G Chir Vol. 32 - n. 6/7 - pp. 310-315
June-July 2011

clinical practice

Papillary carcinoma in a thyroglossal duct remnant. Three case reports and discussion on management

Y. WANG, Q. JI, Y. WU, D. LI, Y. ZHU, C. HUANG, Q. SHEN, Z.WANG, L. ZHANG, T. SUN

SUMMARY: **Papillary carcinoma in a thyroglossal duct remnant. Three case reports and discussion on management.**

Y. WANG, Q. JI, Y. WU, D. LI, Y. ZHU, C. HUANG, Q. SHEN, Z.WANG, L. ZHANG, T. SUN

Objective. *To report three cases of papillary thyroglossal duct carcinoma (TDCa), and to discuss the diagnostic and therapeutic methods.*

Case reports. *We studied the clinical, pathological findings of the tumor, treatment and outcome data on 3 patients treated at our Institution for a papillary TDCa carcinoma and we compared the results with the published cases. Preoperative Fine Needle Aspiration (FNA) and intraoperative frozen section exam was performed in patients 1 and 2. Following the Sistrunk operation (SO), limited thyroidectomy were performed on patients 1 and 2, due to benign lesion. Neck dissections were performed on patients 2 and 3 (second operation after initial SO in other Institute), due to regional lymphadenopathy. The diagnosis of papillary TDCa was confirmed in all cases. Lymph nodes metastases were identified in patients 2 and 3. All patients were treated with levothyroxine therapy. After a median follow-up of 59 months, all patients are alive without recurrence.*

Conclusions. *Papillary TDCa is a rare malignancy with excellent prognosis. FNA and intraoperative frozen section exam are the most useful methods for confirmatory diagnosis. Resection of the thyroglossal duct carcinoma by the Sistrunk operation is an adequate surgical approach. Further thyroidectomy should be limited to one either lobe or pyramidal lobe in high risk patients. Total thyroidectomy is recommended only when there is clinical evidence of multifocal malignancy in thyroid gland. Postoperative hormone suppression is advocated.*

RIASSUNTO: **Carcinoma papillare in residuo del dotto tireoglosso. Valutazioni sulla gestione terapeutica di tre casi.**

Y. WANG, Q. JI, Y. WU, D. LI, Y. ZHU, C. HUANG, Q. SHEN, Z.WANG, L. ZHANG, T. SUN

Obiettivo. *Descrivere tre casi di carcinoma papillare del dotto tireoglosso (CDT) e discutere dei metodi diagnostici e terapeutici.*

Pazienti e metodi. *Abbiamo analizzato i dati clinici e anatomopatologici, il tipo di trattamento e i risultati ottenuti in tre pazienti ricoverati nel nostro Dipartimento per CTD papillare. Abbiamo confrontato i nostri risultati con quelli riportati in letteratura.*

Casi clinici. *I pazienti 1 e 2 sono stati sottoposti ad agoaspitrato (FNA, fine needle aspiration) preoperatorio ed esame istologico estemporaneo. Dopo l'intervento di Sistrunk (IS), nei pazienti 1 e 2 abbiamo realizzato una tiroidectomia limitata per lesioni benigne. Una dissezione linfonodale del collo è stata eseguita nei pazienti 2 e 3 (secondo intervento dopo iniziale IS in altro ospedale) per linfoadenopatia evidente. Nei tre casi è stata confermata la diagnosi di CDT papillare e nei pazienti 2 e 3 le metastasi linfonodali. Tutti i pazienti sono stati quindi sottoposti a terapia con levotiroxina a dosi soppressive. A un follow-up medio di 59 mesi, i pazienti sono tutti viventi in assenza di recidiva.*

Conclusioni. *Il CDT papillare è un raro tumore con prognosi eccellente. FNA ed esame istologico estemporaneo sono gli esami più utili per confermare la diagnosi. La resezione del tumore con IS è il trattamento appropriato. In pazienti ad alto rischio va associata una tiroidectomia di un lobo o della piramide. La tiroidectomia totale è indicata solo in presenza di evidente multifocalità neoplastica. È consigliabile la terapia ormonale postoperatoria tireosoppressiva.*

KEY WORDS: Thyroglossal duct remnant - Papillary carcinoma - Thyroidectomy.
Residuo dotto tireoglosso - Carcinoma papillare - Tiroidectomia.

Introduction

Thyroglossal duct carcinoma (TDCa) is malignant tumor arising within a thyroglossal duct remnant (TDR) or a thyroglossal duct cyst (TDC). This is an extremely rare condition as approximately 200 cases have been reported in the literatures since the first description by Bretano in 1911 (1,2) . There have been fewer than 10 cases reported in China (3,4) .

Fudan University, Shanghai, China
Department of Head & Neck Surgery, Cancer Hospital
Department of Oncology, Shanghai Medical College

In this article, we report three cases of papillary TDCa, and discuss the current opinions concerning management.

Case reports

The study was approved by the Human Research Ethics Board at the Cancer Hospital, Fudan University, Chin, and informed consent was obtained from each patient for use of their data within the study.

One hundred twelve patients who underwent surgical treatment for TDRs TDCs between 1995 and 2007 were identified from the database of Department of Head & Neck Surgery, at Cancer Hospital, Fudan University, Shanghai, China. Three patients were found to have TDCa. The medical records of these patients were reviewed and their pathologic specimens were re-examined. The information includes clinical, pathological findings of the tumor, treatment and outcome data.

Table 1 shows preoperative, operative, pathologic, and postoperative follow-up data of the patients. All the patients were female with a mean age of 40.7 years (33-46). Patients 1 and 2 were initially treated in our Institute. Patient 3 was transferred to our Institute because of the malignant pathologic findings after initial surgical treatment by Sistrunk operation (SO) in other Hospital. No previous neck irradiation or other predisposing factor was reported when medical history was reviewed.

In all three patients, asymptomatic anterior midline neck mass was the Chief Complaint. The neck masses were all firm and located in the supra-hyoid area. Patient 1 had no other associated masses, while patient 2 had a 1.5cm mass in the right lobe of the thyroid and an enlarged lymph node in the neck. Patient 3 was found to have bilateral lymph node enlargement.

Patients 1 and 2 underwent ultrasound exam, which demonstrated solid masses in the midline of the upper neck and a 5mm nodule in right thyroid lobe in patient 1, and a 1.5cm mass in right lower lobe and a 3cm enlarged lymph node in right lateral neck in patient 2. Patient 3 underwent preoperative computerized tomography (CT) and ultrasound exam that revealed bilateral enlarged lymph nodes and normal thyroid gland.

Patients 1 and 2 underwent SO which consists of excision of the entire tract of the thyroglossal duct, the midportion of the hyoid bone,

TABLE 1 - PROFILE OF THE THREE PATIENTS WITH PAPILLARY THYROGLOSSAL DUCT CARCINOMA IN OUR STUDY.

Variable	Patient 1	Patient 2	Patient 3
Age (year)	46	33	43
Gender	Female	Female	Female
History of the midline mass	3 year	1 month	1 year
TDR diameter (cm)	4	3	1.6
FNA	Tumor may generate from thyroid tissue	Papillary carcinoma	Not performed
Initial treatment	SO, lobectomy, unilateral neck dissection	SO, lumpectomy	SO
Secondary procedure	-	-	Bilateral neck dissection
Pathologic finding	Papillary carcinoma	Papillary carcinoma	Papillary carcinoma
Cyst wall invasion	No	Yes	No
Pathology of thyroid	Nodular goiter	Thyroid adenoma	-
Lymph node metastases	No	Yes	Yes
Levothyroxine therapy	Yes	Yes	Yes
Follow-up (years)	6	6	2
Recurrence	No	No	No
Current status	Alive	Alive	Alive

TDR, thyroglossal duct remnant; FNA, fine needle aspiration; SO, Sistrunk operation.

and a portion of the base of the tongue. During the operation there were no obvious signs of invasion to surrounding tissues. Because of the abnormities found in thyroid by ultra-sound, lobectomy (patient 1) and a lump-ectomy (patient 2) were performed, respectively. A modified neck dissection was performed in patient 2 because of the regional lymphadenopathy. Patient 3 underwent a second operation, which included bilateral modified radical neck dissection. The thyroid gland was not resected as no abnormalities were noted during preoperative exams and intraoperative exploration.

Histological examination of the TDCa tumors showed papillary carcinoma with epithelial lining and normal thyroid tissue in all cases (Fig. 1). No lymph node structure was found in all these midline mass. In patient 2, cyst wall and hyoid bone invasion were found. The thyroid specimen showed benign thyroid tissue in patients 1 and 2. Metastatic papillary carcinoma was present in lymph nodes in patients 2 and 3. Based on the Joseph's and Widstrom's criteria, all patients were diagnosed as papillary TDCa.

After surgery, all patients were treated with levothyroxine therapy at suppressive dose. After a median close follow-up of 59 months (range 26 to 77 months), all patients are alive with no evidence of recurrence in remained thyroid gland or other sites.

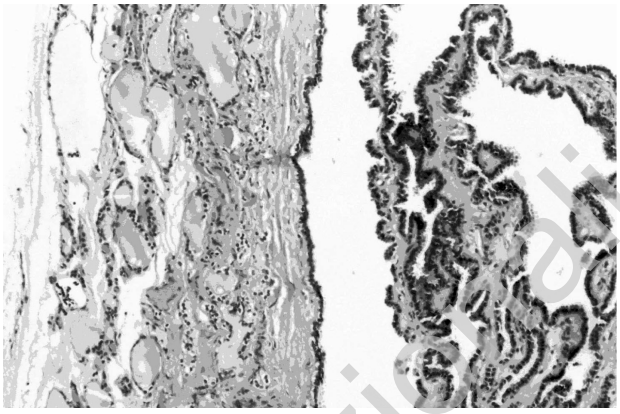

Fig. 1 - Microscopic image of the thyroglossal duct carcinoma showing the papillary carcinoma and the epithelial lining (Hematoxylin and Eosin, ×100).

Discussion

The thyroglossal duct (TD) is formed during the embryologic development of thyroid, and it usually disappears in the 9th to 10th week of fetal life. If the remnant of the TD fails to involute, it can persist as cyst, duct, or ectopic thyroid tissue. TDCa is a malignant tumor, which arises within the thyroglossal duct remnant. Papillary carcinoma is the most common histologic subtype, occurring in 80%-90% of patients, and squamous cell carcinoma constitutes about 5%, while other rare types includes Hürthle cell carcinoma and anaplastic carcinoma (1,2). Medullary carcinoma has not been reported because of the absence of parafollicular C cell in TDRs.

TDCa is rare, with around 200 cases reported in the literature since the first description by Bretano in 1911. There have been fewer than 10 cases reported in China. Because of the obscurity of TDR, it's hard to calculate the exact incidence of TDCa. Most writers can only compare the cases of TDCa with TDR they've treated, and the proportion is around 1:100 (6,7). In our study, it's around 3:100. TDCa arises more often in females (female:male, 1.5:1; 100% female in this study), and the mean age of patients is 39.2 (range 6~81); about 79% patients are from 20 to 60 years old (8).

The clinical presentation of TDCa is often similar to that of TDC. The history ranges from 10 days to 40 years (5). Usually, asymptomatic anterior midline neck mass is the Chief Complaint. In most cases, the diagnosis of malignancy is not made until surgical operation, just like in our patient 3. The malignancy should be suspected when the remnant is hard, fixed, or if it is associated with lymphadenopathy.

With ultrasound exam, the carcinoma may appear as a mural lesion in the cyst, sometimes with microcalcification, or as a tumor invading the cyst wall (16). Carcinoma may be seen as a small peripherally based mass in relation to a cyst, a solid mass in the course of the thyroglossal duct, or a complex invasive mass also in the midline of the neck on CT or MRI. CT may reveal calcification in cases of carcinoma, within either the primary carcinoma mass or a metastatic node (17). The presence of calcification in ultra-sound or CT may be a specific marker for carcinoma. In our series, no one showed these specific signs. Nevertheless, these exams helped to reveal the abnormalities in thyroid gland and suspicious nodes. FNA is considered a safe, well-tolerated and cost-effective procedure. In Miccoli's report routine FNA had extremely high sensitivity (100%) and specificity (100%) (18). But, in Yang's report the diagnostic accuracy was only 53%, and the false-negative rate was 47% (19). We found FNA to be a very effective way to enhance preoperative diagnosis. In this study, all patients showed firm midline remnants and solid mass during ultrasound exam which were different from other TDCs. When further FNA revealed tumor - which might generate from thyroid tissue in patient 1, and papillary carcinoma in patient 2 - TDCa was included in the differential diagnosis in these patients.

Some Authors recommended frozen section exam if there are any suspicious findings during the operation. In patients 1 and 2, once the diagnosed frozen section suggested a papillary carcinoma within a TDR, further surgical treatments were performed at the same time. In patient 3 initially treated in another Institute, the surgeon failed to observe the abnormalities of the remnant. Neither preoperative FNA nor the intra-operative frozen section was performed, and the patient was treated as a normal TDC. So, a secondary operation was performed based on the final pathological report. Based upon this experience, we recommend that preoperative FNA or intraoperative frozen section examination be performed for suspicious lesions (Fig. 2).

The recognition of carcinoma arising from a TDR has both clinical and practical importance. The differential diagnosis of these midline malignant lesions includes a primary thyroid carcinoma in the pyramidal lobe, a delphian lymph node with carcinoma metastasis, and a metastatic tumor from a primary in the thyroid gland. It is important to distinguish between these possibilities for selection of the appropriate surgical and adjuvant treatment as well as for prognostic reasons.

Joseph set down strict criteria for the diagnosis of a primary TDCa (5). These included the finding of a thyroglossal remnant that can be distinguished from a lymph node metastasis by the epithelial lining and the thyroid nests within the cyst wall in a patient with a clinically normal thyroid gland. Widstrom also described diagnostic criteria (10): (a) the carcinoma should be in the wall of the TDR; (b) the TDCa must be differentiated from a cystic lymph node metastasis by histological demonstration of a squamous or columnar epithelial lining and normal thyroid follicles in the wall of the TDR, and (c) there should be no malignancy in the thyroid gland; or any other possible primary site. These two Authors both emphasized that there should be no malignancy in the thyroid gland. This definition excludes 11% to 33% patients with synchronous carcinoma in thyroid gland. Possible explanations for the finding of synchronous lesions include multi-focal thyroid carcinoma, or metastastic spread through the TDR (7). In our study, all diagnosis fitted both Joseph's and Widstrom's strict criteria.

Because of the limited number of cases of this rare malignancy, it is hard to draw any specific treatment guidelines. Many investigators agree that the complete excision of the remnant via SO is adequate treatment to the primary disease, especially if the carcinoma lesion is small and the margins are free of tumor. In some reports, the cure rate for the cases without cyst wall invasion was almost 95%, the treatment included SOoperation followed by endocrine therapy (7-11). If there is any sign of invasion to surrounding tissue, wider margins should be considered. Some authors agree that surgical treatment of the thyroid is indicated for: (1) any suspicious lesions found in thyroid gland during preoperative exam or intraoperative exploration, (2) cyst wall invasion, (3) large TDCa lesions (7,9,11). However, the precise details of the procedure on the thyroid gland remain a controversial issue, and focuses on the potential need for a total thyroidectomy (TT). Some authors recommend a TT in patients with TDCa, even without a clinically evident thyroid mass due to concern about multifocal disease (7,9). Others argue that TT is not needed due to the low incidence of microscopic foci finding in "normal" thyroid tissue (12) and the high incidence (as high as 35%) of occult "incidental" thyroid carcinoma in autopsy studies (20).

From our point of view, after careful preoperative scan by high-frequency ultrasound or CT, even possible, the unsuspicious or undetectable multifocal tumors mostly belong to the microcarcinoma rather than metastatic spread. The effect of finding microscopic foci of papillary thyroid carcinoma in thyroid gland has been shown to have no effect on survival (21). In China, lobectomy of the involved thyroid lobe and other limited thyroidectomy is widely suggested as adequate treatment for papillary thyroid carcinoma (PTCa) (22), unless multiple carcinomas are detected in both lobes. So, most surgeons can not accept removal of the total thyroid gland without an obvious lesion to treat TDCa with lower metastasis and death rates, as even experienced surgeons cannot completely rule out the risk of vocal cord paralysis or hypoparathyroidism. Furthermore, in Patel's report, the addition of TT to SO had no significant effect on outcome in the analysis of prognostic factors to study overall survival in 62 previously reported cases (13). According to the reports from China, most patients with TDCa did not undergo TT (3, 4). Our proposal of a definitive algorithm for treatment is listed in Figure 2.We stress that further thyroid surgery is needed when any suspicious lesions are found in the thyroid gland during preoperative exam or intraoperative exploration, or the lesion is very close to the thyroid gland. Even in these cases, we feel that excision should be limited either to one lobe or pyramidal lobe. Total thyroidectomy is recommended only when there is clinical evidence of multifocal malignancy in thyroid gland. In our report, a lobectomy and a lumpectomy were performed on patients 1 and 2 respectively, because of the abnormalities found in thyroid. In patient 3 the thyroid gland was not resected as no abnormalities were noted during intraoperative exploration and preoperative exam. The incidence of cervical metastasis is lower than for papillary carcinoma of the thyroid: it is estimated to be 8%. Most authors agree that a neck dissection should be performed only when cervical metastases are clinically present (14). In our study, modified neck dissections were performed on patients 2 and 3, because of the regional lymphadenopathy, and positive lymph nodes were found in both cases.

Some investigators advocated postoperative hormone suppression and/or radioactive iodine ablation following TT (1, 11). In our study, all these papillary TDCa patients were treated with levothyroxine therapy accomplished by keeping the thyroid-stimulating hormone between 0.1 and 0.5 mIU/L (2, 11), because of the same pathological origin as normal PTC. But, since no evidence of multiple carcinomas or distant metastases, no one was treated with radioactive iodine.

The prognosis of patients with papillary TDCa is excellent. In Bosch's review of 108 cases, only 2 cases had lung or liver metastasis (15). In Patel et al's report, the 10 years overall survival was 95.6% (13). We recommend that thyroid-stimulating hormone levels be checked and

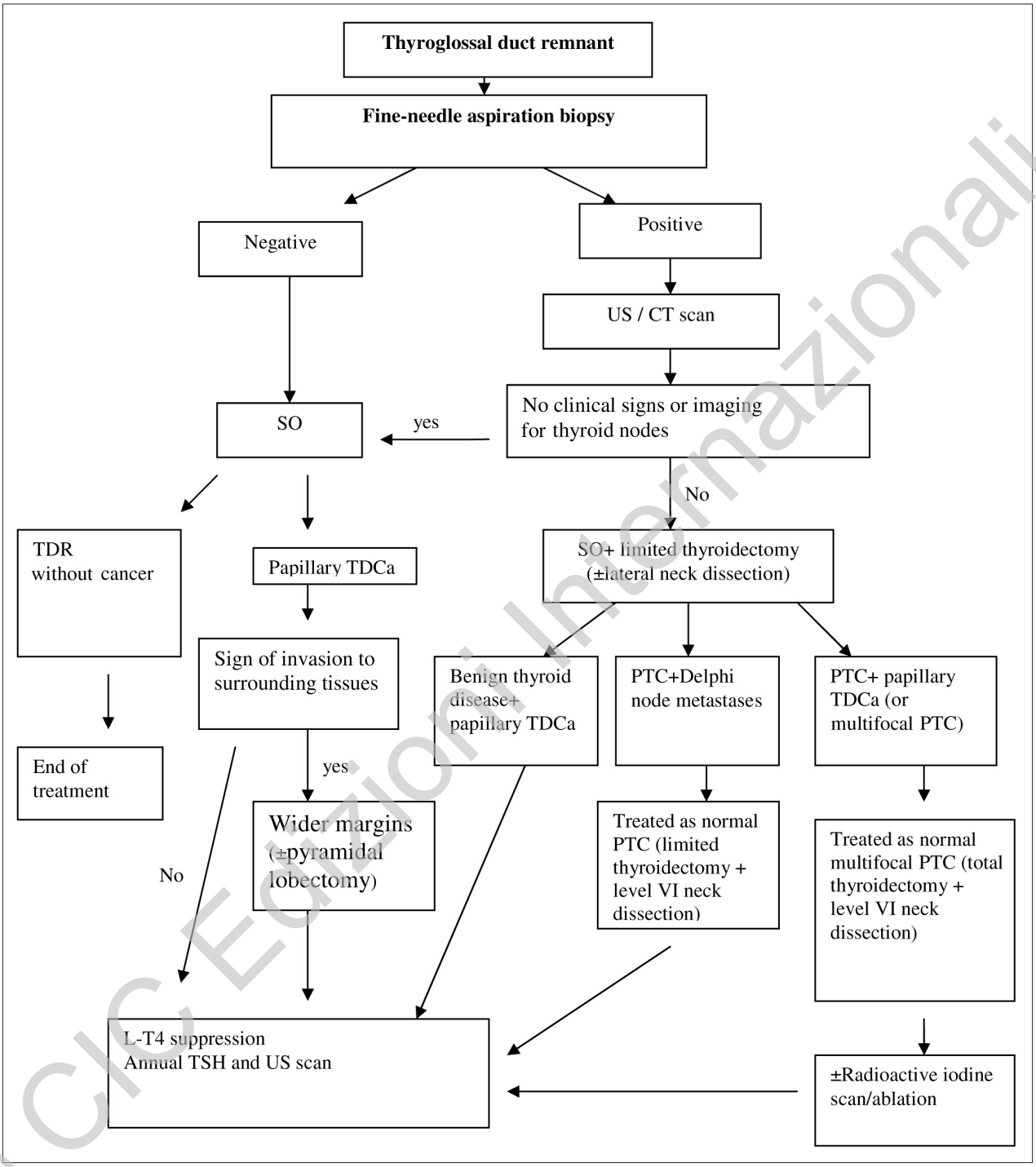

Fig. 2 - Algorithm for diagnosis, treatment, and follow-up of patients with papillary thyroglossal duct carcinoma. US, ultrasonography; SO, Sistrunk operation; TDR, thyroglossal duct remnant; PTC, papillary thyroid carcinoma; TSH, thyroid-stimulating hormone; TDCa, thyroglossal duct carcinoma.

thyroid ultrasound should be included in postoperative follow-up. In our study, there were no clinical or ultrasonographic signs of recurrence or metastasis during the follow-up of three patients.

Conclusion

In conclusion, malignant lesions of TDRs are rare. The preoperative FNA and intraoperative frozen section

exam are the most useful methods confirmatory diagnosis of papillary TDCa, when there is a suspicion that a thyroglossal duct cyst harbors a malignant tumor. Resection of the thyroglossal duct carcinoma by the Sistrunk operation is an adequate surgical approach. Further thyroidectomy should be limited either to one lobe or pyramidal lobe in high risk patients. Total thyroidectomy is recommended only when there is clinical evidence of multifocal malignancy in thyroid gland. Postoperative hormone suppression is advocated.

Statement *- There are no financial or other relationships which may lead to a conflict of interest, and which references any published reports that may duplicate material in this submitted manuscript. The study was approved by the Human Research Ethics Board at the Cancer Hospital, Fudan University, and informed consent was obtained from each patient for use of their data within the study.*

References

1. Chen F, Sheridan B, Nankervis J. Carcinoma of the thyroglossal duct: case reports and a literature review. Aust NZ J Surg 1993; 63(8): 614-616.
2. Kum CK, Goh P, Teh M: Papillary carcinoma arising in a thyroglossal cyst. Aust NZ J Surg 1993; 63(9): 738-740
3. Lv QP, Ma JL. Thyroglossal duct carcinoma: 1 case report. Chinese Arch Otolaryngol Head Neck Surg 1999; 6(4).249-250.
4. Xu SZ. Thyroglossal duct carcinoma: 1 case report. Jilin Medical Journal 2000; 21(6):364-365.
5. Joseph TJ, Komorowski RA. Thyroglossal duct carcinoma [J]. Hum Pathol 1975; 6(6): 717-729.
6. LiVolsi VA, Perzin KH, Savetsky L. Carcinoma arising in median ectopic thyroid (including thyroglossal duct tissue) [J]. Cancer 1974; 34(4): 1303-1315.
7. Heshmati HM, Fatourechi V, Van Heerden JA, et al. Thyroglossal duct carcinoma: report of 12 cases[J], Mayo Clin Proc 1997; 72(4): 315-319.
8. Fernandez JF, Ordo_ez NG, Schultz PN, et al. Thyroglossal duct carcinoma[J]. Surgery 1991; 110(6): 928-935.
9. Plaza CPR, Lopez MED, Carraxco CEG, et al. Management of well-differentiated thyroglossal remnant thyroid carcinoma: time to close the debate? Report of five new cases and proposal of a definitive algorithm for treatment. Ann Surg Oncol 2006; 1:745–752.
10. Widstrom A, Magnusson P, Hallberg O, et al. Adenocarcinoma originating in the thyroglossal duct[J]. Ann Otol, Ann Otol 1976; 85(2): 286-90.
11. LaRouere MJ, Drake AF, Baker SR, et al. Evaluation and management of a carcinoma arising in a thyroglossal duct cyst[J]. Am J Otolaryngol 1987; 8(6): 351-355.
12. Myssiorek D. Total thyroedectomy is overly aggressive treatment for papillary carcinoma in a thyroglossal duct cyst[J]. Arch Otolaryngol Head Neck Surg 2002; 128(4): 464.
13. Patel SG, Escrig, Shaha AR, Singh B, et al. Management of well-differentiated thyroid arcinoma presenting within a thyroglossal duct cyst. J Surg Oncol 2002;7:134-139.
14. Perez MM, Garcia MB, Iturbe CE, et al. Papillary carcinoma arising in a thyroglossal duct cyst: report of two cases[J]. J Oral Maxillofac Surg 1993; 51(1): 89-93.
15. Bosch JL, Kummer EW, Hohmann FR. Carcinoma of the thyroglossal duct[J]. Neth J Surg 1986; 38(2): 36-40.
16. Dedivitis RA, Camargo DL, Peixoto GL, Weissman L, Guimaraes AV. Thyroglossal duct: a review of 55 cases. J Am Coll Surg 2002; 194:274–6.
17. Glastonbury CM, Davidson HC, Haller JR, et al. The CT and MR imaging features of carcinoma arising in thyroglossal duct remnants. AJNR Am J Neuroradiol. 2000 Apr;21(4):770-4.
18. Miccoli P, Minuto MN, Galleri D, Puccini M, Berti P. Extent of surgery in thyroglossal duct carcinoma: reflection on a series of eighteen cases. Thyroid 2004; 14:121–3.
19. Yang YJ, Haghir S, Wanamaker JR, et al. Diagnosis of papillary carcinoma in a thyroglossal duct cyst by fine needle aspiration biopsy. Arch Pathol Lab Med 2000; 124: 139–42.
20. Harach HE, Franssila KO, Wasenius VM: Occult popillary carcinoma of the thyroid. A "normal" finding in finland. A systematic autopsy study. Cancer 1985;56:531-538.
21. Hay ID, Grant CS, van Heerden JA, et al. Papillary thyroid microcarcinoma: a study of 535 cases observed in a 50-year period. Surgery 1992; 112:1139–46.
22. Zhang Lun, Li Shuling: A Long Term Observation of 1 173 Cases with Thyroid Papillary Carcinoma after Surgery. Chinese Journal of Clinical Oncology 2003;30(11):805-808