

Carcinosarcoma thyroid: An unusual morphology with a review of the literature

Dear Editor,

Carcinosarcomas are uncommon tumors; by definition, they have a malignant epithelial and mesenchymal component.^[1] They can occur at all sites where a carcinoma can occur, notably the uterus, breast, thyroid, esophagus and lung. Although uncommon, carcinosarcomas have been described occasionally in the thyroid. Often, these cases do not pose diagnostic difficulty on microscopy, but little literature exists on the biologic behavior and follow-up of these patients. The present case is an addition to this subgroup with some unique features.

A 62-year-old female patient presented to this hospital with a complaint of gradually increasing swelling in the right side of the neck for the last 5 months. There was no dyspnea, dysphagia, pressure symptoms, weight loss or other constitutional symptoms. On local examination, there were multiple lymph nodes at levels II, III and IV. At level II, the nodes formed a large matted mass measuring 6 cm × 5 cm × 5 cm. There was bilateral asymmetric enlargement of the thyroid lobes, right more than left. Thyroid function tests and antibody levels were unremarkable.

Preoperative fine needle aspiration cytology from the nodal mass showed papillary fragments with classic nuclear features of papillary carcinoma of thyroid [Figure 1c and d]. High-resolution ultrasonography of the thyroid suggested a nodule in the thyroid with multiple ipsilateral nodal metastases. Work-up for the primary tumour elsewhere in the body was negative.

After appropriate investigations, the patient underwent total thyroidectomy with right-sided functional neck dissection. The gland was approached via lateral incision, which was

extended up to the mastoid. Intraoperatively, the right lobe had a nodular appearance, with multiple discrete nodes, and the nodal mass at level II was adherent to ipsilateral external jugular vein and the 10th, 11th and 12th cranial nerves on the right side.

Grossly, the thyroidectomy specimen showed asymmetrically enlarged lobes of thyroid, right more than left. The cut-surface of the right lobe revealed a nodular, well-circumscribed focus measuring 3 cm in maximum dimension. The left lobe was grossly unremarkable [Figure 1a]. Cut-surface of the matted nodal mass (level II) was grossly heterogenous, with a solid grey-white fleshy area and an adjacent area with granular appearance [Figure 1b]. The other nodes at levels III and IV showed granular and cystic areas.

Mapped sections were taken from both the lobes and the isthmus, including representative sections from lymph nodes at all levels.

Sections from the thyroid parenchyma did not show any evidence of a tumor focus even after extensive sampling. Sections from the fleshy areas of the matted level II mass revealed interlacing short fascicles and sheets of spindle-shaped cells with pleomorphic vesicular nuclei and bipolar cytoplasmic processes. Frequent mitoses were noted. Interspersed between these cells were follicles lined by cuboidal cells and filled with colloid. These cells had round to oval nuclei with overlapping, clearing, longitudinal grooves and intranuclear inclusions [Figure 2a-c]. There was no evidence of residual peripheral lymphoid tissue in this mass. Sections from the granular areas and the rest of the lymph nodes showed metastatic papillary carcinoma thyroid with classic morphological features [Figure 2d].

An extensive panel of immunomarkers was performed to ascertain the nature of the spindle cells. The epithelial cell component was positive for pancytokeratin, cytokeratin-19, thyroid transcription factor-1 and thyroglobulin. The spindle cells were positive for vimentin but negative for S100 and all the above-stated markers. The luminal colloid showed thyroglobulin positivity. Calcitonin was negative in both cell types [Figure 3].

A diagnosis of ‘carcinosarcoma thyroid with papillary carcinoma and undifferentiated sarcoma components’ was made. The patient received adjuvant radiotherapy with thyroxine supplementation. She is presently on follow-up with no evidence of recurrence or metastasis after 12 months of primary diagnosis.

Carcinosarcoma is defined as a malignant tumor composed of malignant epithelial and mesenchymal elements (World Health Organization, WHO 1999).^[2,3] The proof of coexistence of two malignant components depends on demonstration of two different cell lineages as in the present case by immunohistochemistry. Like at other sites, carcinosarcoma in the thyroid is a very rare neoplasm with fewer than 25 cases reported in the English literature. In addition, there are five cases reported in other languages [Table 1].^[4-8] Most of these reports have described

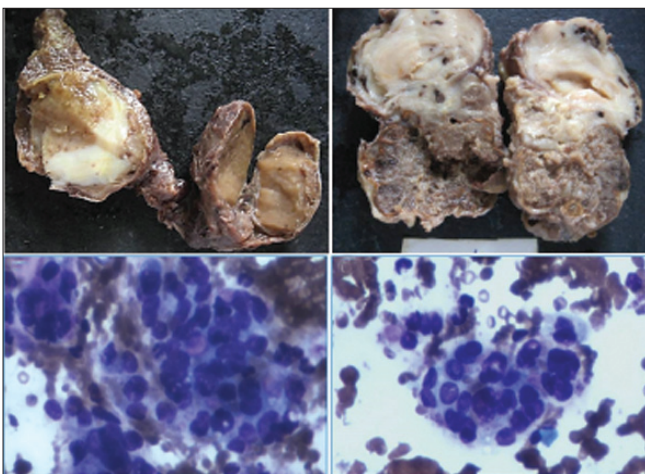


Figure 1: Cut-surface of the (a) main thyroid gland and (b) mass at level II showing granular and adjacent grey-white fleshy areas. (c and d) Fine needle aspiration smears showing classical morphological features of papillary carcinoma thyroid with nuclear overlapping, swirling, longitudinal folds and intranuclear inclusions

Table 1: Summary of all reported cases of carcinosarcoma thyroid

Reporter; year [ref]	Surgical details	Morphology	Follow-up
Al Sobhi <i>et al.</i> ; 1997 ^[14]	Details available for 7/17 cases; two cases had total, 6 subtotal and 1 partial thyroidectomy	OS-CA (9), FS-CA (5), SA-CA (3)	Available for 8 patients; average duration of survival for available patients=6 months
Giuffrida <i>et al.</i> ; 2000 ^[15]	Total thyroidectomy+lymph node dissection+chemotherapy	FC+SA	Died after 6 months
Znati; 2006 ^[16]	Radical thyroidectomy	FC+SA	Died in few days
Okon <i>et al.</i> ; 2003 ^[17]	Surgery+chemotherapy	SA+HC	Died within 2 months
Vlasov; 1973 ^[4]	–	SA+SqC	–
Villard; 1970 ^[5]	Article in French		
Hájek; 1966 ^[6]	Article in Czech		
Herrero; 1961 ^[7]	Article in Spanish		
Bagolan; 1952 ^[8]	Article in undetermined language		
Naqiyah <i>et al.</i> ; 2010 ^[11]	Total thyroidectomy	FC+SA	-
Present case	Total thyroidectomy+neck dissection	PC+SA	12 months till date (please clarify-you have mentioned 12 months in the text) s

CA=Carcinoma, SA=Undifferentiated sarcoma or unspecified, OS=Osteosarcoma, HC=Hurthle cell carcinoma, PC=Papillary carcinoma, SqC=Squamous cell carcinoma, FS=Fibrosarcoma, FC=Follicular carcinoma

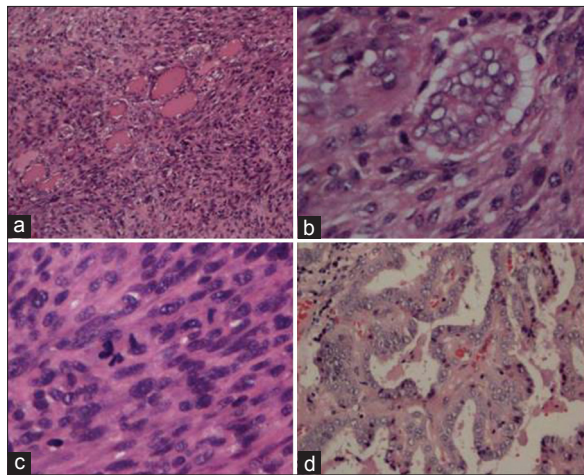


Figure 2: Sections from the level II mass showing (a) predominantly spindle cell component with few follicles filled with colloid (H and E, $\times 100$), (b) follicles lined by cuboidal cells showing nuclear crowding and clearing (H and E, $\times 400$), (c) spindle component showing hyperchromasia and brisk mitotic activity (H and E, $\times 400$) and (d) adjacent areas showing classical papillary carcinoma (H and E, $\times 200$)

carcinosarcomas as aggressive, fatal neoplasms, with patients surviving only for a few months post diagnosis or surgery, even after adjuvant therapy. We were unable to obtain the details of adjuvant therapy that was given in other cases, even after an exhaustive English websearch.^[9-11]

The WHO classification for tumors of thyroid categorizes carcinosarcoma as a variant of anaplastic carcinoma.^[12] However, the cell of derivation of anaplastic carcinoma is an epithelial cell. In contrast, carcinosarcomas (at whatever site) show two distinct cell lineages – epithelial and mesenchymal. Although sarcomas with co-existing differentiated thyroid carcinoma (follicular,^[13] adenocarcinoma^[14]) have been described as early as 1956, the term ‘carcinosarcoma’ did not gain acceptance. This was due to: (1) arguments that sarcomatoid areas represent dedifferentiation in well-differentiated thyroid carcinomas

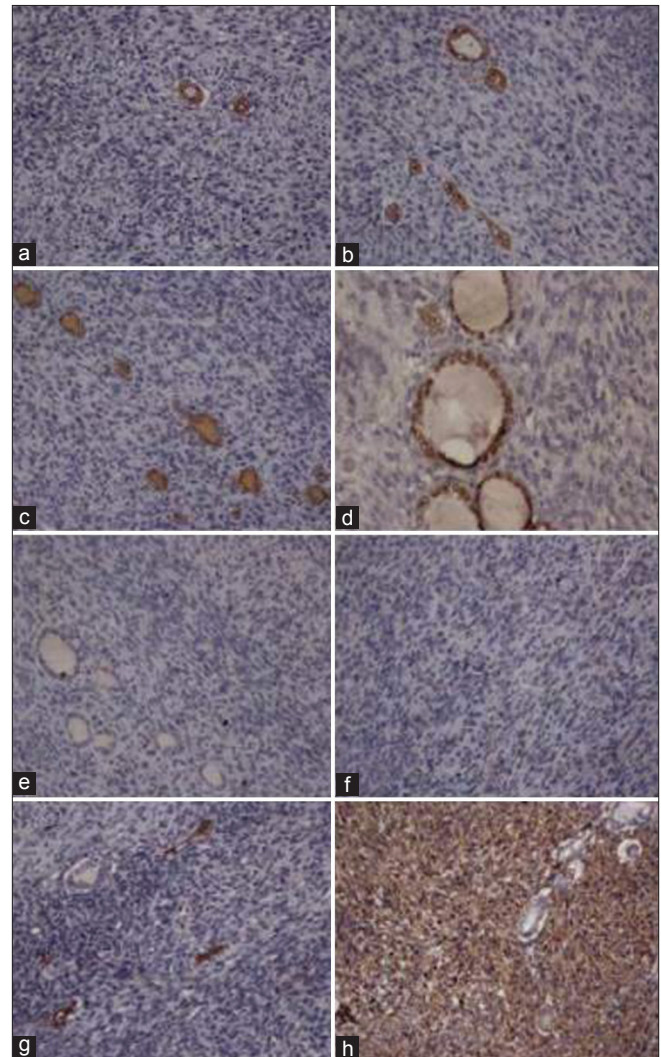


Figure 3: Immunohistochemistry results. (a) Pancytokeratin. (b) Cytokeratin-19. (c) Thyroglobulin and (d) transcription factor-1 positive in the epithelial component but negative in the adjacent spindle cell component. (e) Calcitonin is negative in both components. Spindle cell component is negative for (f) S-100 and (g) Smooth muscle actin (SMA) but strongly positive for (h) vimentin

and (2) the term ‘coexisting carcinoma and sarcoma’ was thought to be better because both components have variable rates of progression and hence different prognostic implications.

In 1997, Al-Sobhi *et al.*^[10] reviewed 17 cases reported as carcinosarcoma of the thyroid. Since then, there have been few additional reports, most of which have confirmed the highly aggressive nature of this neoplasm.^[9,15,16] For many of these patients, clinical data, surgical details and follow-up are not available. Most cases, including the present case, have been reported in females over 50 years of age. History of nitrosurea use was present in one case,^[10] although other cases have not recorded any such exposure.

All reported cases have followed a uniformly fatal course with patients barely surviving beyond a few months. Many of these metastasize or locally invade the adjacent structures to cause respiratory embarrassment. Resection should be complete and all lymph nodes adjacent to the thyroid should be excised.^[10] There is no definite data available as to the response of these patients to chemotherapy. Some authors have advocated the use of radiotherapy as these tumors are thought to be radiosensitive.^[17] Radiotherapy was used in the present case and the patient presently does not have evidence of metastasis or recurrence after 12 months of follow-up. Thus, good local control may be possible with adjuvant therapy.

This case is unique in two aspects: (1) despite extensive search, a primary was not detected in the thyroid. Possible explanations for this include either origin in an ectopic thyroid tissue or regression of the primary tumor in the thyroid after metastasis. (2) Unlike other reported cases, a combination of papillary carcinoma thyroid and undifferentiated sarcoma has never been reported in the literature.

To conclude, although the present WHO clubs carcinosarcoma along with anaplastic carcinoma thyroid, yet, we propose recognition of ‘carcinosarcoma-thyroid’ as a distinct entity, different from anaplastic carcinoma. Anaplastic carcinoma is an aggressive malignancy and the sarcoma-like morphology in this tumor is possibly due to dedifferentiation of an epithelial malignancy; in contrast, the carcinosarcomas at all body sites are thought to originate from a malignant epithelial cell and a malignant mesenchymal cell. Therapies and prognosis for the former subset are well defined, with almost all patients having a uniformly fatal outcome within few months after a tissue diagnosis. However, in the present case, the patient had a good postoperative survival. Thus, patients who have carcinosarcomas could fare better prognostically than frank anaplastic carcinomas. Further reports of these cases are needed to help prognosticate and determine the best treatment approach.

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