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Free thyroid transfer to anterolateral thigh for prevention of radiation induced hypothyroidism: An initial experience

Rakesh Katna[a,b], Nikhil Kalyani[a,*], Akshay Deshpande[a,b], On behalf of Mumbai Oncology Group – Head and Neck

[a] Jaslok Hospital and Research Centre, Pedder Road, Mumbai, India
[b] Bombay Hospital and Research Centre, Marine Lines, Mumbai, India

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ABSTRACT

Aim: Radiation induced hypothyroidism (RIHT) is one of the commonest late side effects of radiation therapy and is seen in more than half of patients and affects quality of life significantly. We report our initial experience on feasibility of free microvascular transfer of thyroid gland out of radiation field to prevent development of RIHT.

Material and methods: A prospective pilot study was undertaken during August 2017 to May 2018. Six Patients with stage III/IV patients of oral cavity cancers who required wide excision/composite resections with microvascular free flap (ALT) reconstruction and adjuvant radiation therapy were enrolled. A written informed consent was obtained from all patients prior to the procedure.

Results: The mean age of cohort was 51 years with tongue most common site of primary cancer. The free transfer of thyroid gland to anterolateral thigh was done using microvascular technique. The mean additional time for procedure was 51 min. All patients had successful transfer with no associated immediate complications. Patients were followed up with Tc99 scan, USG Doppler and biochemical assay at routine intervals in *peri* and post-operative period to assess the anatomical and physiological function of the transferred gland. At median follow up of 8 months, 5 patients were euthyroid and remaining one had biochemical hypothyroidism. All patients had functional thyroid gland in anetrolateral thigh. Five patient were alive, one patient died due to disease.

Conclusion: This is a small and early feasibility study for free thyroid gland transfer and validates the previously published data. The selected group of patients who have high chances of developing RIHT may benefit from this strategy. Further validation of the technique may be explored in a larger cohort.

1. Introduction

Head and neck cancers constitute majority of cancers in Indian subcontinent and > 60% present at loco-regionally advanced stage [1]. Stage III/IV cancers of head and neck require complex surgery with reconstruction followed by adjuvant radiation/chemo-radiation therapy [2]. Radiation therapy induced acute and late side effects have been well documented in literature. Radiation induced hypothyroidism (RIHT) is one of the commonest late side effects of radiation therapy. RIHT is seen in more than half of patients and affects quality of life significantly [3–5]. RIHT requires lifelong supplementation of thyroid hormone, resulting in long term side effects of replacement therapy and treatment compliance issues [6,7]. Free thyroid transfer is a unique concept and has been described recently as a strategy to prevent RIHT [8]. We report our initial experience on feasibility of free microvascular transfer the thyroid gland out of radiation field to prevent development of RIHT.

2. Material and methods

A prospective pilot study was undertaken. Patients with stage III/IV patients of oral cavity cancers were selected. All patients required wide excision/composite resections with microvascular free flap reconstruction. Patients planned for bilateral neck irradiation were selected as they would have higher chances of RIHT. Patients were enrolled for the procedure after discussion in multidisciplinary tumor board. A written informed consent was obtained prior to procedure.

* Corresponding author at: Department of Radiation Oncology, Jaslok Hospital and Research Centre, Pedder Road, Mumbai 400026, India.
E-mail address: nikhil.kalyani@yahoo.com (N. Kalyani).

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3. Procedure

All patients underwent detailed workup for primary cancer and appropriate investigations as per protocol in department of head and neck surgery. Preoperatively apart from routine workup the patient group underwent laryngeal examination using Hopkins scope for assessment of vocal cords movement, ultrasonography (USG) of thyroid gland and thyroid function tests to rule out thyroid nodules or neoplasm. All patients included in study underwent tumor excision and neck dissection along with anterolateral thigh free flap reconstruction. Patients with bilateral nodes or primary disease escaping into neck were not selected for the procedure. All patients received adjuvant treatment as per the histopathology report of the surgical specimen.

4. Free thyroid transfer

After taking routine neck incision (horizontal collar) for neck dissection ipsilateral thyroid gland harvest was done before proceeding with neck dissection to prevent any tumor seeding. Thyroid gland on ipsilateral side was accessed between SCM and strap muscles. The gland was identified and its superior thyroid artery and vein was identified dissected and preserved. The external branch of superior laryngeal nerve was dissected medial to the superior thyroid artery and preserved. Superior thyroid vein and middle thyroid vein wherever present was dissected and preserved. Both superior and inferior parathyroid glands preserved along with their vascular supply and left back in tracheoesophageal groove. The lobe of thyroid gland was harvested along with its intact blood supply. The contralateral lobe was not accessed or dissected at all. Special care was taken to not to damage the surface veins on the thyroid gland. After harvesting the thyroid gland rest of neck dissection and surgery for primary tumor was completed.

Anterolateral thigh flap was simultaneously harvested by the plastic reconstruction team. The harvested thyroid gland was anastamosed with descending branch of lateral circumflex artery and vein in thigh. The excision of tumor and neck nodes were performed by head neck team and reconstructive team went ahead with reconstruction of primary defect as planned (Fig. 1).

5. Monitoring and follow up

Immediate postoperative monitoring of vascular anastomosis was done using USG color Doppler every 6 hourly as per institution protocol for flap monitoring. Viability of the gland was assessed using Tc 99 was done at day 7, at 6 weeks and 6 months (Fig. 2). Biochemical function of thyroid gland was also assessed at same intervals followed by every 3 monthly. Vocal cord examination documented at day 3 and at six weeks post-surgery.

6. Results

Between August 2017 to May 2018, 6 patients were enrolled in the study. The mean age of the cohort was 51 years with tongue being commonest site of primary disease.

Four patients had stage III disease while remaining 2 patients had stage IV disease at presentation. All patients were planned for adjuvant bilateral neck irradiation along with primary tumor bed. Five patients completed adjuvant treatment, remaining one did not take adjuvant radiation.

Total time for the thyroid transfer was calculated and documented as follows: the time taken to harvest thyroid gland in neck along with anastomosis time of superior thyroid vessels with lateral circumflex femoral vessels. This mean additional time required thyroid transfer was 51 min ranging from 41 to 58 min.

All 6 patients had successful transplant with no associated complications. There was no episode of bleeding, anastomosis compromise, seroma or infection reported. Four patients had transient biochemical hyperthyroidism which was managed with help of endocrinology team in post-operative period. Thyroid levels became normal within 2 weeks of surgery for all patients. This was an unexpected event. There was no recurrent laryngeal nerve injury, EBSLN injury, temporary or permanent hypocalcemia or hypothyroidism documented.

All patients showed viable thyroid tissue in thigh in the scan and normal TSH function at different time intervals as per study protocol. At median follow up of 8 months (range 3–14 months), 5 patients were alive, four of which were disease free. One patient died due to disease having loco-regional recurrence and distant metastasis. Five patients were euthyroid with functional thyroid gland in anterolateral thigh till last follow up. One patient developed biochemical hypothyroidism after 9 months post-transplant in spite of having functional thyroid gland in thigh (Table 1).

7. Discussion

Advanced head and neck cancers are managed with surgical resection followed by radiotherapy with or without concurrent chemotherapy. Radiation/chemo-radiation affects thyroid function in patients and is one of documented long term side effects of radiotherapy in nearly half of patients.

Radiation induced hypothyroidism was first reported in 1929 by Grover et al. The hypothyroidism post-radiation sets in because of vascular damage parenchymal damage induced by radiotherapy in long term [9]. Various studies have evaluated this side effect of radiation and reported incidence in around 55% patients and peaks around at 11 month post-radiotherapy while ranging from 3 months to 7 years [10–13]. Newer radiation techniques like IMRT has been more recently used and are fast gaining acceptability as standard technique for radiotherapy for head and neck cancers but it has reported higher

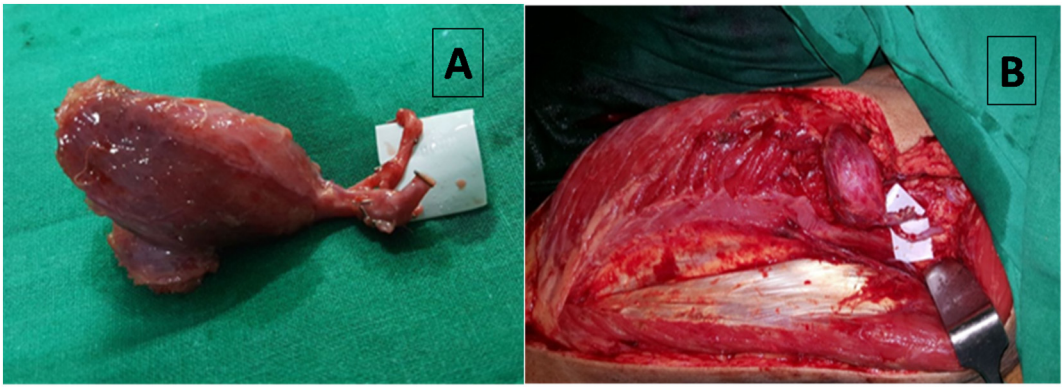

Fig. 1. A. Thyroid gland harvest. B. Anastamosis of thyroid vessels with lateral circumflex vessels.

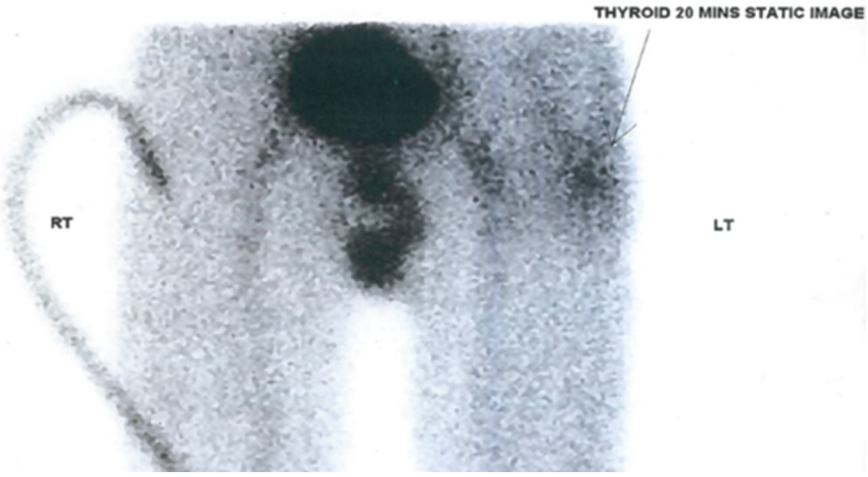

Fig. 2. Tc 99 scan showing uptake in transplanted thyroid in thigh.

Table 1
Patient follow up status and results.

Patient	Month of surgery	Tc 99 scan (uptake in thigh)	Thyroid function	Adjuvant radiotherapy	Oncological outcome
KM	August 2017	Yes	Euthyroid	No	Alive with loco-regional recurrence and distant mets
MT	August 2017	Yes	Euthyroid	Yes	NED
PJ	August 2017	Yes	Hypothyroid	Yes	NED
HS	Nov 2017	Yes	Euthyroid	Yes	Died of disease
SL	Oct 2017	Yes	Euthyroid	Yes	NED
RM	May 2018	Yes	Euthyroid	Yes	NED

incidence of RIHT as compared to conventional 3DCRT [14].

Radiation induced hypothyroidism is underreported and underestimated and many patients with subclinical hypothyroidism are not documented. Thyroid hormone replacement to avoid hypothyroid state is fraught with compliance issues, hormone monitoring and tedious dose titrations [6,7]. There have been reports of using thyroid tissue as auto transplantation like parathyroid in Graves disease and thyroiditis but not documented in patients with radiation therapy [15,16]. The strategy to prevent advent of hypothyroidism by free microvascular transfer of thyroid gland was proposed successfully by Harris et al. in 2017.

Apart from Harris et al. who published their data on free thyroid transfer recently there has been no more studies validating the success of the procedure [8]. We present our early data on feasibility of this surgical procedure (free microvascular thyroid transfer) in Indian population. The main differences in our series and Canadian series are the site of primary tumor and transfer site of gland (thigh compared to forearm). We believe that the implantation site of thyroid gland in thigh is cosmetically superior and easier than implanting in forearm. This is due to superficial location of gland in forearm making it more prone to infection, injury, skin graft loss and a visible bulge in forearm. Four out of six patients in our study experienced transient biochemical hyperthyroidism during post-operative period which has not been seen and reported by Harris et al.

This procedure is mainly useful where bilateral neck is being irradiated in adjuvant setting after a microvascular reconstruction like tongue cancers, middle one third mandible defects and lip cancers. There was a concern of tumor seeding so thyroid gland harvest was performed before primary surgery of oral cavity and neck. The thyroid gland after dissection was left with vascular pedicle intact which was disconnected just prior to anastomosis. The surgical expertise of the team performing harvest of gland should be of the highest order and knowledge of microvascular techniques is must in order to prevent damage to nerves and small vessels of thyroid gland. The risk of damage to recurrent laryngeal nerve and superior laryngeal nerve is potentially there though we had none so far in our cohort. Other complications like bleeding, hematoma and compromise of gland vascularity may happen and utmost care should be taken to avoid that. There is no additional major increase in surgery time and can be viewed as small adjunct procedure with primary reconstruction.

We here have presented the early data regarding feasibility and need long term follow-up for these patients along with further enrollment of patients to successfully translate it into an acceptable method to prevent RIHT.

8. Conclusion

This is a small and early feasibility study for free thyroid gland transfer and validates the previously published data regarding its feasibility. The selected group of patients who have high chances of developing RIHT may benefit from this strategy and can obviate the need of hormone replacement. Our future work will include increased follow-up of this group of patients.

Conflict of interest

None.

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