Aggressive Behaviour of Solid Arrangement Pattern in Differentiated Papillary Carcinoma of Thyroid

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Abstract
The prognosis and overall outcome of solid growth pattern in differentiated papillary carcinoma of thyroid is controversial. While general consensus suggest outcomes similar to typical papillary carcinomas others demonstrate a more aggressive biology. We present a case of differentiated papillary carcinoma of thyroid with solid growth pattern presenting with neck swelling and widespread skeletal metastases. The areas of bone lesions showed avid $^{131}$I concentration on a postoperative large dose $^{131}$I whole body scan and was treated with $^{131}$I subsequently. The present case suggest that the solid architecture in a papillary thyroid carcinoma may be indicative of an aggressive clinical course, contrary to the common opinion that it does not adversely influence its biologic behaviour and thus emphasize the need to reexplore the prognostic significance of histopathologic subclassification along with an assessment of histologic grade and expression of molecular risk factors in this particular tumour subtype.

INTRODUCTION
Multivariate analysis has shown histopathologic subtype to be an independent prognostic factor in papillary carcinoma of thyroid. Areas with solid growth pattern are present in around 20% of papillary carcinomas and have been reported in greater than 30% of cases with papillary carcinoma following the Chernobyl nuclear accident. When the solid growth represents 50% of the tumour mass, a diagnosis of solid variant of papillary carcinoma may be made. The nuclear features are the same as papillary carcinoma. The clinical course of solid arrangement is a matter of debate with many of the opinion that these lesions behave similarly as typical papillary carcinoma and should not be designated as more aggressive. We present a case of papillary carcinoma of thyroid with solid patterns of growth which presented with neck swelling and widespread skeletal metastases.

CASE REPORT
A 35 year old male presented with 2 cm x 2 cm neck swelling involving right lobe of thyroid of one year duration. A fine needle aspiration cytology of the neck swelling revealed it to be a papillary carcinoma of thyroid. The patient was referred for surgery and a total thyroidectomy was done. The histopathology report of the specimen demonstrated it to be a differentiated papillary carcinoma of thyroid with solid patterns of growth (Figs. 1 and 2). Postoperatively the case was referred back to us for further management. The Chest roentgenogram (Posteroanterior and left lateral oblique view) revealed multiple expansile rib lesions with a soft tissue mass eroding the left 8th rib (Figs. 3 and 4). A whole body bone scan with 20 mCi $^{99m}$Tc labeled methylene diphosphonate (MDP) was performed which demonstrated focally increased concentration in the right clavicle, right scapula and areas surrounding multiple osteolytic ribs lesions (Fig. 5). A large dose scan with 4.2 mCi $^{131}$I showed areas of focally increased concentration in chest bilaterally (Fig. 6) corresponding to the bony lesions seen in the chest X-ray and bone scan. Concentration was also seen in the neck (Fig. 7) with a 24 hour neck uptake of 1.73%. A 229.5 mCi $^{131}$I was administered orally. Post-therapy scan showed concentration in all the bony lesions seen in the chest X-ray and bone scan. Additional concentration was also seen in both sides of the pelvis (Fig. 8). A CT scan of chest done at a later date showed several osteolytic expansile rib lesions associated with a soft tissue mass eroding the left 8th rib. The lesions were solid and did not show necrosis (Fig. 9). The second large dose scan with 4.02 mCi $^{131}$I done six months later showed a neck uptake of 0.36% at 24 hours with a small focal uptake persisting in the thyroid bed. The previous bony lesions also demonstrated tracer concentration this time. The serum thyroglobulin level was > 800 ng/ml (Normal range in a post-total thyroidectomy patient : Off Eltroxin - 20 ng/ml and on Eltroxin - 10 ng/ml) and serum TSH level was > 100 µIU/ml (normal : 0.25 - 5.1 µIU/ml).
Another 255 mCi $^{131}$I was administered. The patient has been advised to report after one year for a follow up large dose $^{131}$I scan and further management.

**DISCUSSION**

Papillary thyroid cancer (PTC) is the predominant form of thyroid carcinoma which can occur at any age but is usually found in the 3rd to 5th decade of life with a female preponderance of 2 to 3:1. The commonest mode of presentation is a solitary thyroid nodule and the tumour has a propensity to lymphatic spread. The tumours tend to be biologically indolent and usually have an excellent prognosis.
But in a certain subset, papillary carcinoma runs a more virulent course and can be a killer disease. Papillary carcinoma that behave aggressively are usually aneuploid but the concurrent presence of other unfavourable prognostic factors diminishes the significance of this finding. The biological behaviour of PTC has been related to several factors e.g. age at diagnosis, sex, presence or absence of extrathyroidal extension, microscopic variants, tumour size, capsular invasion, multicentricity, distant metastases and DNA ploidy. Poor prognostic factors include older age (> 40 years) at diagnosis, male sex, large tumour size, extrathyroidal growth and adverse histopathological subtypes. While at one end papillary microcarcinoma has an excellent prognosis, the tall cell and columnar cell variants have a much less favourable outcome. The term “Poorly Differentiated Carcinoma” was introduced by Sakamoto et al and their criteria were mainly based upon the presence of "solid, trabecular and/or scirrhous growth pattern". But others have considered insular carcinoma, tall cell and columnar cell variants and poorly differentiated carcinoma with primordial cell component under the same rubric and have not found convincingly that solid growth pattern is of adverse prognostic significance. The histological features usually quoted as not related to prognosis include relative proportions of papillae and follicles, presence or absence of fibrosis, and the presence or absence of solid areas and squamous metaplasia. But controversies exist regarding this practice. Nishida et al have considered tumours with more than 10% of solid, trabecular or scirrhous architecture as “poorly differentiated”. Study by Akslen et al revealed that tumour’s solid areas have an increased occurrence of mitotic figures and vascular invasion. The solid growth pattern, though thought to have a similar clinical outcome as a typical papillary carcinoma, can run an aggressive course as cited in the presented case. However, all the metastatic lesions in the case showed avid $^{131}$I concentration and were treated by the same. The patient is being followed up for assessing the outcome. The present case demonstrates that appropriate attention should be paid to address the prognosis of the solid tumour architecture in differentiated papillary thyroid carcinoma and a pooled data from the analyses of several centres needs to be evaluated before coming to a definite conclusion in this regard. This should be accompanied by assessment of histological grade based on key features e.g. nuclear atypia, tumour necrosis and vascular invasion, which
are known to be associated with aggressiveness in other tumours as well as assessment of various growth factors and angiogenesis factor expression in this particular histologic subtype. This will also help in deciding whether they should be placed under the descriptive term “poorly differentiated” or should be designated as a specific entity.

REFERENCES


