Original Article

Differentiated thyroid carcinoma in paediatric and adolescent age group: 10-year experience in a university hospital in Saudi Arabia

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ABSTRACT

Background and Objective: To describe the clinical presentation, surgical intervention and treatment, complications, tumour histopathology characteristics, follow-up and survival of 23 patients at or below the age of 21 at the time of diagnosis of differentiated thyroid carcinoma (DTC) diagnosis.

Materials and Methods: A retrospective medical chart review of 23 patients diagnosed with DTC and treated in our institute from January 2003 to December 2013 was done. Pertinent data were collected regarding clinical presentation, workups, surgical intervention and treatment, postoperative complications, histopathology, follow-up events and survival.

Results: The median age at diagnosis was 17 years. 15 patients (65.2%) had papillary carcinoma and 7 patients (30.4%) had papillary carcinoma with follicular variant. Multifocality and extrathyroidal extension were found in 11 (47.8%) and 6 (26.1%) patients respectively. 21 patients underwent total thyroidectomy with neck dissection and were subjected to thyroid ablation with radioactive iodine (radioiodine) and thyroid stimulation hormone (TSH)-suppressant thyroxine replacement therapy. Median follow-up was 6.6 years. Recurrence occurred in 1 patient. No significant postoperative complications were observed.

Conclusion: Appropriate investigations should be carried out to exclude thyroid cancer in children and adolescents presenting with a neck mass. Total thyroidectomy with appropriate cervical lymph node dissection, followed by radioiodine ablation therapy and TSH-suppressant thyroxine replacement therapy is the recommended option to manage children and adolescents with DTC. Neck examination should be part of the routine clinical examination in the paediatric and adolescent age group. A local elaborate genetic database for this disease is essential and may help compare its behaviour with that seen in other populations.

Keywords: Adolescent, cancer, differentiated, paediatric, Saudi Arabia, thyroid

INTRODUCTION

Thyroid cancer in the paediatric age group is a rare malignancy, but its incidence rate has increased in recent decades.[1-3] In Saudi Arabia, thyroid cancer, in general, accounts for about 9% of all malignancies and about 12% of all newly diagnosed female cancers.[4] Differentiated thyroid carcinoma (DTC) is very rare before the age of 10; its incidence is increasing with age.[3,5] It accounts for about 1.5-2% of all childhood cancers and for <5% of all-ages thyroid carcinomas.[6,7] Childhood thyroid cancer is less common in males and shows female predominance with male:female ratio of about 1:3.8. DTC comprises 90 - 95% of all childhood thyroid cancers.[2] The risk factors for the development of thyroid carcinoma in paediatric patients include female sex, puberty, family history of thyroid cancer, head and neck irradiation, previous or coexisting thyroid disease and iodine deficiency.[8-10] Despite aggressive characteristics, prognosis is better than what is seen in the adults.[11] Some studies have suggested a rather conservative surgical approach[12] while more studies recommend a more aggressive management with total thyroidectomy, appropriate cervical lymph node dissection, radioiodine ablation therapy

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(RIA) and appropriate thyroid hormone suppressive therapy.[5-7,13,14] The purpose of this retrospective study was to examine the clinical features, surgical intervention and treatment, tumour histopathology characteristics, postoperative complications, follow-up and survival of 23 paediatric and adolescent patients with DTC treated at an endocrine surgery tertiary care facility, during a 10-year period (2003–2013). We have also followed the patients to detect and treat any possible side-effects of RIA therapy with special attention to fertility issues. The cut-off age of 21, which is used in this study, has also been used in other similar studies.[15]

MATERIALS AND METHODS

Between 2003 and 2013, 490 patients diagnosed with thyroid cancer were treated at our institution. Among them, 23 patients were ≤21 years of age at the time of diagnosis, which represents 4.69% of all age groups. This retrospective study was an analysis of 23 patients' data. The following information was gathered by reviewing the electronic and paper files of the patients: Gender, age at presentation, area of residence in Saudi Arabia, presenting symptoms, thyroid hormone status, metastasis (locoregional or distant), extent of thyroid surgery, extent of cervical lymph node dissection, histopathology characteristics of the tumour, postoperative complications, radioiodine treatment, mean duration of follow-up, recurrence (the reappearance of disease, with new radioiodine uptake or biopsy-proven disease in a patient who was free of disease evident by absence of palpable disease and negative radioiodine scan) and survival. RIA was prescribed within 1 - 3 months after surgery at our thyroid cancer clinic (the RIA therapy was executed in other hospitals in Riyadh city, as we did not have the facility to provide RIA therapy, but patients came back to our institution for follow-up after they completed their RIA therapy). Indications and dosage of RIA therapy in our patients were based on the American Thyroid Association (ATA) guidelines.[16] A radioiodine whole body scan was done within 5 days following RIA. The paediatric dose of RIA was calculated based on the patient's body weight (around 2.0 mCi/kg). All our patients (except the 2 patients with micropapillary carcinoma) received thyroid stimulation hormone (TSH)-suppressant thyroxine replacement therapy according to ATA guidelines.[16] This study was approved by the ethical review board at our institution.

RESULTS

Twenty-three patients with DTC were diagnosed and treated throughout the study period (January 2003–December 2013). Demographics are shown in Table 1. Of these 23 patients, 69.6% were females and 30.4% were males with a female:male ratio of 2.28:1. About 70% of the study group was between the ages 16 and 21 years of age and 30.4% were between the ages 10 and 15 years of age. The median age at presentation was 17 years (range: 10 - 21 years). Table 1 also shows the specific regions from where these patients came from Saudi Arabia and why the central province in the country takes predominance. This is explained by many factors one of which is that, the central province is one of the the biggest and most heavily populated province in Saudi Arabia with some patients and families having to reside there temporarily for treatment, adding to the inaccurate initial documentation of patients' addresses. Table 2 shows the presenting symptoms and family history of our patients, where all our patients presented with anterolateral neck mass (either thyroidal in origin or an enlarged cervical lymph node), 6 patients (26.1%) had some degree of pressure symptoms, 2 (8.7%) had minor voice change, 3 patients (13.0%) had a family history of malignant thyroid disease, 3 patients (13.0%) had a family history of benign thyroid disease. The average duration of symptoms was 11.5 months. None of our patients had a history of radiation exposure (whether natural radiation or therapeutic radiation). They all had a normal thyroid function test at presentation. Preoperatively, all our patients had: Detailed history and physical examination, thyroid function test, ultrasound of the thyroid and neck, fine needle aspiration biopsy from the thyroid lesion or

Table 1: Demographic characteristics of patients

Characteristics	*n*	Percentage
Gender		
Males	7	30.4
Females	16	69.6
Age group in years		
10 - 15	7	30.4
16 - 21	16	69.6
Area of residence		
North	3	13.0
South	3	13.0
Central	15	65.2
East	1	4.3
West	1	4.3

Table 2: Presenting symptoms and family history

Presenting symptoms	*n*	Percentage
Anteriolateral neck mass	23	100.0
Voice change	2	8.7
Pressure symptoms	6	26.1
Positive family history of cancer thyroid	3	13.0
Positive family history of benign thyroid disease	3	13.0

any suspicious lymph node, vocal cord exam ination and chest X-ray.

Tables 3 and 4 show that total thyroidectomy was performed in 21 patients (91.3%) and lobectomy and isthmectomy were performed in 2 patients (8.7%). The final pathology for these 2 patients was papillary microcarcinoma (PMC), 5 mm and 7 mm in diameter respectively, with no signs of infiltration or extension beyond the capsule of the lesion. Ultrasound of the remaining thyroid tissue in the PMC patients showed a normal thyroid tissue, so no further thyroid surgery or thyroid remnant ablation was done in these 2 patients but they were put on a therapeutic dose of thyroxine. Tables 3 and 4 also show that no cervical lymph node dissection of any sort was performed on the PMC patients. Tables 3 and 4 also show that paratracheal lymph node dissection (only) was done in 9 patients (39.1%), and a combination of paratracheal with lateral neck dissection was done in 12 patients (52.2%).

Tumour histopathology reports of our patients [Table 5] show that there was 1 patient (4.3%) who had follicular carcinoma, 7 patients (30.4%) had follicular variant of papillary carcinoma, and the remaining 15 patients (65.2%) had papillary carcinoma. The mean tumour size was 2.4 cm. There were two cases of micropapillary carcinoma (8.7%) (sizes 5 mm and 7 mm respectively). Tumour multifocality was seen in 11 patients (47.8%). Extrathyroidal extension of the tumour was seen in 6 patients (26.1%).

Table 3: Extent of thyroid surgery

Procedure	*n*	Percentage
Lobectomy and isthmectomy (papillary microcarcinoma patients)	2	8.7
Total thyroidectomy	21	91.3

Table 4: Extent of neck dissection

Extent of dissection	*n*	Percentage
Paratracheal	9	39.1
Paratracheal and lateral neck	12	52.2
Not done (papillary microcarcinoma patients)	2	8.7

Table 5: Histopathology characteristics of tumour

Characteristics	*n*	Percentage
Papillary	15	65.2
Paratracheal lymph node metastasis	13	56.5
Multifocality	11	47.8
Lateral neck node metastasis	8	34.8
Papillary with follicular variant	7	30.4
Thyroiditis	7	30.4
Extrathyroid extension	6	26.1
Papillary microcarcinoma	2	8.7
Follicular	1	4.3
Mean tumour size	2.4 cm	

Twenty-one cervical lymph node dissections were done in this study group. All these dissections recovered positive lymph nodes. The pathology report shows thyroiditis in the non-cancerous thyroid tissue in 7 patients (30.4%). Postoperatively, there was no permanent voice change, yet 5 patients (21.7%) had temporary hoarseness of voice, which recovered in due course of time. Temporary hypocalcaemia was seen in 7 patients (30.4%), while permanent hypocalcaemia that required calcium and vitamin D replacement therapy was seen in 1 patient (4.3%), who had extensive multifocal disease with extra-thyroidal extension and extensive lateral and paratracheal lymph node involvement.

Postoperative bleeding and wound infection were not seen. Follow-up of these patients was scheduled at every 6 months for the following: Clinical examination, serum TSH levels, thyroglobulin, T4, chest X-ray and neck ultrasound. During follow-up visits, attention had been paid to the side-effects of RIA therapy, especially for fertility issues, which was not noticed at all in patients in this series who married after treatment. 2 patients failed to follow-up 2 years postoperatively. The mean duration of follow-up was 6.6 years. There was a single disease recurrence, which was seen 3 years after initial surgery (total thyroidectomy with paratracheal and lateral neck lymph node dissection, tumour size of 5.0 cm, papillary type with extra-thyroidal extension and extensive nodal metastasis and lymphovascular invasion). The recurrence in this 16-year-old boy was in the lateral neck group of lymph nodes (three positive lymph nodes). All our 21 patients (2 patients failed to follow-up) are alive, asymptomatic and disease-free at the time of writing this paper.

DISCUSSION

It is well-known that the natural history of DTC is dissimilar in children and adults, children usually present with advanced disease with lymph node metastasis.[3,14,17] Prognosis incongruity is not yet well understood; maybe the thyroid gland during childhood is more prone to oncogenic stimuli. DTC accounts for 1.5 - 2% of all paediatric cancers[6] and for <5% of all-ages thyroid carcinomas.[6,7] In Saudi Arabia, there is no detailed cancer database at the national level, which elaborates on the molecular and genetic issues of thyroid cancer in children.

In this retrospective study, the percentage of female patients is about 70% and that of the male patients is about 30%, which is in agreement with similar

studies.[2,3,7,14,18,19] All the patients in this study had the clinical symptom of anterolateral neck mass with normal thyroid function test at presentation, which was also consistent with other studies.[2,3,7,8,13] The rate of postoperative complications was low in this series, which is in agreement with many similar studies.[3,6,7,17,20] Distribution of tumour histopathology demonstrated 65.21% papillary thyroid cancer, 30.43% follicular variant papillary carcinoma, 4.34% follicular carcinoma and 8.69% PMC; this result was consistent with earlier similar series.[2,5,7,14,18] All the patients in this series (except the 2 patients with PMC) had cervical lymph node metastasis. This rate (91.3%) is higher than that reported by Pazaitou-Panayiotou *et al*.,[5] but it is in agreement with what has been reported by Harness *et al*. (88%) and Landau (80%).[7,14] Cervical lymph node metastasis is a frequent sign in children/adolescent population.[2,5-7,14] Patients with cervical lymph node metastasis usually require a higher dose of radioiodine to achieve ablation.[2,5,13] In this series, the mean tumour size was 2.4 cm, multifocality presents in 11 patients (47.8%), metastasis to locoregional cervical lymph nodes was seen in the central compartment only in 39.13% and in both the central compartment and the lateral neck in 52.17%. Distant metastasis is more likely to present in younger male patients with multifocal tumour and primary tumour size greater than 2 cm.[2,6,15] In this series, we found that the disease burden in the positive cervical lymph nodes was not heavy in the majority of our patients, plus the fact that 70% of our patients were females and between the ages of 16 and 21 years. This may explain the absence of distant metastasis in our patients at the time of presentation. In addition to this, the possibility of genetic factors may somehow have limited the spread to the locoregional area. The optimum surgical procedure to deal with DTC in children is still a debatable issue; however, the great majority of the published literatures recommend total thyroidectomy and central lymph node sampling; and in patients with clinically involved cervical lymph nodes, a modified neck dissection should be done.[3,5,7,14] Postoperative TSH-suppressant thyroxine replacement therapy has become part of the management of DTC in children.[3,5,13,14,17,20] On the other hand, postoperative adjuvant RIA therapy is being used widely as reported in many series.[2,3,5-7,11,14,17,20] Radioiodine treatment has been found to be safe and effective in the management of metastatic cases.[7] In this series, all patients (except the PMC patients) have received adjuvant radioiodine therapy according to the recommendations of the ATA.[16]

We have closely followed-up 21 patients (mean follow-up duration is 6.6 years), all of them are alive and disease-free at the time of writing this paper. Since it is possible that the risk of recurrence is related to the length of follow-up, of longer duration of follow-up will give more reliable conclusions. Regarding postoperative complications, there were seven cases of temporary and one case of permanent hypocalcaemia. Five patients had temporary voice change, which recovered in due course of time; these findings are in concordance with similar studies.[7,20]

It might be of interest to compare our findings in this study with a similar study conducted on a totally genetically different population. Pazaitou-Panayiotou *et al*. from Greece reported a series of 23 patients diagnosed with DTC, patients aged 8 - 20 years, 15 females and 8 males, with a median follow-up of 5.5 years with almost the same median age at presentation like ours in this series.[5] In the Greek series and at the time of diagnosis, there were 3 cases of pulmonary metastasis and 2 cases of mediastinal metastasis. The surgical procedures performed were exactly the same in both series. Papillary thyroid carcinoma was present in 91.3% of the Greek study while it was 95.6% in ours. Multifocality and PMC percentages were the same in both series. The extra-thyroidal extension of the disease was present in 52.1% in the Greek study while it was 26.1% in our series. Cervical lymph node metastasis was seen in 78.2% in the Greek study while it was 91.3% in our series. As far as recurrence of the disease is concerned, there were six cases (26%) of recurrence in the Greek study and 1 (4.34%) in our study. The most likely logical explanation of the points of differences in both series was the technique of cervical lymph node dissection along with the genetic factors which influence the behaviour of the disease, both at presentation and during follow-up period.

CONCLUSION

We found that most of our patients had papillary carcinoma and the primary tumour was multifocal with a mean tumour size of 2.4 cm. In a paediatric/adolescent patient, a neck mass should always alert the clinician to the possibility of thyroid cancer. Total thyroidectomy and appropriate cervical lymph node dissection along with RAI treatment plus TSH-suppressant thyroxine therapy is the recommended management to deal with DTC in paediatric/adolescent patients. Further local studies with a larger number of patients and a longer follow-up period of time are needed for better understanding of this disease. In addition, a local thyroid cancer database with emphasis on the molecular and genetic levels is needed to be done in this country, which would greatly help explain the disease behaviour and benefit planning treatment strategies for such a disease.

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