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ORIGINAL ARTICLE

Analysis of Pattern of Laryngotracheal Invasion by Papillary Thyroid Carcinoma and Their Management: Our Experience

Pradipta Kumar Parida[1] · Karthik Herkal[1] · Chapity Preetam[1] · Pradeep Pradhan[1] · Dillip Kumar Samal[1] · Saurav Sarkar[1]

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Abstract To analyse the pattern of laryngotracheal invasion (LTI) by papillary-thyroid-carcinoma (PTC) and outcomes of their management. We undertook a retrospective chart review to study patterns of LTI by PTC and to evaluate outcomes of surgical modalities used to treat PTC with LTI. Out of 246cases of PTC, 26-cases had LTI (male-12, female-14, mean-age-55.6 years, range 42–73 years). Common clinical presentation were neck swelling, respiratory distress/stridor and vocal cord paralysis in 100%, 8 (30.8%) and 10 (38.5%) cases respectively. PTC was staged according to AJCC-TNM staging system (T4a-24, T4b-02, N1a-12, N1b-14, M0-25, and M1-01). CT-scan showed obvious LTI and tracheal narrowing in 11(42.3%) and 18(69.2%) cases respectively. All cases underwent total thyroidectomy with central-compartment-clearance. Unilateral and bilateral lateral-neck-dissection was performed in 08 and 06cases respectively. Pattern of Intra-operative LTI were as follows: trachea-13cases, trachea and cricoid-05cases, thyroid cartilage-6cases, trachea, cricoid and thyroid cartilage-2 cases and intra-luminal involvement in 4cases. Modified Shin's staging was used to stage LTI. LTI were superficial, deep-extra-luminal and intra-luminal in 13, 09 and 04cases respectively. LTI was managed by shave-excision, window-resection of trachea, sleeve-resection of trachea and anastomosis, partial laryngectomy and total-laryngectomy in 13,02,04,05 and 2 cases respectively. All patients received radio-active-iodine (RAI) and TSH-suppression-therapy post-operatively. Mean follow-up period was two-years (range 18–30 months). One-case had radio-iodine non-avid local recurrence with lung metastases one-year post-operatively. Shave-excision is adequate for tumours not infiltrating into outer perichondrium. Tracheal-resection and total/partial laryngectomy may be required in cases with laryngo-tracheal cartilage or intra-luminal involvement. Adequate surgical excision along with postoperative RAI and TSH-suppression-therapy gives good loco-regional disease control in PTC with LTI.

Keywords Papillary thyroid carcinoma · Extra-thyroidal extension · Thyroidectomy · Tracheal resection

Introduction

Most of differentiated thyroid cancers (DTC) are usually indolent disease with favourable prognosis. Still there is about 8 to 26% of thyroid gland malignancy have shown to invade adjacent structure like trachea, larynx and esophagus which leads to increased cause specific mortality and morbidity rates [1–3]. Laryngotracheal invasion (LTI) by papillary thyroid carcinoma (PTC) worsens the prognosis. Local invasion into airway has cause specific death rate of 50 percent in DTC [4]. These subset of patients were found to have higher recurrence rate and lower survival time even after surgical excision.

Invasion to laryngo-trachial structure occurs in stepwise manner from superficial layer into deep structure and in more advanced cases intra-luminal involvement is found. It is classified according to Shin [5].

With reference to present classification systems by the Union for International Cancer Control (UICC) and the

✉ Pradipta Kumar Parida
drpradipta04@gmail.com

[1] Department of ENT and Head Neck Surgery, All India Institute of Medical Sciences, Sijua, Patrapara, Bhubaneswar, Odisha 751020, India

American Joint Committee on Cancer (AJCC), the widely invasive thyroid cancer (TC) is classified as potentially operable (T4a, e.g., involving of the airway, esophagus, or muscles) or usually not operable (T4b, e.g., invasion of large arteries or the prevertebral fascia) [6, 7].

Various treatment modalities are available according to extent of involvement of laryngo-tracheal structures starting from total thyroidectomy along with laryngo-tracheal excision to post-operative radio iodine ablation [8]. Extent of resection to treat LTI is controversial. It ranges from "shave excision" that may leave microscopic disease to radical excision and reconstruction.

We undertook a retrospective chart review to study patterns of laryngotracheal invasion (LTI) by papillary thyroid carcinoma (PTC), histo-pathoogical variants and to evaluate outcomes of laryngo-tracheal resection or shave excision with post-operative radioiodine remnant ablation (RRA) in the treatment of LTI from PTC between April-2016 to May-2019 at our centre.

Materials and Methods

This study is a retrospective study of chart review of 246 PTC patients presented to our tertiary care hospital from april 2016 to may 2019. Twenty six out of 246 patients had LTI and those cases were included in study. The case records were reviewed for demographics, clinical presentations, various investigation modalities used for evaluation and to make diagnosis, types of surgeries patients received, pattern of LTI and their management and postoperative adjuvant therapy.

Aims and Objectives of Study

To study the patterns of LTI by PTC, histo-pathoogical variants of PTC and outcome of various management modalities for LTI from PTC.

Inclusion Criteria

Patient with FNAC proven resectable PTC with LTI underwent surgery as primary modality of treatment.

Exclusion Criteria

1. patient with unresectable primary disease, recurrent disease or revision surgery, 2. patients not willing for surgery and 3. patients with uncontrolled diabetes and hypertension.

A detailed history was elicited regarding neck wselling, voice change, respiratory distress and stridor. Local and physical examination was carried out for all the patients. All patients were investigated by Thyroid function tests, ultrasonography of thyroid and neck, and fine needle aspiration cytology. The preoperative diagnosis of PTC was made by FNAC. Preoperative fibre-optic laryngoscopy was done for all cases to check for vocal cord mobility and to visualise any intra-luminal bulge or growth. Preoperative contrast enhanced computer tomography(CECT) done to estimate extent of extrathyroidal invasion and nodal metastasis. For distant metastasis chest radiography along with CECT chest and abdomen was done in all patients preoperatively. American Joint committee on Cancer(-AJCC) TNM staging system (8th edition) was used to stage the disease. Modified Shin staging [9] of laryngotracheal invasion in thyroid cancer (stage-1: perilaryngotracheal adhesion, Sage-2: Invasion of the cartilage, stage-3: Invasion into intercartilagenous space and/or mucosa without intraluminal manifestation and stage-4: Intraluminal tumour/involvement) was used to stage the LTI as shown in Table 1.

All patient underwent total thyroidectomy with central neck node dissection with or without lateral neck dissection and resection of extrathyroidal involved tissue under general anesthesia. All cases received post-operative radio iodine ablation (RIA) and TSH suppression therapy.

Parameter Studied

Demographic data, patterns of LTI by PTC, histo-pathoogical variants of PTC and surgical modalities used for treatment.

Statistical Analysis

Descriptive Statistics were used to analyse the data.

Results

Age and Gender

Out of 246 cases of PTC, 26-cases had surgically confirmed LTI from PTC (male-12, female-14, Mean age-55.6 years, Range 42–73 years). The data for these 26 cases were analysed (Table 1).

Clinical Features

Common clinical presentation were neck swelling, respiratory distress/stridor and vocal cord palsy in 100%, 8(30.8%) cases and 10(38.5%) cases respectively s(Table 1).

Table 1 Demographics details, clinical features, CT findings, staging, operative procedure and post-operative adjuvant therapy

Characteristics	Number/%
Demography	
Age	55.6 years
Mean age	42–73 years
Range	12:14
Gender (M:F)	
Clinical presentation (number/%)	
Neck swelling	100% cases
Respiratory distress/stridor	8(30.8%) cases
Vocal cord palsy	10 (38.5%)cases
CT findings	
Tracheal narrowing	18(69.2%)
Laryngotracheal invasion	11(42.3%)
Clinical staging	
T category	
T4a	24
T4b	02
N category	
N 1a	12
N1b	14
M category	
M0	25
M1	01
Surgery	
Total thyroidectomy with central compartment clearance	26 (100%)
Unilateral lateral compartment dissection	08 (30.8%)
Bilateral lateral compartment dissection	06 (23.1%)
Histopathology report	
Classical	20
Follicular	04
Tall cell variant	02
Multifocal	20

Investigations

Thyroid function test was normal in all cases. FNAC in all cases was suggestive of papillary carcinoma of thyroid (Bethesda type-VI). CT scan showed obvious LTI and tracheal narrowing in 11(42.3%) and 18(69.2%) cases respectively (Figs. 1, 2, 3).

Staging

Final staging (TNM) was done based on histopathological findings, intraoperative findings and radiological findings.

T Category

Twenty four cases had T4a and two cases were in T4b. *N Catagory*: Twelve cases had N1a disease and 14 cases had N1b disease. M category: Distance metastases were present in lungs (M1) in 2 cases.

Surgical Management

Pre-operative tracheostomy was done in two cases who presented with severe stridor. Both the cases had ipsilateral vocal cord paralysis along with gross invasion of larynx by the tumor. All cases were operated under general anesthesia. The anesthesia was administered through tracheostomy tube in two cases and in rest 24 cases orotracheal intubation was carried out under fibre-optic guidance. All cases underwent total thyroidectomy with central compartment-clearance with or without lateral-neck-dissection. Lateral neck dissection was done in 14-cases (Unilateral-8 and bilateral -6). Pattern of Intra-operative LTI were as follows: trachea-13cases, trachea and cricoid-05cases, thyroid cartilage-6cases, trachea, cricoid and thyroid cartilage-2 cases and intra-luminal involvement in 4cases. Modified Shin's staging was used to stage LTI. LTI were superficial, deep-extra-luminal and intra-luminal in 13, 09 and 04cases respectively. LTI was managed by shave-excision, window-resection of trachea, sleeve-resection of trachea and anastomosis, partial laryngectomy (resection of thyroid-lamina along with surrounding involved tissue) and total-laryngectomy in 13,02,04,05 and 2 cases respectively (Table 2) (Figs. 1, 2, 3, 4).

R0 resection for primary tumor could be achived in all cases. The metastatic lymph node could be removed in all cases except in two cases and in these two cases the lymph nodes were enchasing the common carotid artery and these lymph nodes were shaved out from the carotid artery.

Postoperative Complications

One patient developed postoperative infection with partial anterior tracheal necrosis after shave resection and bilateral neck dissection. It was managed by wound debridement with primary closure of tracheal defect under antibiotic cover. Post–operative chyle leak was present in 6 cases which was managed by dietary modification and pressure dressing.

Histopathology

Histological types were classical, follicular and tall cell variants in 20-cases, 4-cases and 2-case respectively. Lymph node dissected out in central compartment

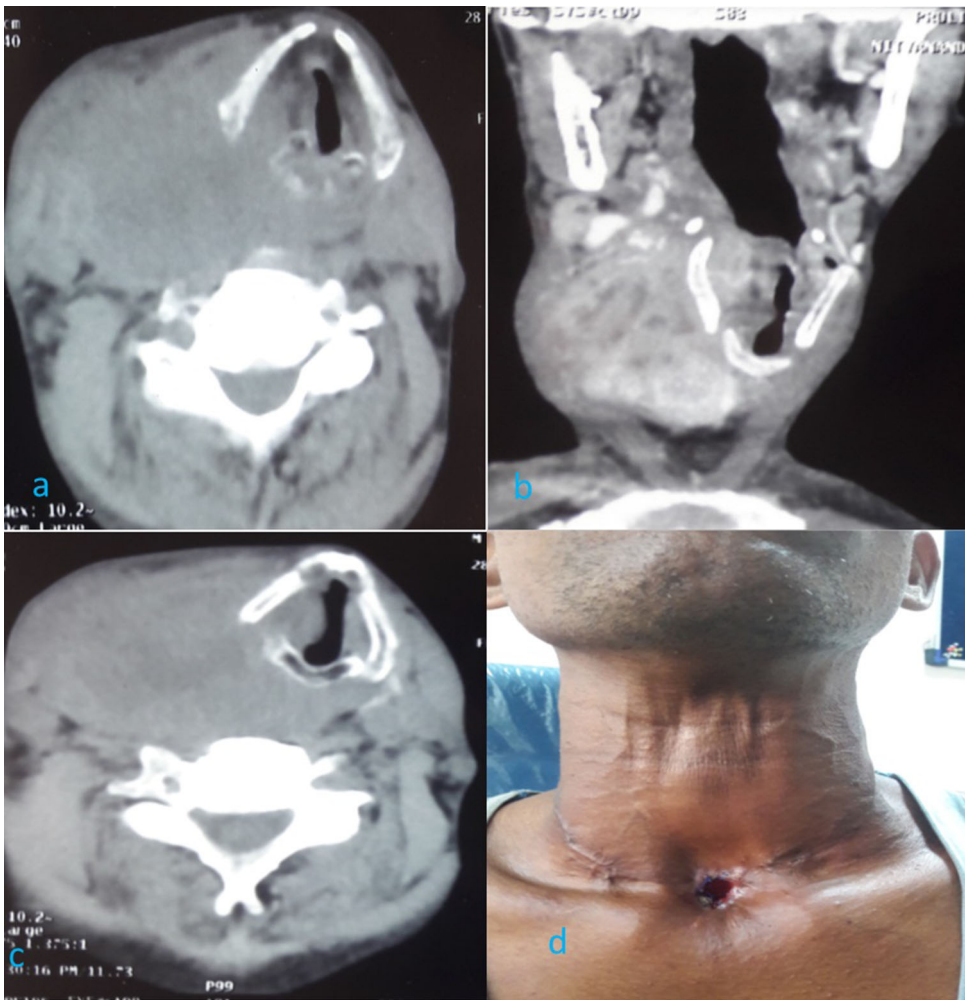

Fig. 1 **a**, **b**, **c** CT-scan showing gross involvement larynx intra-luminal extension (stage-4 involvement). **d** Postoperative clinical photograph after excision of tumor and total laryngectomy

dissection were positive for metastases in all cases. All lateral neck dissectiuon specimen were positive for metastasis.

Post-Operative Adjuvant Therapy and Follow Up

Postoperative risk stratification revealed that all case falls under high risk group. Hence, all patient received adjuvant iodine therapy and same was repeated in every six months to one year depending on pretherapy thyroid scan. Radio-iodine remnant ablation (RRA) was done in 24 patients and Radioactive iodine therapy (RAI) treatment in two cases with residual residual neck along the common carotid artery. Response to therapy radio active iodine therapy was excellent, biochemical incomplete response and structural incomplete response in 22 cases, 3 cases and 01 case respectively at the last follow up.

The patients were followed up with postoperative USG neck, serum thyroglogulin and antithyroglobulin antibody level six monthly. Mean follow up period was 24 months (range 18–30 months). One case had local recurrence after one year of follow up and the tumor became radio-iodine resistant with lung metastases was treated with external beam radiotherapy(EBRT). All patients received suprathreshold dose of thyroxine, 100–150 microg daily during follow up period.

Discussion

LTI by PTC is rare. The patients with locally advanced PTC usually presents with hoarseness, stridor, hemoptysis, and dysphagia depending upon the structure involved [10]. Radiographic evaluation indicated in cases with large tumors or symptoms and signs suggestive of extrathyroidal extension. Ultrasound, CT, and MRI are commonly used modalities to assess the primary tumor and its extension. Ultrasound with or without FNAC is the initial investigation of choice for any thyroid swelling. CT scan helps in delineating the primary tumor, presence of metastaic lymph node and the extent of extrathyroidal extension. The advantage of MRI over CT scan is that it does not interfere

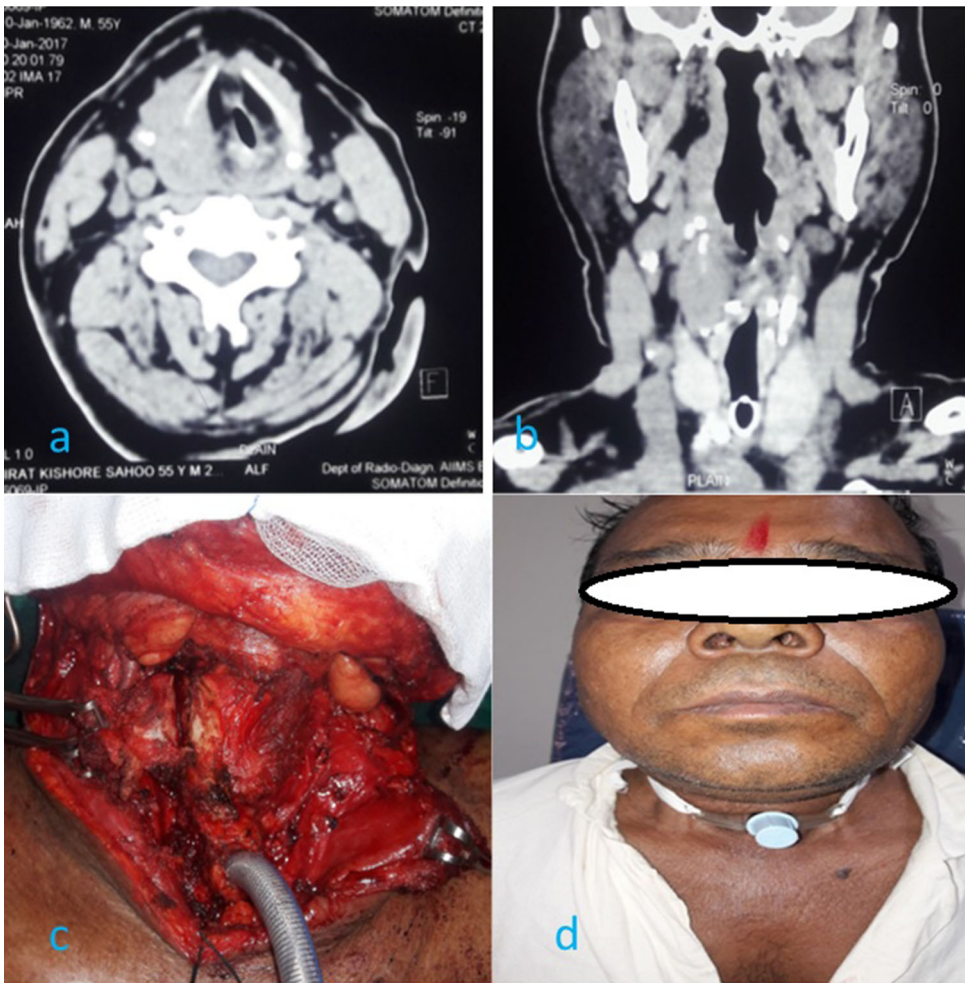

Fig. 2 **a**, **b** CT scan showing involvement of larynx by the tumor without intraluminal extension (stage-III involvement). **c** Intra-operative photograph showing tumor invading into rirght thyroid lamina. **d** Post-operative photographs showing the patient tolerating tracheostomy tube corking

with Postoperative RAI. Fibre-optic laryngoscopy and Tracheoscopy or bronchoscopy may be required to assess the vocal cord mobility and to visualize intraluminal involvement.

PTC is primarily treated surgically and followed by RIA carries a good prognosis. The known prognostic factors for PTC are age, gender, extra-thyroidal or extracapsular extension, tumor histology, primary tumor size, and distant metastasis [11]. The decreasing order of structures involved by extrathyroid spread are the strap muscles (53%), recurrent laryngeal nerve (47%), trachea (37%), esophagus (21%), lateral neck structures including the great vessels and vagus nerve (30%), and larynx (12%) [12]. These structures are involved either by spread of the primary tumor or from etranodal extension of level VI metastatic lymph node [13]. Presence of extrathyroidal extension worsens the survival and increases the risk of loco-regional control of the disease. Ten-year overall survival rates is reduced to 45% in patients with extrathyroidal extension compared with 91% for those who have encapsulated tumors [14]. The surgical planning in treatment of LTI from PTC depends on invasion site, depth of invasion into the wall and vertical and Horizontal extent of invasion-new 2. Aerodigestive tract invasion by thyroid tumors can be subdided into three types: superficial, deep extraluminal and intraluminal involvement. Superficial invasion may be managed by shave excision. Deeper invasions, however, require complete wall resections. Complete radical excision is the ideal treatment for locally advanced disease but resection of critical structures like larynx, trachea and recurrent laryngeal nerve is associated with significant morbidity. The conservative approaches such as peeling or shaving technique reduces morbidity and preserves the function but carries a high risk of leaving behind disease in situ leading locoregional recurrence. Postoperative radioactive iodine (RAI) with or without external beam radiotherapy (EBRT) should be considered to manage microscopic disease after shave excision.

In our centre among the 26 cases, the Pattern of Intra-operative LTI were as follows: trachea-13cases, trachea and cricoid-05cases, thyroid cartilage-6cases, trachea, cricoid and thyroid cartilage-2 cases and intra-luminal involvement in 4cases. The LTI in our cases were managed as proposed by Dralle et al. [1]. Dralle et al. classified the

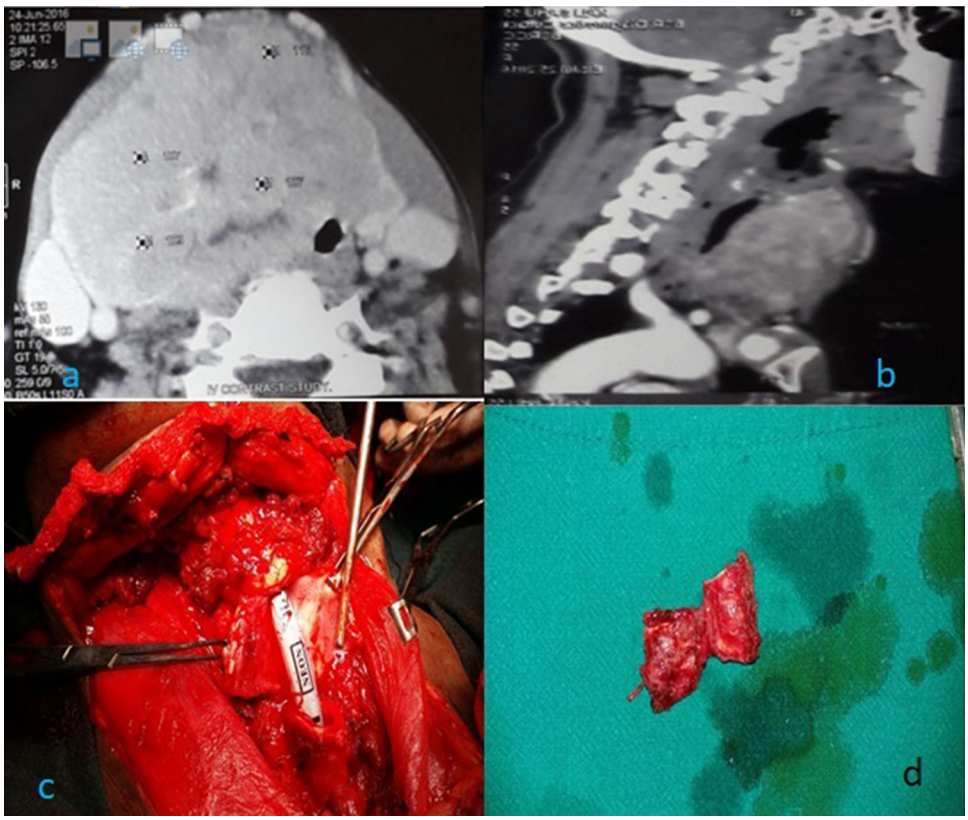

Fig. 3 **a**, **b** CT scan showing the narrowing of trachea along with grade -4 involvement of tracheal cartilage. **c** Intra-operative photograph showing resection of involved segment of trachea. **d** The resected segment of involved trachea

Table 2 Pattern of laryngotracheal invasion and their management

Structure(s) involved	Type of excision
Trachea: 13	
Stage-I: 06	Shave excision
Stage-II: 03	Window resection
Stage-III: 02	Sleeve resection and anastomosis
Stage-IV: 02	Sleeve resection and anastomosis
Both trachea and cricoid cartilage:05	
Stage-I:05	Shave excision
Thyroid cartilage:06	
Stage III (infiltration into the cartilage with no intra-luminal extension: 04	Partial laryngectomy (Resection of thyroid lamina along surrounding tissue)
Stage IV (intra-luminal extension): 02	Total laryngectomy
Trachea, cricoids and thyroid: 02	
Stage-I: 02	Shave excision

complete wall resection on larynx and trachea into six types: 1. window resection within the laryngotracheal area, 2. window resection of tracheal wall, 3. circular wall resection within the laryngotracheal area, 4. circular wall resection of the trachea, 5. laryngectomy, and 6. cervical evisceration-dralle et al. The distinguished three main type of resections are: 1. non-circumferential wall resection (window resection), 2. circular wall resection (sleeve) resection with anastomosisand 3. resection without reconstruction including laryngectomy and permanent tracheostomy.

Management of Laryngeal Involvement by PTC

The surgical options are peeling or shave procedure, partial laryngectomy, and total laryngectomy depending on extent and depth of invasion of larynx. Shave excision may be adequate in the absence of gross invasion of the perichondrium. There is no difference in survival between radical resection and shave procedures when all gross disease is completely resected [10, 12, 15] in patients with laryngeal involvement. Thyroid cancer invading the laryngeal cartilage without intraluminal involvement may be more amenable to parial laryngeal surgery because of the lateral location of tumors [10, 16]. Friedman et al. [17] found that up to 50% of the external laryngeal framework could be removed keeping the internal laryngeal architecture intact. Half of the thyroid cartilage and approximately 30% of the cricoid may be safely resected without complex reconstruction or tracheotomy-dralle et al. Total laryngectomyis indicated in cases with intraluminal invasion, or lack of larynx function [18–20]. It gives good local control for extensive larynx invasion by PTC [21]. Incomplete

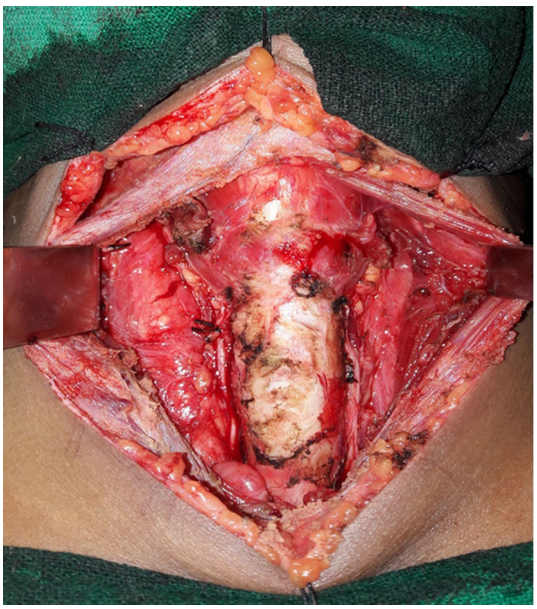

Fig. 4 Intraoperative photographs showing shave excision for superficial tracheal invasion from papillary thyroid carcinoma

resection of laryngeal involvement is usually associated with higher recurrence rates and worse survival in comparison to radical resection [19].

Management of Tracheal Invasion

Shin et al. [5] divided tracheal incolvement into four stages depending on depth of infiltration into the tracheal wall by the PTC from outward to within: stage 1: carcinoma abuting external perichondrium but does not invade it, stage–II: carcinoma invading cartilage or causing cartilage destruction, stage III: carcinoma invading past cartilage into the lamina propria of the tracheal mucosa with no elevation or penetration of the mucosa, stage IV: carcinoms invading the tracheal mucosa, visible as bulge or ulcer within the lumen. Stage-1 tracheal invasion can be managed by shave excision producing equivalent surgical outcome in term of local and regional recurrence, distant metastasis, or overall survival as in patients with invasive well differentiated thyroid cancer without airway involvement. Both shave procedure and more radical resection for early lesions give similar survival [10, 12, 15, 22] and local control rates [10, 21]. Patients with stage II or higher tracheal invasion requires airway resection and reconstruction. Sutotal resection without airway resection in these cases was associated with a much higher recurrence rate [17, 23, 24] (79%) and a shorter mean overall survival (1.5 years) [19, 23, 25]. Shave procedure leaves behind macroscopic disease in situ. This may lead high locoregional recurrence and poor survival for these patients. Hence shave procedures should be reserved for carefully selected group of patients like poor general physical conditions, coexistence morbidities like uncontrolled DM HTN, extensive distant mestasis [10, 12, 15, 17, 23, 26] as the radical excision produces additional morbidity [27, 28].

Management of Cricoid Involvement by PTC

Early cricoid cartilage invasion can be treated by either shave excision or by window resection and primary closure. Subglottic invasion via direct cricoid cartilage invasion or through the cricothyroid membrane should be treated by total laryngectomy.

Adjuvant Therapy

Considering the increased risk for postoperative locoregional recurrences and distant metastasis, the postoperative adjuvant therapy is mandatory in locally invasive PTC [29].

The commonly used adjuvant therapy in these high risk group of patients are RAI, THS Suppression and external beam radiotherapy. These adjuvant therapy improves locoregional control, decreased distant metastasis, and fewer cancer-related deaths in patients [29–31].

RAI/RRA

In our series, all patients received RRA. All patients showed very good response to it except one patient. In this patient, the tumor became RAI non-avid. This may be because of de-differentiation of the tumor tissue. The ATA guideolines for definite indications of post-operative RRA are: Gross extrathyroidal extension Incomplete tumor resection Distant metastases Nodal metastasis more than 3 cm in largest dimensions and FTC with extensive vascular invasion. Postoperative RAI ablation improves locoregional control, decreased distant metastasis, and fewer cancer-related deaths in patients [31]. But Tsang et al. [32] demonstrated improved local control but no survival advantage for treatment with RAI. Aggressive histologic variants of thyroid cancer is more common in patients with locally advanced disease. These tumors may not concentrate radio-iodine effectively causing RRA less effective.

TSH Supression Therapy

American Thyroid Association recommends TSH suppression below 0.1 mU/L for high risk cases. Mcgriff NJ et al. in a metaanalysis demonstrated that hormone suppression therapy decreases the adverse clinical outcomes in thyroid cancer [30]. In our series, all cases were high risk

cases and all cases received postoperative TSH suppression.

External-Beam Radiotherapy (EBRT)

There is no indications for EBRT if the tumor along extrathyroidal extension was completely excised. But postoperative EBRT is indicated in patients with gross residual or unresectable locoregional disease and radioactive iodine non-avid residual or recurrence tumor in elderly patients [33]. EBRT may improve locoregional recurrence in this setting, overall survival is unchanged [33].

In our series, one case with stage IV tracheal invasion treated by sleeve resection and anastosis had locol recurrence one year after surgery. The recurrent tumor in this patient was RAI non-avid and was treated by EBRT. There was no mortalitry in our series during the follow up period.

Limitation of our study is the realtively small sample size with shorter follow up period. Multicentre study involving larger number of patient is required to assess the long term outcomes of various surgical modalities of treatment for PTC with LTI.

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Code Availability Not available.

Compliance with Ethical Standards

Conflict of interest Nil.

Ethics Approval The study was approved by institutional ethics committee.

Consent to Participate Not applicable.

Consent for Publication Not applicable.

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