Anaplastic Thyroid Carcinoma in a Young Woman: Case Report

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Carcinoma Anaplásico de Tireoide em uma Paciente Jovem: Relato de Caso

Carcinoma Anaplásico de Tiroides en una Mujer Joven: Reporte de Caso

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ABSTRACT

Introduction: The anaplastic thyroid carcinoma is a rare, aggressive tumor, and it affects mainly women over the age of 60 years, being less common in younger people. It is believed that this tumor appears due to the loss of differentiation in well differentiated thyroid carcinomas. Low iodine ingestion has also been suggested. Despite multimodal intervention attempts, prognosis is poor. **Case report:** A 41 year-old female patient underwent a total thyroidectomy because of the rapid growth of a thyroid mass, associated with radiological suspicion of malignancy. The macroscopic evaluation showed that the tumor had a lobulated shape, necrotic and hemorrhagic areas, and poorly-defined margins. Microscopic findings confirmed an anaplastic thyroid carcinoma, characterized by the proliferation of spindle and osteoclast-like multinucleated cells, associated with a well differentiated papillary thyroid carcinoma. **Conclusion:** Despite its rarity, the anaplastic carcinoma should be thought as a possibility when evaluating a thyroid neoplasia, and differential diagnosis must be considered cautiously, since it can be misleading for other tumors, such as lymphomas and sarcomas. In addition, it is important to point out the necessity to admit it even when the patient does not belong to the typical epidemiological group.

Key words: thyroid neoplasms; thyroid carcinoma, anaplastic/pathology; thyroid cancer, papillary; neoplasms.

RESUMO

Introdução: O carcinoma anaplásico da tireoide é um tumor raro e agressivo, que afeta principalmente mulheres com idade acima de 60 anos, sendo menos comum em pessoas mais jovens. Acredita-se que esse tumor surja em razão da perda de diferenciação em carcinomas bem diferenciados de tireoide. Uma baixa ingestão de iodo também foi sugerida. Apesar das tentativas de intervenção multimodal, o prognóstico é ruim. **Relato do caso:** Paciente do sexo feminino, 41 anos, submetida à tireoidectomia total, por causa do rápido crescimento de massa tireoidiana, associada à suspeita radiológica de malignidade. A avaliação macroscópica mostrou que o tumor apresentava formato lobulado, áreas necróticas e hemorrágicas e margens mal definidas. Os achados microscópicos confirmaram um carcinoma anaplásico de tireoide, caracterizado pela proliferação de células multinucleadas fusiformes e osteoclásticas, associadas a um carcinoma papilar de tireoide bem diferenciado. **Conclusão:** Apesar de sua raridade, o carcinoma anaplásico deve ser considerado uma possibilidade na avaliação de uma neoplasia tireoidiana, e o diagnóstico diferencial deve ser levado em conta com cautela, pois pode ser confundido com outros tumores, como linfomas e sarcomas. Além disso, é importante ressaltar a necessidade de considerá-la mesmo quando o paciente não pertence ao grupo epidemiológico usual.

Palavras-chave: neoplasias da glândula tireoide; carcinoma anaplásico da tireoide/patologia; câncer papilífero da tireoide; neoplasias.

RESUMEN

Introducción: El carcinoma anaplásico de tiroides es un tumor agresivo poco común y afecta principalmente a mujeres mayores de 60 años, siendo menos común en adultos más jóvenes. Se cree que este tumor surge debido a la pérdida de diferenciación en carcinomas tiroideos bien diferenciados. También se ha implicado una baja ingestión de yodo. A pesar de los intentos de intervención multimodal, el pronóstico es malo. **Reporte del caso:** Paciente de 41 años fue sometida a tiroidectomía total por rápido crecimiento de una masa tiroidea, asociada a sospecha radiológica de malignidad. La evaluación macroscópica mostró que un tumor voluminoso con áreas necróticas y hemorrágicas y márgenes mal definidos. Los hallazgos microscópicos confirmaron un carcinoma anaplásico de tiroides, caracterizado por la proliferación de células multinucleadas fusiformes y similares a los osteoclastos, asociado con un carcinoma papilar de tiroides bien diferenciado. **Conclusión:** A pesar de su rareza, el carcinoma anaplásico debe considerarse una posibilidad al evaluar la neoplasia tiroidea. Se deben considerar cuidadosamente los diferentes diagnósticos, ya que pueden confundirse con otros cánceres, como linfomas y sarcomas. Además, es importante señalar la necesidad de considerarlo incluso cuando el paciente no pertenece al grupo epidemiológico habitual.

Palabras clave: neoplasias de la tiroides; carcinoma anaplásico de tiroides/patología; cáncer papilar tiroideo; neoplasias.

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INTRODUCTION

Anaplastic thyroid carcinoma (ATC) is a rare undifferentiated and aggressive neoplasm[1]. The tumor is diagnosed predominantly in women with mean age of 66.5 years[2]. Its incidence is declining worldwide and is associated with the improvement of iodine supplementation and consequently with the reduction of the prevalence of endemic goiter[3]. It is believed that ATC can develop in the context of goiter.

There is also association among differentiated carcinomas of thyroid and ATC which corroborates the idea that the latter is caused by the loss of differentiation of papillary and follicular carcinomas. In despite of these associations, it is not yet clear whether goiter and differentiated tumors share the same molecular routes in the creation of ATC[4]. The most recurrent mutations of ATC affect the *TP53* and beta-catenin protein (*CTNNB1*) genes[5].

Mean survivorship of patients is five months, and survivorship rates of one- and five-years account for less than 20%[6] and 12%[7], respectively. In average, 41% of the patients with ATC have metastases at the diagnosis, most commonly detected in the lungs, mediastinum, liver and bones causing 51.5% of the deaths[2].

In addition, metastases to regional lymph nodes[8] are quite common. Overall survivorship is quite low even with multimodal intervention protocols[1], which include surgical resection for patients in clinical conditions and in stage compatible with surgical management associated with radiation – preferentially intensity-modulated radiotherapy (IMRT) – and chemotherapy, especially doxorubicin associated with cisplatin[3,9].

For the patients at more advanced stages of the disease, with no perspectives of cure, surgeries and other palliative therapies can be applied[9]. The present case addresses not only a rare neoplasm but also with uncommon presentation. The Institutional Review Board of "*Faculdades Pequeno Príncipe*" approved the study, CAAE: 43092821.2.0000.5580.

CASE REPORT

41-year-old woman sought medical care because of a sore cervical mass. The patient referred progressive growth in the last two months and local pain. There were no comorbidities, tobacco or alcohol use. Physical examination revealed node in thyroid's right lobe. The node was indurated, appeared well-defined and had nearly 6 cm. Computed tomography (CT) of the patient's neck showed a large solid mass with poorly-differentiated margins, originating in the right lobe of the thyroid, extending to the mediastinum. The images also showed necrosis and probable spread to trachea and internal jugular vein, in addition to cervical lymphadenomegaly. Thoracic CT revealed multiple nodular opacities with density of soft parts in different dimensions invading the pulmonary parenchyma, predominantly peribronchovascular and subpleural, suggestive of metastases.

Because of the rapid growth and suspected radiologic characteristics of malignancy, total thyroidectomy was performed. During surgery, it was detected extrathyroidal extension of the neoplasm with tracheal and internal jugular spread (Figure 1).

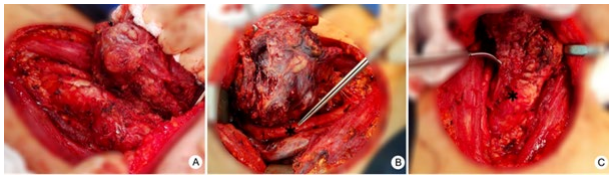

Figure 1. A. Enlarged thyroid neoplasm; **B.** Neoplasm spreading to internal jugular vein (asterisk); **C.** Adherence to trachea (asterisk).

The macroscopic exam of the 140.0-gram specimen showed a 9.0 cm tumor at the right lobe spreading through the whole thyroid lobe. The tumor was poorly-defined and presented a heterogeneous, lobulated and fleshy surface on cut section with necrotic and hemorrhagic areas (Figure 2).

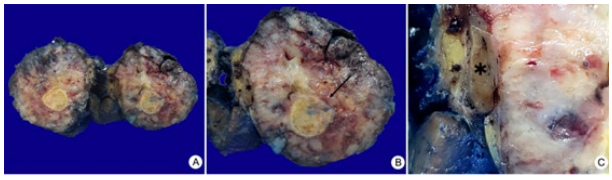

Figure 2. A and B. Macroscopic image of the right lobe of the bisected thyroid nearly completely replaced by the solid neoplasm with necrotic areas (highlighted by arrow); **B.** Residual normal thyroid is seen at the left side (asterisk); **C.** Fleshy surface on cut section and detail of residual non-neoplastic thyroid (asterisk).

During the microscopic evaluation, a spindle cell neoplasia, with numerous osteoclast-like multinucleated cells and elevated mitotic index (up to 17 mitosis/2 mm^2) was diagnosed as compatible with ATC. Diffuse and perineural angiolymphatic invasions have also been detected, as well as extra-thyroid extension (Figure 3). Half of the dissected lymphatic ganglia of the specimen revealed the presence of metastasis. The neoplastic invasion of the wall of the jugular vein was confirmed.

The tumor was accompanied by a 0.9 cm classical variant papillary carcinoma of thyroid. The immunohistochemistry exam revealed positivity for the thyroid transcription factor-1 (TTF-1), as well as for the paired-box gene 8 (PAX8) in papillary carcinoma. On the other hand, fusocellular neoplasm was negative for both markers and for markers of other tissue lineage confirming the diagnosis of ATC (Figure 3).

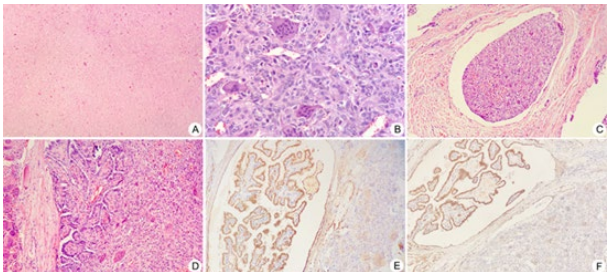

Figure 3. Histopathological and immunohistochemistry characteristics. **A.** ATC with low magnification (40x, H&E); **B.** Detail showing spindle multinucleated osteoclast-like cells and mitotic figures (400x, H&E); **C.** Angiolymphatic invasion (100x, H&E); **D.** Transition from well-differentiated papillary carcinoma to ATC (100x, H&E); **E.** TTF-1 showing positivity in papillary carcinoma and negativity in ATC (100x, IHQ); **F.** PAX8 showing positivity in papillary carcinoma and negativity in ATC (100x, IHQ).

After surgery, the patient initiated the first cycle of chemotherapy with doxorubicin and cisplatin, and was referred to radiotherapy, but she did not resist and died because of lung complications. The evolution of the neoplasms from diagnosis to death was six months.

DISCUSSION

ATC is a rare thyroid cancer accounting for only 1% to 2% in average of the thyroid tumors in the whole world[3]. The female-to-male ratio is 2:1[8] and typically affects older adults, especially in the sixth and seventh decades of life[10]. There are reports, although rare, in younger patients, including an extreme case of a 5-year-old child[11-13]. The present patient stands out as she is two decades younger than the epidemiological age-range.

Macroscopic findings of ATC reveal a bulky yellow mass with necrotic and hemorrhagic areas. It is an invasive tumor, spreading to soft tissues and other structures around the thyroid[10]. The size is variable and those smaller than 7 cm are associated with lower mortality rates[6]. As the patient's tumor was 9 cm, poor prognosis was anticipated.

ATC is characterized by undifferentiated follicular cells with variable microscopic features. The three main histopathological subtypes include sarcomatoid, giant cells and epithelial patterns which can overlap in the same tumor or appear individually. Additional rare variants are paucicellular, rhabdoid, lymphoepithelioma-like, angiomatoid and small cell[8]. All the types are characterized by nuclear atypia with high mitotic activity and typically associated with necrotic areas. Acute inflammatory infiltrate, osteoclast-like giant cells and even heterologous differentiation as bone and cartilage inside the tumor can be found[5]. Vascular invasion is often present[8]. Although ATC has different histopathologic growth patterns, it does not appear to be associated with patient prognosis so far[14].

The main differential diagnoses for ACT include medullary thyroid carcinoma and poorly differentiated, sarcomas, squamous cells carcinoma, lymphomas and chronic fibrosing thyroiditis[2]. The main types of lymphomas that need to be differentiated are large diffuse B cell lymphoma and anaplastic lymphoma[10].

According to immunohistochemistry, thyroglobulin and expression of TTF-1 appear to be absent in ATC because it is an undifferentiated carcinoma. In some situations, PAX8 can be present, while AE1/AE3 cytokeratin cocktail is usually positive, as well as p53 protein. The expression of the antigen Ki-67 is usually high, indicating elevated proliferation of neoplastic cells[10]. Immunohistochemistry is essential for differential diagnosis between ATC and other undifferentiated carcinomas as well as lymphomas and melanoma[14].

ATC is detected earlier than differentiated carcinomas due to its high aggressiveness and the prompt beginning of clinical symptoms, but often at advanced stages[10]. Most patients present symptoms of neoplastic local extension such as dyspnea, dysphagia, cough and hoarseness[4]. Recurrent symptoms in most cases are the feeling of growing mass in the neck, pain and hemoptysis[2]. The young patient presented a painful growing mass but none of the other characteristic symptoms.

The American Joint Committee on Cancer (AJCC/TNM)[15] classification of malignant tumors attributes stage IV to every ACT when diagnosed. The tumor of the present case was classified as pT4b pN1, that is, stage IVB[15].

ACT is an extremely aggressive neoplasm and clinical risk factors such as manifestation of acute symptoms, age over 75 years old, male patients and leukocytosis are associated with worse prognosis[3]. Distant metastases are independent risk factors for poor outcome[6].

The treatment is multimodal and in most of the cases includes surgical resection associated with radiotherapy and/or chemotherapy, specially doxorubicin. New approaches as neo-adjuvancy and immunotherapy, mainly when mutation of *BRAF* V600E occurs, have been showing promising results for patients survivorship[9]. Yet, better response rates are around 20%[3]. Because of the dismal prognosis, a quick diagnosis is very important for these therapeutic strategies to be promptly implemented.

CONCLUSION

ATC is an aggressive tumor, and it is considered uncommon among thyroid carcinomas. Despite its rarity, ATC cannot be ignored as a potential diagnosis. Its microscopy is variable and can simulate other neoplasms such as sarcomas, lymphomas, and other carcinomas, which highlights the importance of keeping a wide spectrum in the differential diagnosis. Furthermore,

although the population younger than 60 years does not have a typical epidemiological profile, the diagnosis of ATC cannot be rejected as this case report has clearly demonstrated.

CONTRIBUTIONS

All the authors contributed to the conception and/or design of the study, data acquisition, analysis and interpretation, wording and critical review and approved the final version to be published.

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DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

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REFERENCES

1. Haymart MR, Banerjee M, Yin H, et al. Marginal treatment benefit in anaplastic thyroid cancer. Cancer. 2013;119(17):3133-39. doi: https://doi.org/10.1002/cncr.28187
2. Smallridge RC. Approach to the patient with anaplastic thyroid carcinoma. J Clin Endocrinol Metab. 2012;97(8):2566-72. doi: https://doi.org/10.1210/jc.2012-1314
3. Nagaiah G, Hossain A, Mooney CJ, et al. Anaplastic thyroid cancer: a review of epidemiology, pathogenesis, and treatment. J Oncol. 2011;2011:542358. doi: https://doi.org/10.1155/2011/542358
4. Steggink LC, van Dijk BA, Links TP, et al. Survival in anaplastic thyroid cancer in relation to pre-existing goiter: a population-based study. Am J Surg. 2015;209(6):1013-9. doi: https://doi.org/10.1016/j.amjsurg.2014.06.027
5. Smallridge RC, Ain KB, Asa SL, et al. American Thyroid Association guidelines for management of patients with anaplastic thyroid cancer. Thyroid. 2012;22(11):1104-39. doi: https://doi.org/10.1089/thy.2012.0302
6. O'Neill JPaul, Shaha AR. Anaplastic thyroid cancer. Oral Oncol. 2013;49(7):702-6. doi: https://doi.org/10.1016/j.oraloncology.2013.03.440
7. Hvilsom GB, Londero SC, Hahn CH, et al. Anaplastic thyroid carcinoma in Denmark 1996-2012: a national prospective study of 219 patients. Cancer Epidemiol. 2018;53:65-71. doi: https://doi.org/10.1016/j.canep.2018.01.011
8. Lloyd RV, Osamura RY, Klöppel G, et al., editors. WHO classification of tumours of endocrine organs. 4th ed. Lyon (France): International Agency for Research on Cancer (IARC); 2017. (World Health Organization classification of tumours; vol. 10).
9. Bible KC, Kebebew E, Brierley J, et al. 2021 American Thyroid Association guidelines for management of patients with anaplastic thyroid cancer. Thyroid. 2021;31(3):337-86. doi: https://doi.org/10.1089/thy.2020.0944
10. Deeken-Draisey A, Yang GY, Gao, et al. Anaplastic thyroid carcinoma: an epidemiologic, histologic, immunohistochemical, and molecular single-institution study. Hum Pathol. 2018;82:140-8. doi: https://doi.org/10.1016/j.humpath.2018.07.027
11. Sharma SC, Sakthivel P, Raveendran S, et al. Anaplastic carcinoma thyroid in a young child - an extremely rare occurrence. Acta Medica (Hradec Kralove). 2018;61(4):150-152. doi: https://doi.org/10.14712/18059694.2018.134
12. Salazar-Mejía CE, Pérez-Arredondo LA. A giant mass in the neck of a young men: a case of anaplastic thyroid cancer. Pan Afr Med J. 2018;30:151. doi: https://doi.org/10.11604/pamj.2018.30.151.15156
13. Li M, Milas M, Nars C, et al. Anaplastic thyroid cancer in young patients: a contemporary review. Am J Otolaryngol Head Neck Surg. 2013;34(6):636-40. doi: https://doi.org/10.1016/j.amjoto.2013.07.008
14. Keutgen XM, Sadowski SM, Kebebew E. Management of anaplastic thyroid cancer. Gland Surg. 2015;4(1):44-51. doi: https://doi.org/10.3978/j.issn.2227-684X.2014.12.02
15. Amin MB, Edge SB, Greene FL, et al., editors. AJCC cancer staging manual. 8th ed. Chicago: American Joint Committee on Cancer, Springer; 2017.

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