

Case Study: Oncological Management of a Patient with Papillary Thyroid Cancer

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Abstract—The following case study presents the management of stage III Differentiated Thyroid Cancer (DTC) patient in an NHS hospital in London, UK during period of 2004-2005.

Keywords—Differentiated Thyroid Cancer, Oncological Management, Papillary, Thyroid Cancer, Stage III.

I. INTRODUCTION

THYROID cancer is relatively uncommon and accounts for roughly 2% of all human malignancies worldwide [1], [2]. In Europe and US about three out of 100 000 people develop a thyroid malignancy [3]. It accounts for less than 0.5% of all cancers in England and Wales [4]. It is twice more common in women than men [5]. Thyroid cancer is more prevalent in the young and the elderly although all age groups can be affected [6]. The most common histological types of thyroid cancer are papillary, follicular, medullary and anaplastic. Papillary and follicular tumours are known as differentiated thyroid cancer, DTC [7]. The survival rate varies with the histological type and tumour differentiation and is high for Papillary Thyroid Carcinoma, PTC and low for Anaplastic tumours [3]. The incidence of thyroid cancer is rising worldwide [8]. The aim of this essay is to critically discuss the management of a patient with PTC focusing on Radiotherapy treatment. However it will include a general overview of the presenting symptoms and diagnostic workup.

II. BACKGROUND

A. Case presentation

The patient is an 84 years old retired male, with a diagnosis of advanced stage papillary thyroid carcinoma with lymph node metastases. There is no family history of thyroid disease which reduces the risk of malignancy. A genetic inheritance factor has not been well established for DTC, although about 3% of PTC cases are familial [9]. Patient also suffered from hypertension.

B. Clinical Presentation

He presented with a five months history of hoarseness. A change in voice is one of the presenting symptoms of advance disease and is usually caused by compression of the larynx or invasion of the recurrent laryngeal nerve [10]. There were no other presenting symptoms. Besides voice deterioration patients with DTC can present with other symptoms

depending on how advance the disease is. Other Symptoms of advanced disease include cough, dysphagia, odynophagia, a sense of fullness and pressure in the neck, hemoptysis or dyspnoea at rest or on exertion (patients with lung metastases), vocal cord palsy due to involvement of recurrent laryngeal nerve and bone pain (due to blood bourne spread) which is more common in Follicular thyroid cancer [11]. In rare cases lungs and bone metastases are first presenting symptoms [12]. PTC is more likely to cause regional lymph node metastases than distant metastases, which is more common in children and adolescents therefore enlargement of the cervical lymph nodes is one of the presenting symptoms [3]. This explains the presence of lymphadenopathy in case of our advanced stage patient which points to likelihood of PTC.

III. DIAGNOSTIC WORK UP

A number of investigations were carried out to diagnosis, stage and grade the disease as well as to decide on an appropriate and effective treatment plan. These investigations are discussed below:

A. History and Physical Examination

There was no history of previous irradiation of the neck. PE revealed a hard mass extending retrosternally mainly on the left side and fibre optic endoscopy (Laryngoscopy) confirmed the recurrent left laryngeal nerve palsy. On PE patient found to have some of the features which were indicative of malignancy as suggested by Shaha and Patel [6] such as old age, male sex, vocal cord paralysis and a hard and fixed mass.

B. Ultrasound (US)

US of the neck confirmed a solid multinodular mass with multiple nodes which suggested high risk of malignancy. The incidence of malignancy in a solid thyroid nodule is high and ranges from 15-20% [6]. A thyroid ultrasound is therefore commonly performed as an initial evaluation of a thyroid mass to distinguish between solid versus a cystic mass and to confirm whether a clinically solitary nodule is indeed a single thyroid nodule and not a dominant nodule within a multinodular goiter [13]. Besides identifying the extent and localization of the primary and coexisting thyroid nodules it is used to diagnosis enlarged cervical nodes [3]. Kouvaraki and colleagues [14] reported that US plays an important role in preoperative detection of lymph node or soft tissue metastases in neck compartments believed to be uninvolved by PE in a high percentage of patients. This facilitates complete resection of disease and minimizes recurrence.

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C. Fine Needle Aspiration (FNA)

US helped direct FNA. FNA of the thyroid mass confirmed the presence of Papillary Carcinoma. Histopathology of pretracheal node confirmed extracapsular and vascular invasion in the patient. FNA is the most cost effective and accurate initial test available today. Its accuracy, sensitivity and positive predictive value exceeds 90% [6].

D. Imaging

A CT scan of neck, thorax and abdomen was performed and confirmed the presence of a thyroid mass in the patient's neck but did not show the nodes so well. It showed expansion of left thyroid lobe which extends retrosternally and was deviating trachea to the right within the neck. There was no tracheal compromise. No mediastinal adenopathy or parenchymal abnormality was noted. A CT scan is not routinely used in patients with thyroid masses but it may be of great help in evaluating large tumours those with substernal extension [6] which is why its use is justified in the diagnostic work up of this patient. PET scanning is mainly used to determine recurrent or metastatic disease where thyroid tumour cells have lost their iodine trapping ability [15]. MRI is not commonly used for routine evaluation of thyroid nodules but may help in picking up incidentalomas [6]. Chest X-ray was done to rule out lung metastases as DTC often metastasizes to lung. Thyroid scintigraphy is discussed later in the essay.

E. Thyroid Function Test and CBC

Thyroid Function Test was performed to Include measurement of Serum thyroid hormones, TSH and thyroglobulin levels [13]. CBC has no role in detection of PTC but can give information about thyroiditis or Medullary carcinoma [5].

IV. STAGING

Based on patient's medical history, record and diagnostic work up, the patient was staged as T3 N1A M0 according to TNM staging. This means tumour was > 4cm in greatest dimension and limited to thyroid, involvement of ipsilateral cervical nodes and absence of distant metastases. Combining TNM status and Age (>45yrs) placed patient into stage 111 group.

V. MANAGEMENT OF DIFFERENTIATED T3N1AMO THYROID CANCER

Management of the stage 111 Papillary Thyroid Carcinoma was based on the prognostic factors and included Surgery, Radioactive Iodine Ablation, External beam Radiotherapy and Thyroid Stimulating Hormone, TSH suppression.

Age > 45 years, Tumour size > 4 cm, advanced tumour grade, Male sex, Extrathyroidal invasion and distant metastases have a negative impact on survival and classify patients into high risk group [16].

A. Surgery

Surgery was decided as first line treatment. Zidan and colleagues [17] state that surgical resection is the first line of treatment in the management of most thyroid cancers in order to achieve local disease control. The main surgical options are total lobectomy, sub-total thyroidectomy (total lobectomy with contralateral subtotal lobectomy) and total thyroidectomy, TT. To decide which procedure to carry out depends on the risk of local recurrence and the anticipated use of Radioactive Iodine (I-131) [10].

The plan was to conduct total Thyroidectomy (TT) and level VI selective neck dissection on the patient but the surgeon ended up carrying out sub-total thyroidectomy only. The goal of the surgery was to remove all tumour tissue in the neck and reduce the risk of recurrence. Sub-total thyroidectomy instead of TT was carried out presumably because the surgeon found it difficult to preserve parathyroid glands and also had to sacrifice recurrent laryngeal nerve on the side of the tumour due to left vocal cord palsy. Due to the old age of the patient it was important to maintain a good quality of life postoperatively and therefore sub-total thyroidectomy was preferred to avoid permanent hypoparathyroidism and vocal cord injury. The aim of thyroid surgery is not to cause complications and morbidity by damaging recurrent laryngeal nerves, vocal cord or parathyroid glands so every effort is made to preserve these structures and that's why sub-total thyroidectomy was carried out. Gimm [3] reported decreased morbidity after lobectomy or sub-total thyroidectomy as opposed to TT. This technique is further justified by Clark [18] who state that leaving a small remnant of normal thyroid tissue on contralateral side of tumour, which can be ablated subsequently with radioactive iodine therapy, is a preferable approach in such cases. In this case one of the reasons to initially opt for TT was the high risk of recurrence associated with our high risk group patient. TT maximizes disease free survival, overall survival and quality adjusted life expectancy in patients with PTC irrespective of risk group classification. Even sub-total thyroidectomy is associated with decreased risk of recurrence than lobectomy [19]. According to guidelines of Northern Cancer Network, UK introduced in 1999 all patients with tumours greater than 1 cm in diameter were recommended to undergo TT and radioactive ablation and TT resulted in reduced thyroid remnant [20]. Total or sub-total thyroidectomy also facilitates the routine use of Radioiodine ablation at a later date and to use serum thyroglobulin in the follow up of patients which is difficult in the presence of normal thyroid tissue [6]. The patient did not have a neck dissection mainly to avoid any further morbidity. A meta-analysis of nine studies showed no relation between lymph node status at presentation and survival although several studies did show an increased risk of tumour recurrence [1]. Thus due to the limited life expectancy of the patient it was decided not to perform neck dissection.

B. Radioactive Iodine Therapy

Post operatively the patient had a scintiscan (Whole body scan), which showed residual disease in the thyroid bed and

Right Lobe. It is used to identify hyperfunctioning or non functioning thyroid tissue, to detect occult or minimal cancer, to detect primary tumour or distant thyroid metastases [21]. Consequently a therapeutic dose of oral I131 (2.9GBq) was given to ablate remnant thyroid tissue, to treat any residual disease in the Right thyroid lobe and any occult distant metastases. Bomford and Kunkler [5] propose a therapeutic dose of 3GBq to destroy remaining thyroid tissue. Mazzaferri and Kloos [7] reported low cancer recurrence, distant recurrence and cancer death rates (the latter for age>40yrs) in patients with tumours > than 1.5cm. Radioactive Iodine ablation of remnant thyroid tissue in patients with PTC and FTC who have undergone TT or subtotal thyroidectomy is important in the detection of metastatic disease and the destruction of the remaining thyroid tissue [17]. However undifferentiated thyroid cancers do not benefit from I-131 therapy [10].

C. Thyroid Stimulating Hormone Suppression

As Radioiodine therapy was scheduled within 4 weeks of surgery the patient was not started on thyroid hormone replacement until after the administration of radioiodine to sufficiently raise TSH levels. The patient was placed on thyroxine therapy to suppress TSH. Irrespective of surgical procedure, all patients should be placed on suppressive doses of long acting thyroid hormone between I131 treatments [21]. It prevents hypothyroidism, minimizes stimulation of tumour growth and improves disease free survival especially in high risk patients [1].

D. External Beam Radiotherapy

The patient was given accelerated hyperfractionated radical EBRT post operatively to treat residual and occult metastatic disease in order to achieve better loco regional control and reduce the risk of recurrence. Where surgery is incomplete EBRT should be used as third line treatment. A retrospective study of 842 patients [22] reported EBRT to be effective in improving loco regional control with gross post operative residual disease in the neck. Mazzarotto and colleagues [23] state that patients at high risk of local relapse may benefit from a course of EBRT. According to revised guidelines issued by American Thyroid Association, EBRT is indicated in patients with age greater than 45 years and with grossly noticeable extrathyroidal expansion seen at time of surgery as well as an increased likelihood of microscopic residual disease [24].

1. Prescription

Phase1 delivered a total dose of 40Gy in 24 fractions (mid plane) in 12 days with two fractions per day. Phase 2 delivered a total dose of 10Gy at 100% in 6 fractions in 3 days with 2 fractions per day. In both phases dose / fraction was 1.67Gy and energy was 6MV. A total dose of 50Gy in 30 fractions over 15days was given using accelerated Hyperfractionation schedule. Ford and colleagues [25] reported that in order to have an impact on local control a total dose of at least 50Gy and higher is needed. Bomford and Kunkler [5] state conventional radiotherapy doses of 50-55Gy in 20-25 fractions

over 4-5weeks using 4-6MV whereas some books state doses as high as 70Gy in 7.5 weeks [21]. Accelerated hyperfractionation involves less dose per fraction than conventional fractionation, more fractions and shortening of overall treatment time by increasing dose per week above 10Gy. Accelerated hyperfractionation results in better tumour control, reduced late normal tissue damage in short period of time than conventional fractionation schedules [26]. This mode of treatment was suitable for the patient due to his old age as it required fewer attendances at hospital to complete his radiotherapy without compromising loco regional control.

2. Technique

Phase1 was simulator planned and Phase2 was CT planned (conformal RT) to ensure that spinal cord tolerance of 46Gy does not exceed. A two phase technique is used where Planning Target volume, PTV includes loco regional lymph nodes and absolute doses from each phase may be modified so that maximum spinal cord dose does not exceed 46Gy [27].

3. Immobilization

The patient was positioned supine with neck extended to avoid the mandible and salivary glands. For phase1 immobilization consisted of a chin strap with arms by the sides. The chin strap was used in preference to an immobilization shell to maximize skin sparing. For Phase2 a custom made beam directional shell was used to ensure reproducibility of spinal cord position. The treatment field on the shell was cut out to minimizing skin reactions. Bomford and Kunkler [5] state that to immobilize the neck a shell is required and patient lies in a supine position with neck extended. The patient's accessories included a one inch thick polystyrene block, a knee rest and a mattress. The 1-inch poly block may be used to prevent spinal cord curvature.

4. Target Volume, Borders and Field Arrangement

For Phase1, TV included thyroid bed and loco regional lymph nodes on both sides of the neck and volume extended from mastoid processes to the carina to encompass the thyroid bed plus cervical, supraclavicular and upper mediastinal lymph nodes for obvious reasons to include loco regional nodal disease (CTV + 5mm margin=PTV). In this setting anterior and under couched field were used. The most common technique for first phase is Anterior-Posterior set of fields whereas oblique anterior fields with wedges are occasionally utilized to avoid the spinal cord [28]. For treatment of thyroid bed only (PH2), an anterior oblique wedged pair of beams was used isocentrically and the upper and lower margins extended from hyoid bone to supersternal notch. Wilson and colleagues [29] have stated similar field arrangements and Target volumes for PH2.

5. Shielding

In phase1 lead shielding was used to protect mandible, sub-mandibular glands and sub apical lung. In phase2 Multileaf Collimators (MLC) were used to conform to the shape of TV and avoid dose to spinal cord. Shielding for mandible and lung tissue should be routinely used [29].

6. Radiotherapy Induced Side Effects

The patient suffered from Mucositis, oesophagitis and erythema as a result of Radiotherapy treatment. These side effects were managed with the use of mouthwash, oral hygiene, aqueous cream on skin and frequent use of sips of water and liquid to maintain moisture and wash down food at mealtimes. White [28] stated similar side effects of treatment. EBRT improves loco-regional control but does not improve survival [30].

E. Chemotherapy

Vini and Harmer [4] have stated that role of chemotherapy is limited in the management of DTC and is reserved for patients with progressive and symptomatic inoperable disease that does not concentrate iodine. American Thyroid association guidelines suggest no role of adjunctive chemotherapy in the management of patients with DTC.

VI. CONCLUSION

In the management of papillary carcinoma (DTC) risk factors play an important role. The goal of treatment is to cure the disease while minimizing the complications of thyroid surgery and side effects of adjuvant therapeutic modalities. Surgery is the main stay of treatment and aims at complete removal of the primary tumour. Adjuvant therapeutic options include Radioactive Iodine and EBRT. In high risk group patients a combined modality approach is indicated. EBRT reduces risk of loco regional recurrence in high risk group and thereby improves patient's quality of life. It does not affect overall survival.

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