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CASE REPORT

Papillary Thyroid Carcinoma in a 5-Year-Old Child—Case Report

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Introduction

Papillary thyroid carcinoma is the most common pediatric thyroid malignancy representing 85–95 % of cases [1]. Pediatric thyroid cancers typically present as neck masses with no associated symptoms and thus come to medical attention at widely varying stages of disease progression [2]. In contrast to adult papillary thyroid carcinoma, pediatric papillary thyroid carcinoma tends to be more aggressive at presentation with higher incidence of multifocality, lymphnode metastases and extracapsular extension. The following case details an aggressive presentation of pediatric papillary thyroid cancer [1].

Case Report

A 5 year old boy presented with 3 months history of multiple swellings in lateral aspect of neck on both sides. Swellings were insidious in onset and gradually progressed in size. There was past history of the patient having tubercular lymphadenitis, at the age of 3 months for which he was treated adequately. There was no family history of thyroid cancer and no history of irradiation. On examination, there was significant bilateral cervical lymphadenopathy and thyroid gland was just palpable and firm. Largest lymph node measured 2×2 cm. Figure 1—Pre op photograph lymphnode marked. Thyroid function tests were normal. Ultrasound scan of thyroid showed hypoechoic lesion on left lobe measured 0.7×0.8×0.9 cm. A diagnosis of carcinoma thyroid with level I, II, III, IV lymphadenopathy was made. Ultrasound scan of abdomen and chest X-ray had no significant abnormality.

Fine needle aspiration cytology was performed from left cervical lymphnode, smears showed epithelial cells in monolayered sheets, small clusters and in discohesion, exhibiting moderate anisokaryosis and regular nuclear membrane without nucleoli. Some of the cell fragments showed papillaroid configurations (Fig. 2). There were a few cells showing prominent intranuclear inclusions and nuclear grooves. Background was clear with a few red blood cells. There was no colloid, psammoma bodies, or lymphoglandular bodies. Cytological diagnosis of papillary thyroid carcinoma was made.

Total thyroidectomy with central compartment clearance and bilateral functional neck dissection was done. Figure 3—Per op photo showing thyroid gland Thyroidectomy specimen measured 4.5×2×0.5 cms. Right lobe measured 2×2×0.5 cm, left lobe measured 2×2×0.5 cm. External surface of isthmus showed grey white nodule measuring 0.5×0.5 cm. Cut section of the left lobe showed grey white areas measuring 0.9×0.5×0.5 cm. Cut section of isthmus showed grey white nodule which measured 0.5 cm across (Fig. 4). Cut section of right lobe was unremarkable. A total of 56 lymph nodes were retrieved from central compartment and right and left functional neck dissection specimens.

Histological sections from grey white nodule from the left lobe and isthmus showed features of papillary thyroid carcinoma (Fig. 5). Tumor showed psammoma bodies and focal extension into perithyroid soft tissue. Thirteen lymph nodes showed metastasis out of 56 nodes retrieved (Fig. 6). A few nodes also showed extracapsular spread. Parathyroids was not identified in the sections studied Final histopathological diagnosis was papillary thyroid carcinoma—left lobe and isthmus

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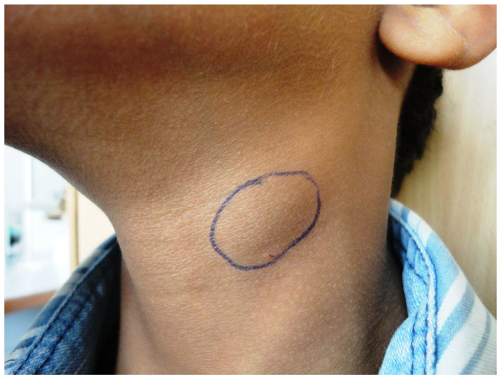

Fig. 1 Pre-op photograph largest lymphnode is marked ms 2×2 cm

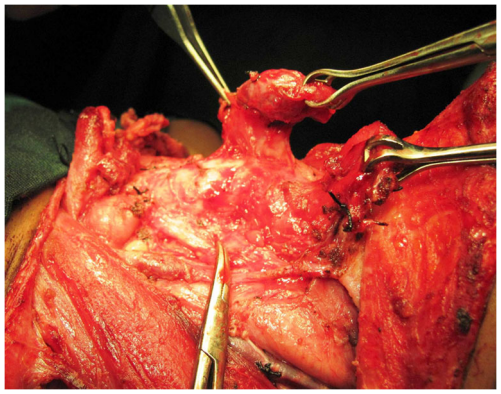

Fig. 3 Per-op photograph showing thyroid gland

with extrathyroidal extension and cervical lymphnode metastasis with extracapsular spread and TNM staging of pT3N1bMx was made.

FISH analysis was carried out on the paraffin—embeded tissue sections by using XL RET BA probe, Green/Orange, MetaSystems GmbH, according to manufacturer's protocol. Slides were counterstained with 10 μl of 4′,6-diamino-2-phenylindole (DAPI; 125 ng/ml, Abbott molecular Inc). Fluorescence microscopy was carried out with an Axioscope microscope. A three filter set (MetaSystems) was used for simultaneous detection of DAPI, Green signal and Orange signal. Several images were processed using ISIS software (MetaSystems GmbH). Each slide was scored by at least three observers.

The FISH results showed positive for the RET rearrangement in the given Papillary thyroid carcinoma patient (Fig. 4) and 10 % of the cells showed RET rearrangement.

Discussion

Pediatric thyroid cancer is rare. Risk factors include a family history and previous radiation exposure. The patient presented, however, had no identifiable risk factors. Sporadic papillary thyroid cancer represented only 1.4 % of newly diagnosed childhood carcinomas in the USA from 1975–1995 according to the SEER database [3]. Interestingly, the incidence among gender lines changes according to age group with males having 6:1 increased incidence at ages 5–9, a similar incidence among males and females from ages 10–14 and a ratio more consistent with adult patients with 5:2 female to male ratio after the age 14 [3].

In one case series of 566 pediatric thyroid carcinomas, the average age at diagnosis was 16 years. Here the patient was 5 years old and presented with 3 months duration of multiple swellings in the lateral aspect of neck [4]. Others have reported thyroid carcinoma in 12 and 18 years [1, 5].

Papillary thyroid carcinoma (PTC) clearly behaves as a different clinical disease in children and adults. Children with locally advanced disease, lymph node involvement, and distant metastasis have better long term prognosis than adults. Children with PTC can be expected to have a normal life expectancy and optimal surgery is the treatment of choice [6].

Papillary or papillary-follicular histology has been shown to be a major risk factor associated with recurrence after surgical resection [7]. The rate of recurrence is 35–45 % in children compared to 5–20 % in adults [6]. However in our case there was no recurrence, over a follow up period of one and half years.

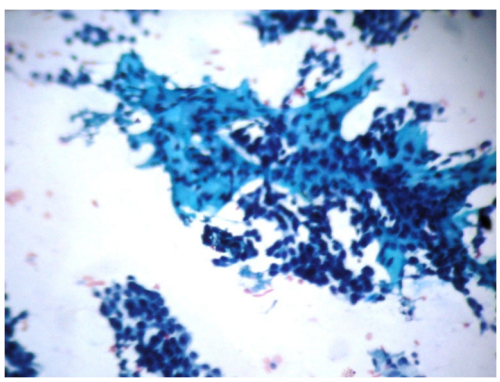

Fig. 2 Microphotograph showing cell fragments with papillaroid configuration (pap, ×10)

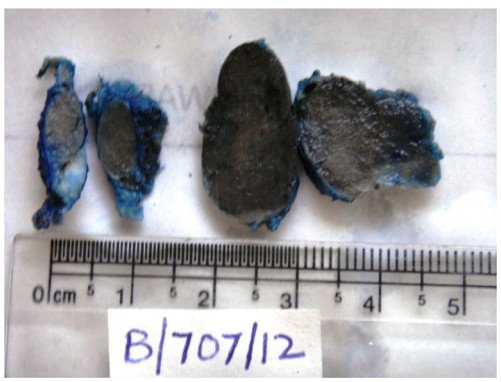

Fig. 4 Gross photograph showing cut section of left lobe of thyroid with irregular grey white lesion and right lobe was unremarkable

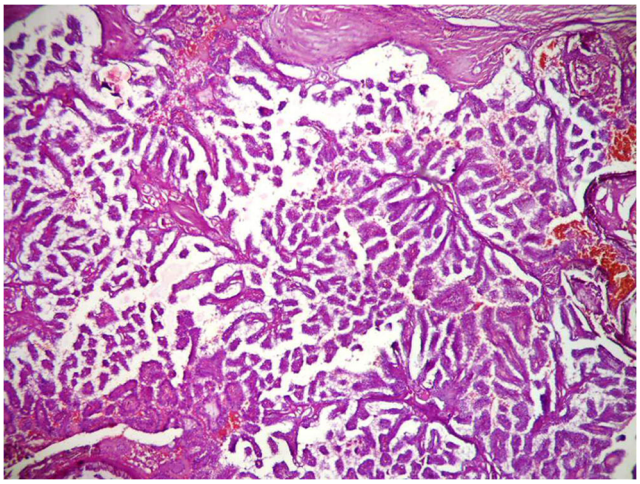

Fig. 5 Microphotograph showing classical features of papillary thyroid carcinoma with papillary areas and nuclear features (H &E, ×10)

Differentiated thyroid carcinomas have a more aggressive clinical behavior in young children with a reported rate of lymph node metastases ranging between 60 and 80 % and lung metastasis in approximately 20 % of the cases at diagnosis [6]. This is best illustrated by a report from cancer center, New York, where out of 327 patients less than 21 years with differentiated thyroid cancer 83 had distant metastasis; 90 % of this group had regional nodal metastasis and 48 % had extrathyroidal extension and all had distant metastasis to the lung at presentation. However, despite the aggressive clinical characteristic of differentiated thyroid carcinoma in their series survival rate was 100 % after 10 years [8]. The bilateral neck dissection specimen of our patient showed multifocal papillary carcinoma metastases, however X-ray chest was normal. Predictive factors for recurrence include younger age (<16 years), regional lymph node involvement or distant metastasis at diagnosis and some histological characteristics such as diffuse-sclerosing papillary variant, noted frequently in children [9].

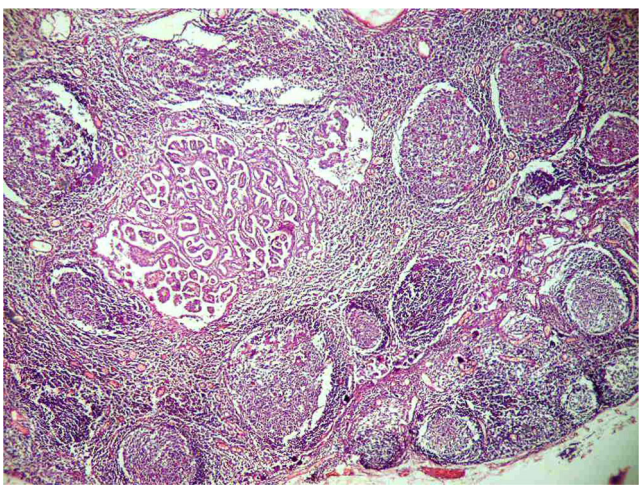

Fig. 6 Microphotograph showing lymphnode metastasis (H &E, ×10)

Diagnosis is often established with a combination of ultrasound, CT scan without contrast, fine needle aspiration cytology. In young children the positive predictive value of FNA (fine needle aspiration) is low, but in our case aspiration cytology was the initial means of diagnosis. In a series of 101 specimens from 82 pediatric patients, the diagnostic sensitivity and specificity of detecting carcinoma was 87 % and 92 % respectively by aspiration cytology [10, 11].

Activation of the RET protooncogene through somatic rearrangements represents the most common genetic alteration in papillary thyroid carcinoma. Three main rearranged forms of RET have been described: RET/PTC and RET/PTC3, which arise from a paracentric inversion of the long arm of chromosome 10, and RET/PTC2, which originates from a 10;17 translocation [12]. There is broad variability in the prevalence of RET/PTC rearrangement, due to different detection methods and tumor genetic heterogeneity [13]. In our study, the FISH results showed positive for the RET rearrangement in 10 % of the cells (Fig. 7).

In one study a total of 69 PTCs and 22 benign lesions were evaluated. Among the PTCs, 13 (18.8 %) showed a RET rearrangement, and 11 (15.9 %) of these carried an inversion (RET/PTC1 or RET/PTC3) in more than 10 % of the nuclei examined. Activated forms of RET were also observed in three adenomas. Several PTCs carried a significant number of cells characterized by a trisomy or a tetrasomy of chromosome 10 [12]. Unbalanced 5;16 translocation was seen in a boy with PTC, who had mental and growth retardation with facial anomalies [14]. Recently HOOK3-RET, is a novel type of RET/PTC rearrangement in papillary thyroid carcinoma. The FISH approach in interphase nuclei represents a powerful tool for detecting, at the single cell level, RET/PTC rearrangements and other anomalies involving the RET chromosome region [15].

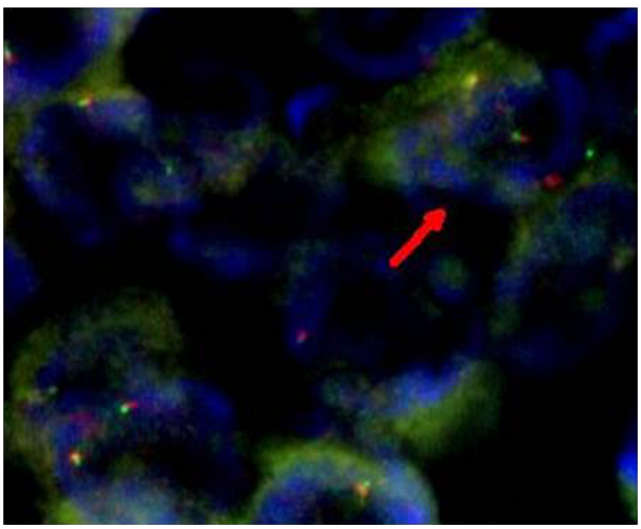

Fig. 7 FISH analysis of RET rearrangement. In the abnormal cell, nuclei exhibiting a rearranged RET gene show a split FISH signal in orange and green in addition to fusion FISH signal. The *arrow* indicates the abnormal cell showing split signals

Many studies recommended total or near total thyroidectomy as the procedure of choice for papillary thyroid carcinoma in children, the indication for total thyroidectomy being the presence of multicentric tumor occurrence and bilateral lobe involvement [6].

We performed total thyroidectomy with bilateral functional neck dissection and central compartment clearance in our patient. Voice was normal after surgery and there was no hypocalcemia in post-operative period. The other issue in the management of children with thyroid cancers is the role and extent of neck dissection. Neck dissection is indicated for palpable metastatic neck nodes but there is no proven efficacy for prophylactic neck dissection in the absence of initial palpable or radiological disease [16]. Standard curative regional neck dissection involves clearance of ipsilateral levels II-V lymph nodes with pre and paratracheal lymph node clearance. Bilateral (levels 2–6) neck dissection was performed in our patient. Radioiodine ablation with 30–150 mCi of I^{131} to destroy any remaining functional thyroid tissue 4 weeks after surgery have been recommended, especially in children under 16 years. Patients require regular follow up and their thyroglobulin levels are monitored, in addition when necessary a diagnostic I^{131} whole body scanning is performed annually [17].

The thyroglobulin level was initially elevated before surgery in this case. Serum Thyroglobulin levels done on recent follow up were near normal levels. Post operative I^{131} uptake scan didn't reveal any significant uptake in the neck or chest. However in view of extensive lymphnode involvement going into mediastinum minimum dose of radioiodine was given 100 mCi. The child is on thyroxine replacement 150 mg/day.

Conclusion

Pediatric papillary thyroid cancer can have a very aggressive initial presentation including a high rate of local lymphnode metastases and relatively high rate of distant metastases compared to adult patients. Although a lifetime recurrence rate is high, the mortality rates are still low. Palpable thyroid abnormalities in children should be viewed with suspicion and worked up for possible malignancy.

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