

# THREE SIBLINGS WITH FAMILIAL NON-MEDULLARY THYROID CARCINOMA: A CASE SERIES

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## INTRODUCTION

- Thyroid carcinoma affects around 63000 people in the U.S yet it remains one of the most treatable cancers <sup>1</sup>.
- It is mainly classified into medullary and non-medullary types. Conventionally, medullary carcinoma was associated with heritability but increasing reports have now begun to associate non-medullary thyroid carcinoma with a genetic predisposition as well.
- It is important to identify a possible familial association in patients diagnosed with non-medullary thyroid carcinoma because these cancers behave more destructively than would otherwise be expected <sup>2</sup>.
- Our case series presents a diagnosis of familial, non-syndromic, non-medullary carcinoma of the thyroid gland in three brothers diagnosed over a span of six years.

## CASE PRESENTATION

We report the history, signs and symptoms, laboratory results, imaging and histopathology of the thyroid gland of three Pakistani brothers from Sindh with non-medullary thyroid carcinoma (NMTC). All three patients were in the age group of 52-58 years old and were diagnosed with NMTC. Only patient 1 and 3 had active complaints of swelling and pruritus respectively, whereas patient 2 was asymptomatic. Patient 2 and 3 had advanced disease at presentation with lymph node metastasis. All patients underwent a total thyroidectomy with patients 2 and 3 requiring a neck dissection as well. No previous exposure to radiation was present in any of the patients. In addition, their mother had died from adrenal carcinoma but also had a swelling in front of her neck which was never investigated. All patients remained stable at follow-up.

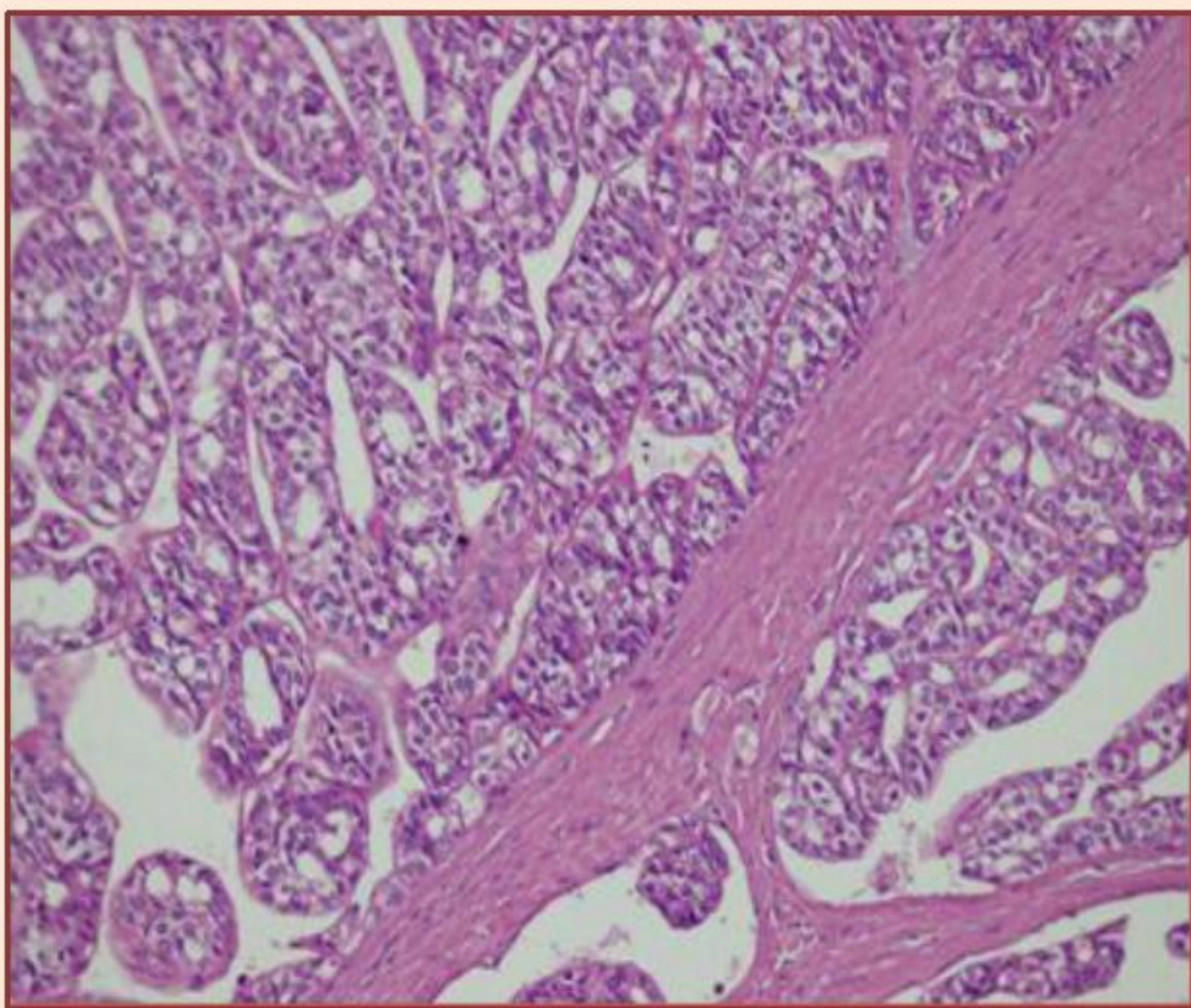


Figure 1. High power view of thyroid neoplasm with follicular arrangement. Nuclear features of papillary thyroid carcinoma are not appreciated.

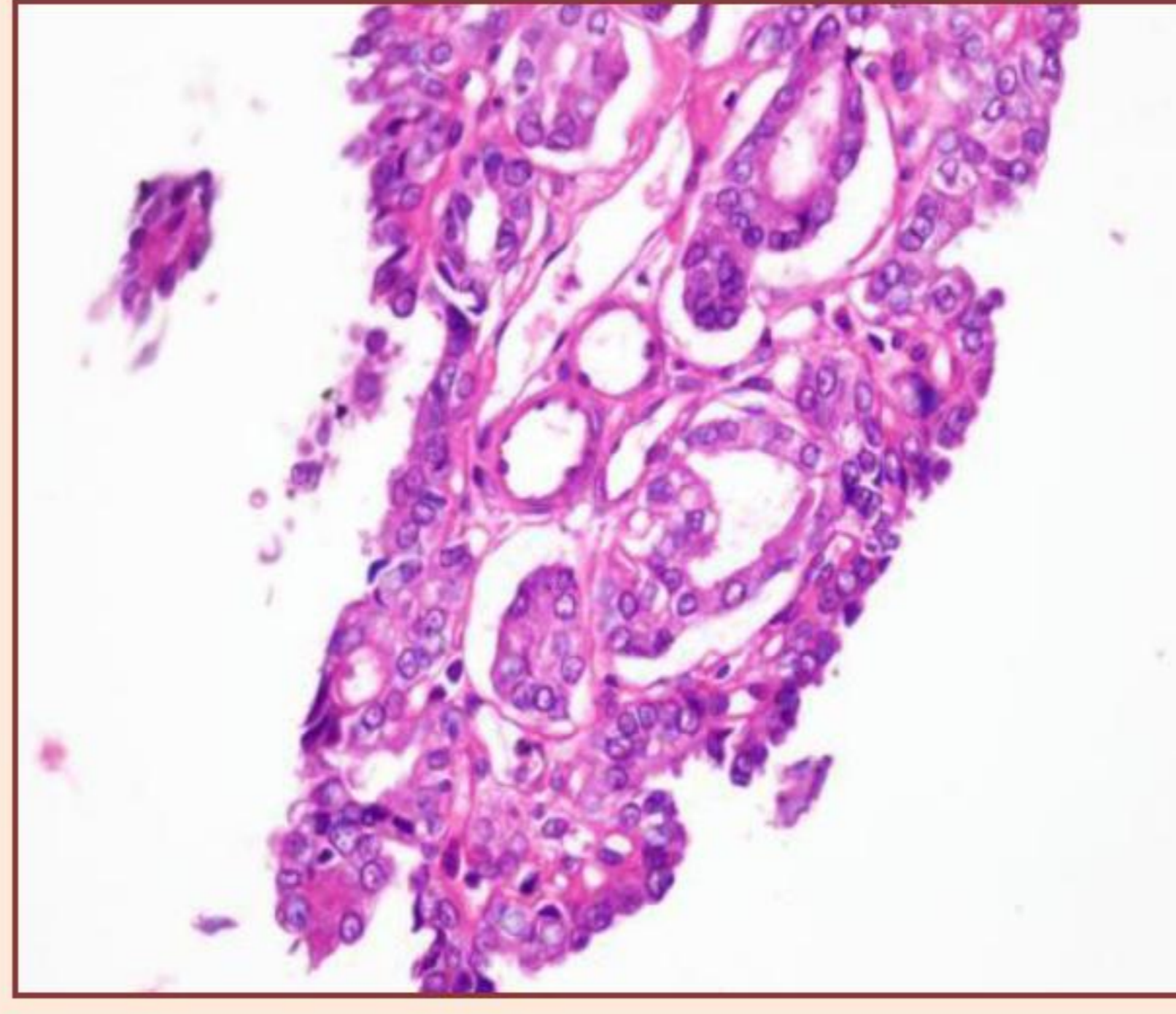


Figure 2: High power view of neoplastic cells exhibiting nuclear enlargement, crowding, clearing, grooves and pseudo-inclusions.

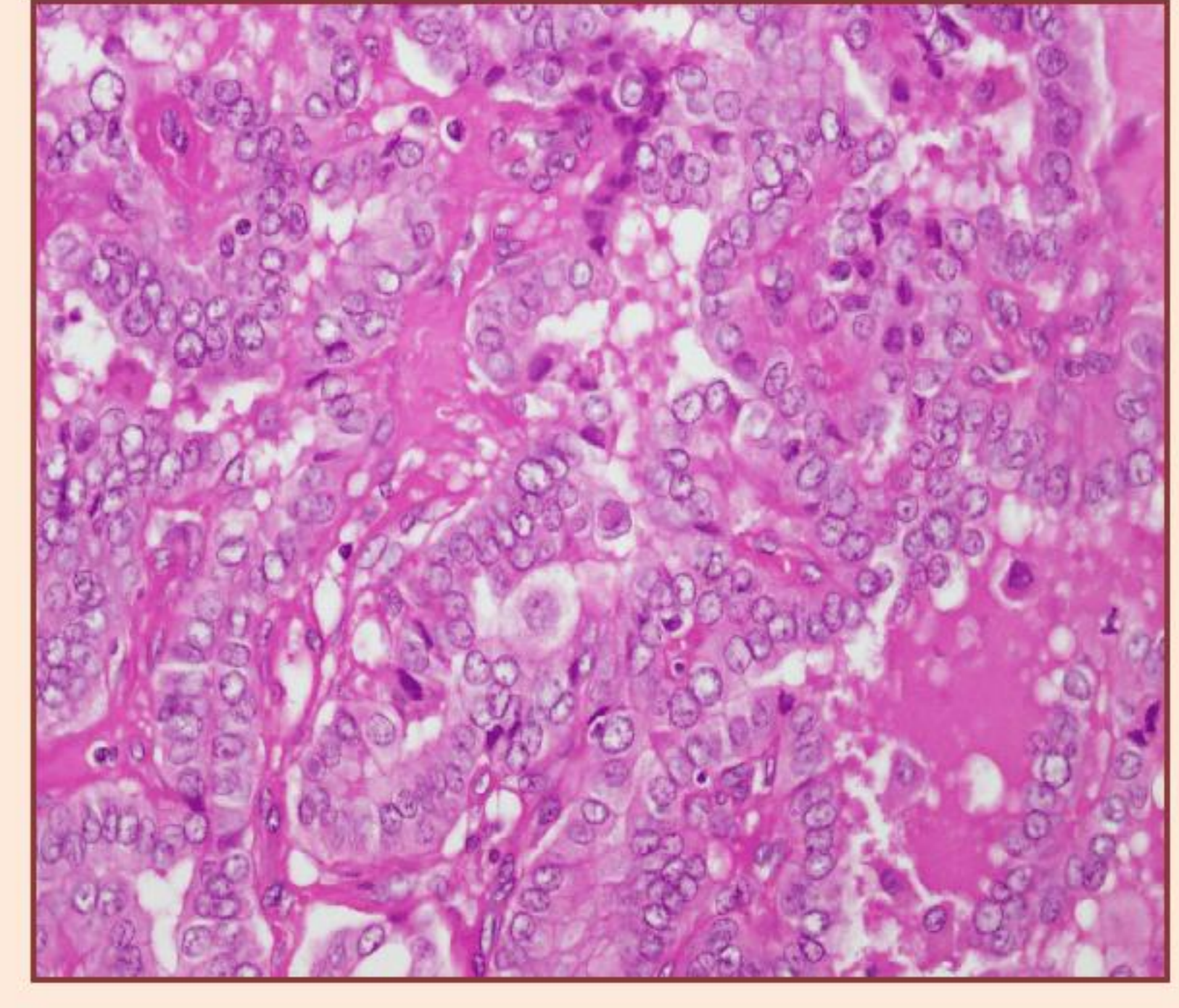


Figure 3: Tumor with intra-nuclear inclusions.

## DISCUSSION

To our knowledge this is the first case series reported of familial non medullary carcinoma of the thyroid from Pakistan. Because the number of affected patients was more than two it is highly unlikely that the NMTC was due to sporadic mutations. No specific gene has been associated with heritability therefore no genetic testing is available to check for the specific gene. Therefore, clinicians have to rely on a strong family history of this variant of thyroid cancer to diagnose familial cases. Charkes et al stated that when 3 or more family members are affected the probability of this due to sporadic mutations is less than 6% thus we believe that FNMTTC in our patients due to sporadic mutations is highly unlikely <sup>3</sup>. Although some researchers argue that familial clustering could be due to environmental exposure and bias due to more aggressive screening in asymptomatic family members, increasing evidence is now accumulating on the heritability of NMTC. All three of our patients had minimal symptoms but advanced disease at presentation. Lymph nodes metastasis was seen in patient 2 and 3 whereas capsular invasion was present in patient 3 only. This aggressive picture is supported by a meta-analysis by Wang et al which showed that FNMTTC is more aggressive at presentation with a higher degree of recurrence due to increased multifocality, extrathyroid invasion, bilateral presentation and lymph node involvement and is associated with less disease free survival as compared to sporadic NMTC <sup>2</sup>.

## CONCLUSION

- As specific gene testing is not available, identification of FNMTTC cases relies on a good family history and detailed pedigree analysis. In cases where clinical data suggest the presence of FNMTTC, ultrasound should be used for screening in close relatives for earlier diagnosis and better outcomes.
- Since FNMTTC is known to be particularly aggressive, patients should be treated with total thyroidectomy and neck dissection and kept under close follow-up with regular evaluations to detect recurrences.

## REFERENCES

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