to developing neoplastic changes (11). In this case, the patient had a history of goiter disease in the form of a multinodular thyroid.

Tumors are usually large-sized averaging 5 cm, solid and light brown to gray. Some show soft consistency and pale areas of necrosis. The growth margins are often pushing, and it may be that the tumor is partly encapsulated. Frequently, there are satellite nodules within the thyroid parenchyma, and in some cases, the growth of multinodular tumors may resemble thyroid goiter. Usually, there is a spreading out of the thyroid capsule and resection margins, but extrathyroidal infiltration is less pervasive than in anaplastic carcinoma (2). In this case, it is sent in the form of tissue pieces with the largest size of 7.5x5x1.5 cm, appearing as solid infiltrative nodules in some parenchyma; some other tissues experience necrosis with partially soft fragile partial consistency, and no spread apparent of tumor cells to the extra thyroid.

Microscopically, the features of this carcinoma, formerly called poorly differentiated carcinoma (insular) with characteristics of "insular" nest growth patterns, are solid to the microfollicular, small uniform tumor cells, variable mitotic activities, and tumor necrosis, sometimes resulting in a pattern of perithelioma. Insular nests are surrounded by thin fibrovascular septa, which are often separated from the nests of tumor cells by artefactual clefts. The tumor cells have a hyperchromatic round nucleus, the nucleoli unclear, and mild nuclear pleomorphism. Sometimes the nucleus may show irregular features, such as "raisin-like", convoluted nuclei reminiscent of papillary carcinomas, but dark chromatin and no pseudo inclusions (12,13).

Some cases of poor differentiation do not show the classical features of "insular" carcinoma, but dominant trabecular patterns; the neoplastic cells have larger nuclear pleomorphism and comedo necrosis. Vascular invasion is identified in cases of large tumors. Extrathyroid infiltration is common but less invasive than anaplastic carcinoma. The Turin consensus criteria, currently used to describe poorly differentiated carcinoma, recommend an algorithm for diagnosis (12).

Although much progress has been achieved in defining poorly differentiated thyroid carcinoma, there are still aspects of diagnosis that require additional investigation (14). Perhaps the most problematic involves the convoluted nuclei of this carcinoma. Although tumors have a nuclei convolution it is unclear whether the convoluted nuclei along with solid/trabecular/insular components is sufficient for the diagnosis of poorly differentiated thyroid carcinomas according to the Turin proposal (15). Most reported cases of poorly differentiated thyroid carcinoma with a convoluted nucleus diagnosed using the Turin criteria also have a mitotic number greater than or equal to 3 mitoses per 10 high-power fields or necrosis tumor (16).

The 2006 Turin Consensus recommends the most accepted algorithm and includes the criteria for diagnosing poorly differentiated thyroid carcinomas (Algorithm 1). According to the proposal, poorly differentiated thyroid carcinomas are defined as follows:

1) Solid growth patterns, trabecular or insular.
2) The absence of conventional nuclear features of papillary carcinoma.
3) At least one of the following features: convoluted nuclei, mitotic activity ≥3x per 10 HPF, and tumor necrosis (17).

In this case, architecturally there was a solid and trabecular pattern (criteria 1), then the nuclear of the papillary carcinoma was not found (criteria 2) and the findings showed necrosis and mitotic ≥3X per 10 LPB (criteria 3), for the diagnostic criteria of poorly differentiated thyroid carcinoma.

In this case, the histopathology showed tumor cells forming an insular and solid pattern infiltrating connective tissue stroma, skeletal muscle, and fat tissue, mild nuclear pleomorphism, mitotic activity > 20 per high power fields, the appearance of a large necrotic area, and hemorrhage.

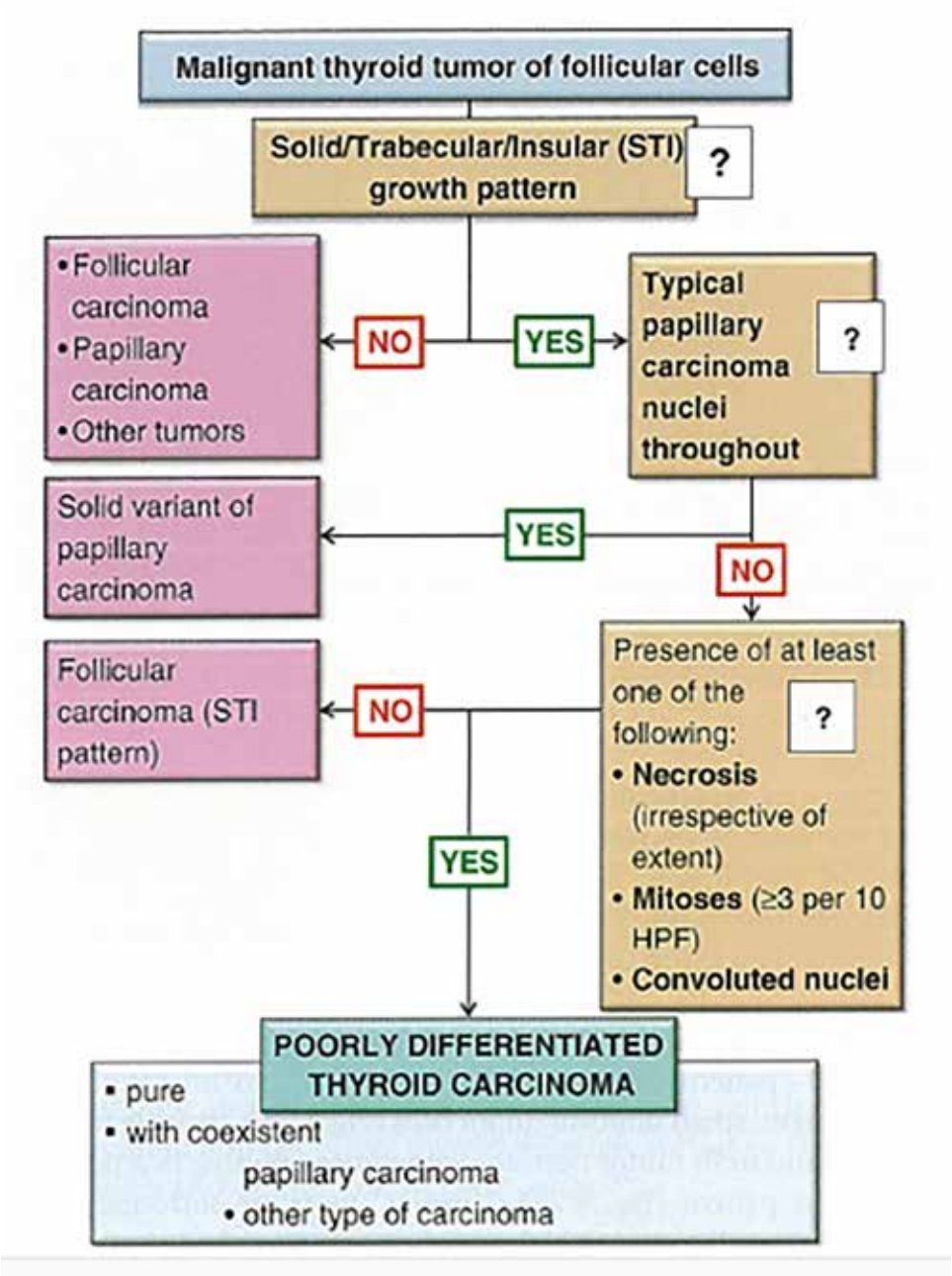

Figure 6. Algorithm for the diagnosis of poorly differentiated thyroid carcinoma using the Turin consensus criteria (Giovanni and Thomas, 2018).

These tumors have wide invasion ability, spread parathyroid soft tissue in 60-70 % of cases, regional KGB metastases in 15-65 %, and distant metastases (most frequently to the lung, followed by bone and other organs such as the brain, liver, skin, spleen, and kidney) in 40 %-70 % of cases. Stage criteria are the same as those used for follicular carcinomas and well-differentiated papillary carcinomas. These tumors have higher pathological tumor-node-metastasis (pTNM) stages than well-differentiated carcinomas (2). Diagnosis of poorly differentiated thyroid carcinoma is usually present in advanced stages of the disease, with extra thyroid extension and extensive local invasion (18). In this case, it shows stage IIIb. Immunohistochemistry is not necessary to make a diagnosis of poorly differentiated thyroid carcinoma; however, immunohistochemistry staining may be used to support the diagnosis. This tumor is positive for PAX8, TTF-1, and thyroglobulin. Compared with well-differentiated tumors, TTF-1 and thyroglobulin staining are generally weaker in poorly differentiated thyroid carcinomas. Although thyroglobulin staining is characteristic of poorly differentiated thyroid carcinoma, it is not completely specific because it can also be observed in benign or malignant thyroid lesions with a dominant pattern of solid/ trabecular (15). In this case, immunohistochemical staining is not performed because the diagnosis can be established morphologically.

In determining the diagnosis of a case that is sometimes difficult, it is necessary to consider the differential diagnosis of medullary thyroid carcinoma, followed by parathyroid carcinoma and carcinoma metastatic to the thyroid gland and immunohistochemistry is useful in resolving difficult cases (12).

Poorly differentiated thyroid carcinoma has an association with a worse prognosis compared with a well-differentiated thyroid carcinoma but the prognosis is better than for anaplastic carcinoma (19). The prognosis mainly depends on lymph node involvement, distant metastases, TNM stages, surgery complete, and response to radioiodine therapy (20).

In most previous research, 5-year survival averaged 60 %-70 %. Recurrences usually develop within the first 3 years. The average time of specific survival is 5 years after diagnosis. Response to radioiodine treatment is generally poor. Prognostic factors related to survival are based on multivariate analysis. There is a poor prognosis with clinicopathological factors: patient age ≥ 45 years, tumor size ≥ 5 cm, macroscopically evident extrathyroidal extension (pT4a) at surgery, and distant metastases (M1) at presentation. Histological and immunohistochemical factors: tumor necrosis, IMP3 immunoreactivity, and oncocytic features then molecular genetic factors Ras gene mutation and downregulation of miR- 150. There is a good prognosis in the case of a histology factor with convoluted (papillary carcinoma-like) neoplastic cell nuclei. Strong prognostic factors are the stage and age of the patient. The presence of a tumor capsule is associated with a good prognosis (2).

CONCLUSION

In this case, a 76-year-old male patient presented with a clinical diagnosis of colli tumor suspected MNT. Based on histopathological examination, he was diagnosed with poorly differentiated thyroid carcinoma infiltrated into the skeletal muscle and fatty tissue (stage IIIb). This patient was still recommended for immunohistochemical examination with TTF-1 and MIB-1 to support diagnosis although morphologically appropriated and included in the Turin proposal criteria.

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