Case Report

Thyroid Disease and Its Varied Presentations: A Series of Unusual Cases, a Tertiary Centre Experience

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Abstract

Introduction: Thyroid diseases, both non-neoplastic processes and neoplasms, are on the rise nowadays and are associated with a preponderance in females. Methods: This is a prospective study of nine (9) unusual cases of thyroid lesions conducted from January 2021 to June 2022, over one and a half years, in our tertiary care centre. Results: The age range was 22 to 75 years. All the cases were females. The different histological subtypes included haemangioma, Riedel's thyroiditis, hyalinising trabecular tumour, anaplastic carcinoma of the thyroid, sclerosing mucoepidermoid carcinoma with eosinophilia, mucoepidermoid carcinoma, metastatic neoplasms, medullary carcinoma of the thyroid (MTC), and follicular carcinoma. Conclusion: Here we present nine (9) rare cases of the thyroid gland, ranging from benign lesions to aggressive carcinomas, such as anaplastic as well as metastatic carcinomas. Among these, hyalinising trabecular tumour and haemangioma were found to be associated with better prognosis, whereas anaplastic carcinoma and the secondaries had the worst outcomes. The prognosis of MTC and follicular carcinoma varies depending on the subtypes and other clinical variables.

Keywords:

Benign, Histopathology, Immunohistochemistry, Malignant, Thyroid

Introduction

The thyroid gland is a large endocrine organ with a potential for massive enlargement [1]. The incidence of thyroid diseases—both non-neoplastic processes and neoplasms—is on the rise nowadays and has a female preponderance. With the advent of modern technologies, thyroid disorders are easier to detect. Early diagnosis and definitive treatment remain the cornerstone of therapy [2]. Here, we have compiled the varied proportions and presentations of unusual thyroid disorders.

This is a prospective study of unusual thyroid lesions conducted over a period of eighteen months, from January 2022 to June 2023, in our tertiary care centre. The study was conducted on nine cases. Informed consent was taken from all the patients. The

patients presented with varied clinical features and sites of lesion. The age range was 22 to 75 years. All the patients were investigated with a complete haemogram, fine needle aspiration cytology, and computed tomography (CT scan). The tissue sections prepared from the surgical resection of the tumour masses in the neck were processed and examined in our department. Gross examination followed by proper light microscopic examination of the tumour mass from the representative paraffin-embedded sections was done. The specimens were later subjected to relevant immunohistochemical examination (IHC) where needed.

Case Report

Case 1: A 75-year-old female presented with a rapidly growing hard mass in the neck. Subsequent investigations, i.e., USG and CT scan, revealed a thyroid nodule with necrosis involving both lobes. Biopsy was done from the excision specimen and sent to the Pathology Department for histopathological examination. FNAC was performed, and the cytology smear revealed a cellular smear with spindle and epithelioid cells showing marked nuclear pleomorphism in the background of necrosis, diagnosed as anaplastic carcinoma of the thyroid (Bethesda category VI). On gross examination, there were multiple tissue pieces, with the largest one measuring 2 × 1 cm. Sections from the tumour mass showed tumour cells arranged in solid sheets with epithelioid and spindle cell patterns. Individual cells were large, highly pleomorphic with prominent nucleoli. Multiple tumour giant cells, mitotic figures (11–14/HPF), and areas of geographical necrosis were also evident [Figure 1A, 1B]. As the histomorphological features were so evident, IHC was not performed. Hence, a diagnosis of anaplastic carcinoma of the thyroid was assigned.

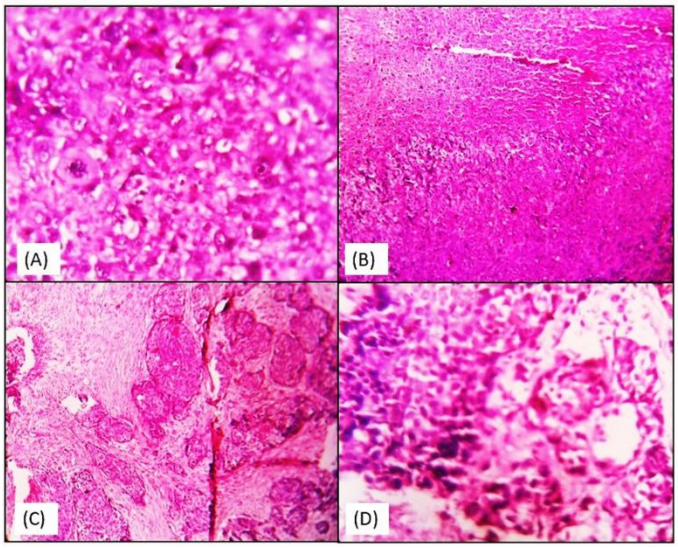

Figure 1: Anaplastic carcinoma of thyroid (A) Section shows tumor cells arranged in sheets and tumor cells are highly pleomorphic with prominent nucleoli (x400, H&E) (B) Section shows areas of geographical necrosis (x100, H&E) Mucoepidermoid carcinoma arising from thyroid gland (C) Section shows solid nests of epidermoid cells with keratinization (x100, H&E) (D) Section shows intermediate cells with pleomorphism (x400, H&E).

Case 2: A 55-year-old female patient presented with a gradually increasing painless neck swelling for 5 months. CT scan revealed an enlarged thyroid gland with infiltration of the trachea. USG-guided FNAC revealed malignant cells in an inflammatory background (Bethesda category II). The patient underwent total thyroidectomy, tracheal resection, and bilateral neck dissection. The tumour mass measured 35 × 22 × 10 mm, with no normal thyroid tissue. There was evidence of transmural invasion of the

trachea along with peritracheal tissue. In the right neck dissection, 5/12 nodes were positive for tumour involvement, and 2/9 nodes were positive in the left neck dissection. Histopathological examination of the excised specimen showed nests and cords of squamoid cells with prominent nucleoli, with mucocytes set in a dense sclerotic stroma with lymphocytes, eosinophils, and plasma cells. Perineural invasion was also noted. Hence, it was reported as a case of sclerosing mucoepidermoid carcinoma with eosinophilia of the thyroid gland (SMECE).

Case 3: A 32-year-old female patient presented with dyspnoea and a neck mass with a history of gradual increase in size. CT scan revealed a tumour mass from the thyroid gland with invasion and destruction of adjacent structures. USG-guided FNAC was performed. The cytomorphological features included epidermoid cells and mucus-secreting cells with background cell debris or mucin, suspicious of malignancy (Bethesda category V). The patient was subjected to radical neck dissection, and the mass was sent for histopathological examination. Grossly, it was a large tissue piece measuring 6 × 6 × 3 cm. The thyroid could not be dissected out as it was tightly encasing the underlying cartilage and was firmly adhered to it. Multiple sections were taken from the mass. Histopathological examination of the excised specimen showed nests and cords of polygonal squamoid cells with eosinophilic cytoplasm and prominent nucleoli, with mucocytes set in a dense sclerotic stroma [Figure 1C, 1D], suggestive of mucoepidermoid carcinoma arising from the thyroid gland.

Case 4: Another 75-year-old female presented with a hard neck mass with dyspnoea and difficulty in deglutition for 2 months. The mass was gradually increasing in size. The patient had a history of right hemicolectomy performed 4 months prior. She was a patient of mucinous adenocarcinoma of the colon. This time, she underwent a USG-guided biopsy from the mass for histopathology. Gross examination showed white, solid, and slimy areas; multiple tissue pieces were received [Figure 2A]. On microscopical examination, histopathological features suggested a mucinous adenocarcinoma, probably metastatic in origin. On immunohistochemistry, the tumour mass was positive for CK20 [Figure 2B], epithelial membrane antigen (EMA), and the Ki-67 index was high but was negative for TTF-1, whereas the surrounding thyroid follicles were positive for it.

Case 5: A 60-year-old female presented with severe dyspnoea and stridor, and a history of dysphagia. Physical examination revealed a stone-hard, painless, voluminous neck mass. CT scan showed an enlarged and heterogeneous thyroid gland with heterogeneous early enhancement and late homogeneous enhancement on contrast, invading the posterior wall of the oropharynx and compressing the trachea and the oesophagus. The vascular structures were displaced but not compressed. Tracheostomy was performed. Subsequent USG (TIRADS 5) and FNAC suggested a diagnosis of anaplastic carcinoma arising from the thyroid gland (Bethesda category VI). Biopsy of the tumour mass revealed follicles which were obliterated by extensive dense fibrous tissue. Adjacent skeletal muscles were also infiltrated. The vein entrapped within the tumour mass also showed inflammation. The diagnosis of Riedel's thyroiditis was made.

Case 6: A 22-year-old female presented with a painful mass in the neck. USG of the thyroid gland and CT scan suggested the presence of a vascular lesion with a nodular mass in the right lobe of the thyroid gland. Hemithyroidectomy was done and sent for histopathology. On gross examination, there were irregular tissue pieces altogether measuring 4 × 3 × 1.5 cm, with attached isthmus measuring 1 × 1.5 × 0.5 cm. Cut section showed a well-circumscribed mass in the upper lobe, which was 1.5 cm in diameter. Microscopical examination revealed a mass composed of ectatic vascular spaces lined by flat endothelial cells in a background of colloid-filled thyroid follicles of varying size and shape [Figure 2C]. The mass was well demarcated by a fibrous capsule. Immunohistochemistry revealed CD34 positivity of the tumour [Figure 2D]. Hence, it was a rare case of haemangioma in a background of adenomatoid goitre.

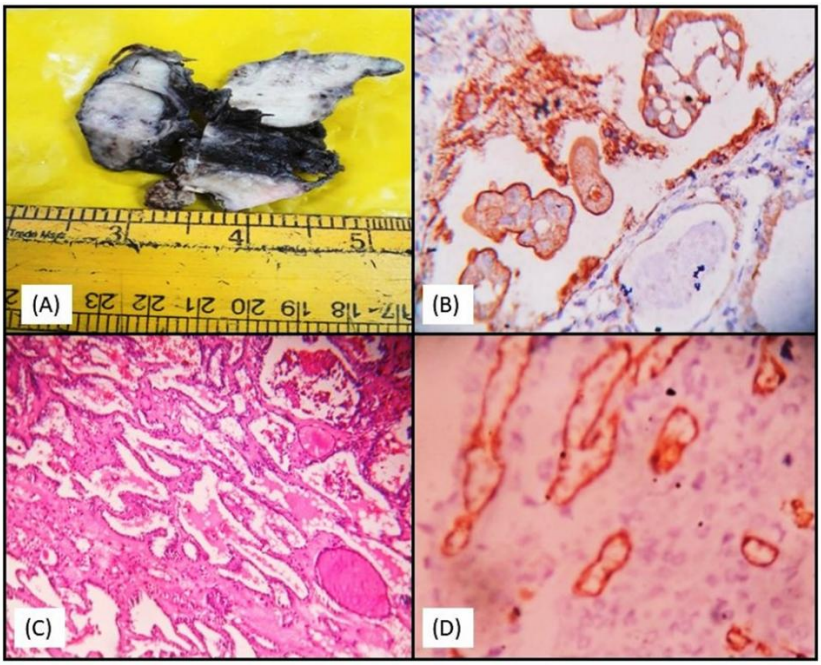

Figure 2: Mucinous adenocarcinoma probably metastatic in origin (A) Gross examination shows white solid and slimy areas (B) IHC staining for CK20 showing positivity (x100) Haemangioma (C) Section shows ectatic vascular spaces lined by flat endothelial cells in a background of colloid filled thyroid follicles of varying size and shape (H&E, x100) (D) IHC staining for CD34 showing positivity (x100).

Case 7: A 70-year-old female patient presented in the surgery OPD with a single lump on the anterior aspect of the neck. USG of the neck revealed a thyroid nodule involving the right lobe (TIRADS 5). Subsequent FNAC from the nodule suggested a diagnosis of medullary carcinoma of the thyroid (Bethesda category VI) [Figure 3A]. The patient underwent subtotal thyroidectomy. On gross examination of the excised thyroid lobe, a nodular area with a firm consistency was noted. Histological sections of the lesion revealed neoplastic cells arranged in a trabecular pattern and in some areas an insular pattern. Individual cells were plasmacytoid-polygonal with round nuclei, salt and pepper chromatin, inconspicuous nucleoli, and amphophilic cytoplasm [Figure 3B, 3C]. Abundant stromal amyloid deposition was noted. Immunohistochemistry for chromogranin [Figure 3D] and synaptophysin [Figure 3E] was positive. Congo red staining was also positive [Figure 3F]. The case was diagnosed as medullary carcinoma of the thyroid (MTC).

Case 8: A 44-year-old female patient presented in the surgery OPD with a painless, gradually increasing neck mass. On examination, it was soft to firm in consistency. Subsequent USG of the neck suggested a thyroid nodule involving the right thyroid gland (TIRADS 3). FNAC from the nodule suggested a diagnosis of papillary carcinoma of the thyroid (Bethesda Category VI). The patient underwent subtotal thyroidectomy. Gross examination of the excised thyroid lobe revealed a well-circumscribed, encapsulated lesion, tan to grey in colour and gritty in consistency. Histologic sections of the lesion revealed a circumscribed lesion with follicular cells arranged in a trabecular growth pattern, associated with abundant dystrophic calcification. Tumour cells showed a spindled morphology with clumped nuclear chromatin and eosinophilic cytoplasm [Figure 4A]. Occasional nuclear pseudo-inclusions and grooves were noted. The case was diagnosed as hyalinizing trabecular tumour of the thyroid.

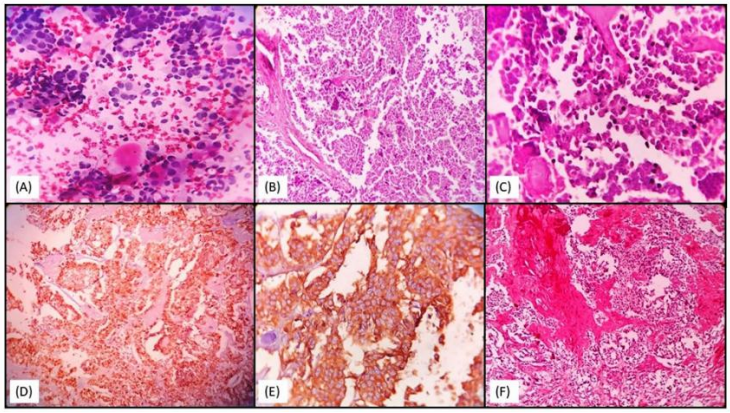

Figure 3: Medullary carcinoma of thyroid (A) Smear shows ovoid, plasmacytoid cells with abundant cytoplasm and eccentric nuclei (x400, LG) (B) Section showsneoplastic cells arranged in a trabecular pattern and somewhere in insular pattern (x100, H&E) (C) Section shows neoplastic plasmacytoid-polygonal cells with round nucleus and salt and pepper chromatin, inconspicuous nucleoli and amphophilic cytoplasm (x400, H&E) (D) IHC staining for chromogranin showing positivity (x100) (E) IHC staining for synaptophysin showing positivity (x400) (F) Positive Congo red staining (x400).

Case 9: A 59-year-old female presented in the surgery OPD with a neck mass. On examination, it was firm in consistency. USG revealed a well-defined lesion (TIRADS 5) in the left lobe of the thyroid. USG-guided FNAC showed microfollicles with nuclear enlargement, overlapping and crowding, and nuclear atypia was also noted. The features were suggestive of follicular neoplasm (Bethesda category IV). Subsequently, she underwent left hemithyroidectomy. On gross examination, multiple cystic areas were noted with various pedunculated masses, the largest measuring 2 × 2 × 1 cm. Histologic examination revealed an encapsulated lesion composed of closely packed thyroid follicles arranged in a solid configuration [Figure 4B]. Capsular invasion was present [Figure 4C]. Hence, it was a case of follicular carcinoma. Subsequently, the patient also had scalp metastasis, which was diagnosed after biopsy from that site [Figure 4D].

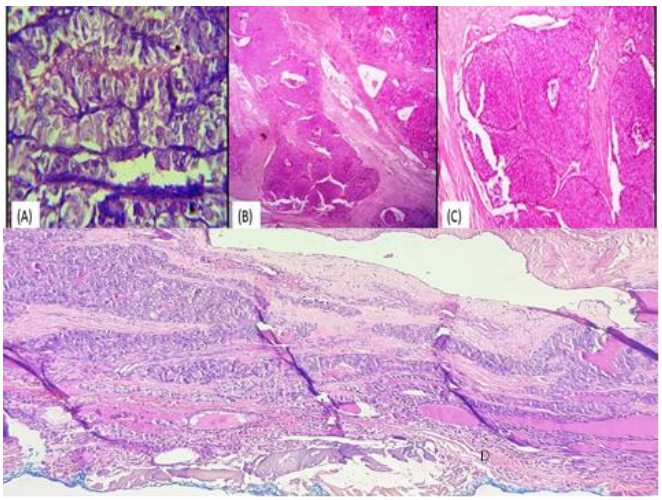

Figure 4: Hyalinizing trabecular tumour of the thyroid (A) Section shows tumor cells arranged in trabecular growth pattern (x100, H&E) Follicular carcinoma (B) Section shows encapsulated lesion composed of closely packed thyroid follicles arranged in a solid configuration (x100, H&E) (C) Section shows capsular invasion (x400, H&E) (D) Section shows bone metastasis in scalp tumour.(x100).

Discussion

Over the past centuries, there has been an extensive worldwide variation in the demography and presentation of thyroid disorders. Among the neoplastic processes, papillary carcinomas are the commonest, followed by follicular carcinoma and others [3]. Anaplastic thyroid carcinomas (ATC) are unusual, accounting for approximately 2% of all thyroid gland cancers. Among the primary malignancies of the thyroid, anaplastic carcinomas are most aggressive and are associated with poor prognosis, with a mean survival of six months after diagnosis. They are responsible for the majority of thyroid cancer-related deaths. Fifty percent of anaplastic carcinoma develops from a pre- or coexistent differentiated carcinoma after a multistep carcinogenesis pathway, induced by loss of P53 tumour suppressor genes [4]. Long-standing cases of goitres or benign nodules should always be followed up carefully and considered for resection if they are not responding to medical therapy and should undergo total thyroidectomy. They have a female preponderance with a female:male ratio of 2:1 and are most prevalent in the sixth to seventh decades of life [3]. Our case was an elderly female. Histologically, ATC shows a mixture of pleomorphic, spindle, and squamoid cells with considerable variation in both the proportion and distribution of these cell types. Additional variants may be seen, which include the pauci-cellular, rhabdoid, small cell, osteoclastic, carcinosarcoma, and lymphoepithelioma-like variants. In 23–78% of ATC cases, a pre-existing or coexisting well-differentiated carcinoma or PDC has been demonstrated.

The differential diagnoses of ATC include Riedel thyroiditis, poorly differentiated carcinoma, papillary carcinomas with squamous differentiation or fasciitis-like stroma, de-differentiated medullary carcinoma, sarcoma, primary or secondary squamous cell carcinoma, spindle epithelial tumour with thymus-like differentiation (SETTLE), and Carcinomas Showing Thymus-Like Differentiation (CASTLE) [5]. ATCs are also shown to be associated with peripheral blood neutrophilia and stromal neutrophilic infiltration due to production of macrophage and granulocyte colony-stimulating factor by the carcinoma cells. Leucocytosis is inversely related to patient survival. Positive staining for Cytokeratin AE1/AE3, TTF-1, and p63 supports the diagnosis of ATC. P53 expression differentiates it from more differentiated thyroid carcinoma. It has a high MIB-1 labelling index.

Chan et al. first described sclerosing mucoepidermoid carcinoma with eosinophilia and showed that they are inadvertently associated with Hashimoto thyroiditis. It has a high female preponderance with a female:male ratio of 7:1 and a median age of 55 years [6]. Our case was a 55-year-old female patient. It most commonly presents as a cold nodule in imaging. Microscopically, it shows a population of epidermoid tumor cells in thin strands and nesting pattern with mild to moderate nuclear pleomorphism, conspicuous nucleoli, pale eosinophilic cytoplasm in a background of dense fibro-hyaline stroma. Foci of squamous differentiation, aggregates of mucous cells, and mucin pools may be acknowledged. Dense lymphoplasmacytic infiltration along with copious eosinophils is found in a sclerosing stroma. Perineural invasion and abolition of median-sized vessels are frequently encountered. The non-tumour thyroid always presents Hashimoto thyroiditis or lymphocytic thyroiditis. The histological features were quite similar in our cases and very striking. Immunohistochemically, the tumour cells were positive for cytokeratin, p63, CD10, and galectin-3 and were negative for thyroglobulin. Unlike its previous consideration as a low-grade malignancy, nowadays extrathyroidal extension and regional lymph node metastasis are common. The most common site of metastasis is lung, followed by bone, liver, mediastinum, and non-contiguous lymph nodes [6]. Our case also showed the involvement of bilateral contiguous lymph nodes as well as infiltration of extrathyroidal tissue.

Mucoepidermoid carcinoma is an extremely rare tumour of the thyroid gland with a female:male ratio of 2:1 and a median age at presentation of 47 years [7]. The tumours are usually asymptomatic with incidental findings, but symptomatic in cases with extrathyroidal extension and distant organ involvement. On microscopic examination, it shows large confluent epidermoid nests

along with mucin-producing cells. The tumour cell nuclei resemble that of papillary carcinoma of thyroid. Occasionally, psammoma bodies are seen. It has a strong association with chronic thyroiditis. IHC showed positivity for PAX-8, thyroglobulin, and TTF-1. Epidermoid cells showed positivity for p63. It is a low-grade malignant lesion and has a median survival of more than 10 years [7]. Highly aggressive variants are reported, with the most common site of metastasis being the cervical lymph nodes. Our case showed a complete destruction of the trachea and surrounding structures with a relatively aggressive course. It is reported to have a 10% incidence of transformation to anaplastic carcinoma.

The most common sources of distant metastasis of mucinous adenocarcinoma to the thyroid gland are kidney, lung, gastrointestinal tract, and breast respectively [8]. In the Asian population, lung carcinoma is the most common site of primary for thyroid metastasis. In our case, a 75-year-old female presented with a gradually increasing hard neck mass. The patient underwent right hemicolectomy after being diagnosed with mucinous adenocarcinoma of the colon. USG-guided biopsy from the mass showed histopathological features suggestive of a mucinous adenocarcinoma. On immunohistochemistry, the tumour mass was positive for Cytokeratin 20, Epithelial Membrane Antigen (EMA), ki-67 index was high but negative for TTF-1, whereas surrounding thyroid follicles were positive for it [9]. The IHC analysis ruled out the possibility of a thyroid primary mucinous carcinoma. Prognosis of these secondary tumours depends upon the stage of the primary tumours.

Riedel's thyroiditis is a rare tumour with a reported incidence of 1.06/100,000 [10]. It is a long-standing inflammatory disease involving the thyroid gland, characterised by extensive fibrosis which extends to the adjacent structures, often leading to partial distortion of the normal glandular architecture. On radiological examination, there are numerous overlapping features simulating that of a carcinoma, hence surgical biopsy remains the mainstay of diagnosis. It shows morphology of a dense inflammatory process often extending to the surrounding tissues, absence of giant cells, lymphoid follicles, granulomas, and oncocytes or any evidence of malignancy [10]. Surgery remains the mainstay of treatment but due to its extensive attachment to surrounding structures, extensive surgery is not possible.

Primary haemangioma of the thyroid gland is an extremely rare tumour with only a handful of reported cases [11]. They are considered as a developmental anomaly related to angioblastic mesenchyme. Histopathology is the mode of diagnosis, defined as multilobated lesion with dilated vascular spaces. The tumours should be resected when conservative management fails and are associated with a good prognosis. The differential diagnosis includes endothelial reactive hyperplasia among benign disorders and also undifferentiated sarcomatoid carcinoma, angiosarcoma, hemangiosarcoma among the malignant ones [12].

Hyalinizing Trabecular Tumours (HTT) are unusual follicular tumours of the thyroid. The reported incidence is 0.44–1.3% [13]. The age range is 21–80 years with a mean age of 50.5 years. It has a female preponderance with a female:male ratio of 6:1. Chronic lymphocytic thyroiditis and multinodular goitre are frequently associated with it. Microscopically, it shows neoplastic cells arranged in trabeculae with areas of hyalinization and often calcification. The cells have low nuclear:cytoplasmic ratio. Mimickers include most commonly papillary carcinoma of thyroid, followed by medullary carcinoma of thyroid and paragangliomas among others. The diagnosis of HTT is favoured by minimal cytologic atypia, low nuclear:cytoplasmic ratios, hyalinized material, and clumped or fine chromatin with absence of nuclear grooves and optically clear nuclei. The labelling index for ki-67 was found to be low in HTT than its malignant mimickers [14]. It has an overall good prognosis.

Medullary carcinoma of the thyroid is an unusual neoplasm, which is associated with certain specific supportive diagnostic markers. It is a tumour of the parafollicular C-cells and it requires special attention as the detection of the precursor lesion (C-cell hyperplasia) and the hallmark genetic mutation in the RET gene [3]. Genetic counselling should be provided to all the patients

with medullary thyroid carcinoma along with RET mutation analysis, and if positive, it must be extended to all the first-degree relatives since germline RET mutations have been identified in 1.5%–7.3% of sporadic medullary thyroid carcinoma [3]. MTC has an overall favourable prognosis, even if the rate of biochemical cure is lower in it than in differentiated types of thyroid cancer.

Follicular carcinoma is a malignant epithelial tumour of the thyroid gland with follicular differentiation. Owing to the incapability of pre-operative imaging, FNAC, and molecular technique to provide a clear-cut distinction between FTC and benign follicular thyroid adenoma, the histopathological evaluation of formalin-fixed, paraffin-embedded tissue sections remains an excellent tool for the definitive diagnosis of follicular carcinoma and the characterisation of its subtypes [3]. It is characterized by the absence of the nuclear features that are typical of papillary thyroid carcinoma. In 2016, the American Registry of Pathology divided FTC into two main types: Minimally invasive FTC and Widely invasive FTC. The majority of the follicular carcinomas belong to the minimally invasive type [3]. This subtype comprises 'minimally invasive FTC with capsular invasion (with no obvious invasion)', 'minimally invasive FTC with limited vascular invasion (< four vessel invasion)', and 'minimally invasive FTC with extensive vascular invasion (≥ four vessel invasion)'. As per the current 2022 World Health Organization (WHO) classification of tumours of endocrine organs, there are three histological subtypes: minimally invasive FTC with capsular invasion only, encapsulated angio-invasive FTC, and with extensive vascular invasion and widely invasive FTC [3].

Conclusion

In this study, we present a series of nine unusual cases involving the thyroid gland, with a wide range of benign inflammatory processes like Riedel's thyroiditis and aggressive carcinomas like anaplastic carcinoma, as well as metastatic carcinomas. Out of these, hyalinising trabecular tumour and haemangioma were associated with better prognosis, whereas anaplastic carcinoma and the secondaries had the worst outcomes. The strongest predictors of survival for patients with MTC are stage of disease and age at diagnosis. Follicular carcinoma is a heterogeneous group of tumours with different malignant potential: minimally invasive (excellent prognosis), encapsulated angio-invasive, and widely invasive FTC (higher risk of recurrence and metastasis). Early diagnosis and management are important to reduce the disease burden as well as prevent further progression to advanced disease, thereby increasing survival.

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