descriptive diagnosis may be given, with a comment on the likely benign nature of these lesions.

Current literature shows that pre-operative diagnosis of ELS is challenging, even with imaging and cytology. The initial working diagnosis prior to surgical resection in our case was that of a parasplenic mucinous cystic lesion. On histology, ELS shows dilated bronchi and bronchioles, alveolar ducts, and alveoli. A well-formed bronchus may be present, but dilated bronchial structures surrounded by a fibromuscular wall with a cartilage plate are more frequently seen. The presence of alveolar structures excludes a bronchogenic cyst.[1] Superimposed infarction, arteritis, infection, and congenital cystic adenomatoid malformations may alter the microscopic features and potentially mimic malignancy (e.g., adenocarcinoma). Herniation of the lung outside the thoracic cavity is unusual and a combination of clinical and radiological findings will be helpful in its exclusion.[1]

The treatment of choice for ELS is surgical excision. It is prudent for pathologists to consider ELS in the differential diagnosis of subdiaphragmatic intra-abdominal lesions in which FNA shows unusual features such as respiratory epithelium or cartilage. Specific imaging investigations may then be applied to ascertain the pre-operative diagnosis of this rare entity, so that appropriate surgical treatment can be planned.

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**Irfan Sagir Khan[1], Darren Chua[2], Benjamin Wong[3], Shi Wang[1], Min En Nga[1]**

*[1]National University Health System, Singapore; [2]Yong Loo Lin School of Medicine, National University of Singapore, Singapore; [3]Woodlands Health Campus, Singapore*

Contact Dr Irfan Sagir Khan.
E-mail: irfan_sagir_khan@nuhs.edu.sg

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## Primary thyroid hyalinising clear cell carcinoma: a rare variant of salivary gland type carcinoma of the thyroid

Sir,

Clear cell carcinoma (CCC) is a rare salivary gland tumour usually arising from minor salivary glands of palate or tongue base, and it was first described by Milchgrub *et al.* in 1994.[1–4] CCC is characterised by small epithelioid cells with clear to eosinophilic cytoplasm and arranged in cords or nests in a hyalinised stroma. CCC usually has a disease-specific fusion of the Ewing sarcoma breakpoint region 1 (*EWSR1*) and activating transcription factor 1 (*ATF1*) gene or cAMP response element modulator (*CREM*).[2,3] Identification of this pathognomonic *EWSR1* rearrangement is important in the diagnosis of CCC. Herein, we report a rare case of primary thyroid CCC.

A 47-year-old woman had no previous history of systemic disease or surgery. In May 2018, a right neck mass was noted but there was no associated symptoms such as pain, tenderness, dysphagia, or odynophagia. She visited our clinic and thyroid sonography revealed a 3.5 cm right thyroid tumour. The first fine needle aspiration (FNA) reported colloid goitre. After 6 months follow-up, the thyroid tumour enlarged and the second FNA showed suspicious for malignancy. Radical thyroidectomy was performed. A white and firm tumour measuring 4.2 × 3.0 cm in size was found in the right thyroid gland (Fig. 1A). Microscopically, the tumour comprised small nests and cords of small polygonal cells with mildly irregular nuclear contours, indistinct nucleoli, and eosinophilic or clear cytoplasm (Fig. 1B,C). Most tumour nests were rimmed by a densely hyalinised stroma, while the spaces between tumour nests were less hyalinised and occasionally associated with a plasmacytic infiltrate. Two of seven level VI lymph nodes were directly invaded by the carcinoma. Immunohistochemically, the tumour cells were positive for cytokeratin (AE1/AE3) and p63 (Fig. 1D,E) but negative for TTF-1, PAX8, thyroglobulin, calcitonin, synaptophysin, chromogranin A, S100, smooth muscle actin, and SOX10. Mucicarmine stain was negative. *EWSR1* gene rearrangement in tumour cells was confirmed by fluorescent *in situ* hybridisation (FISH) using commercial Vysis EWSR1 Dual Color Break Apart FISH Probe (Abbott Molecular, USA) (Fig. 1F). The histological and cytogenetic results confirmed a primary thyroid clear cell carcinoma. After surgery, full-body computed tomography (CT) scans showed no definite mass lesions or lymphadenopathy in the brain, head and neck, chest, abdomen, and pelvis. The patient has been followed for 6 months and there is no local recurrence or distant metastasis.

Primary thyroid salivary gland-type carcinoma is very rare, and mucoepidermoid carcinoma (MEC) and mammary analog secretory carcinoma (MASC) are the two most commonly reported salivary gland-type cancers in the thyroid gland.[5,6] Similar to their salivary gland counterpart, pathognomonic genetic fusions, such as *MAML2* fusion in MEC and *ETV6* fusion in MASC, can also be found in these thyroid salivary gland-type carcinomas.[5–7] Clear cell carcinoma is a rare, low-grade salivary gland malignancy. CCC most commonly arises from minor salivary glands of the oral

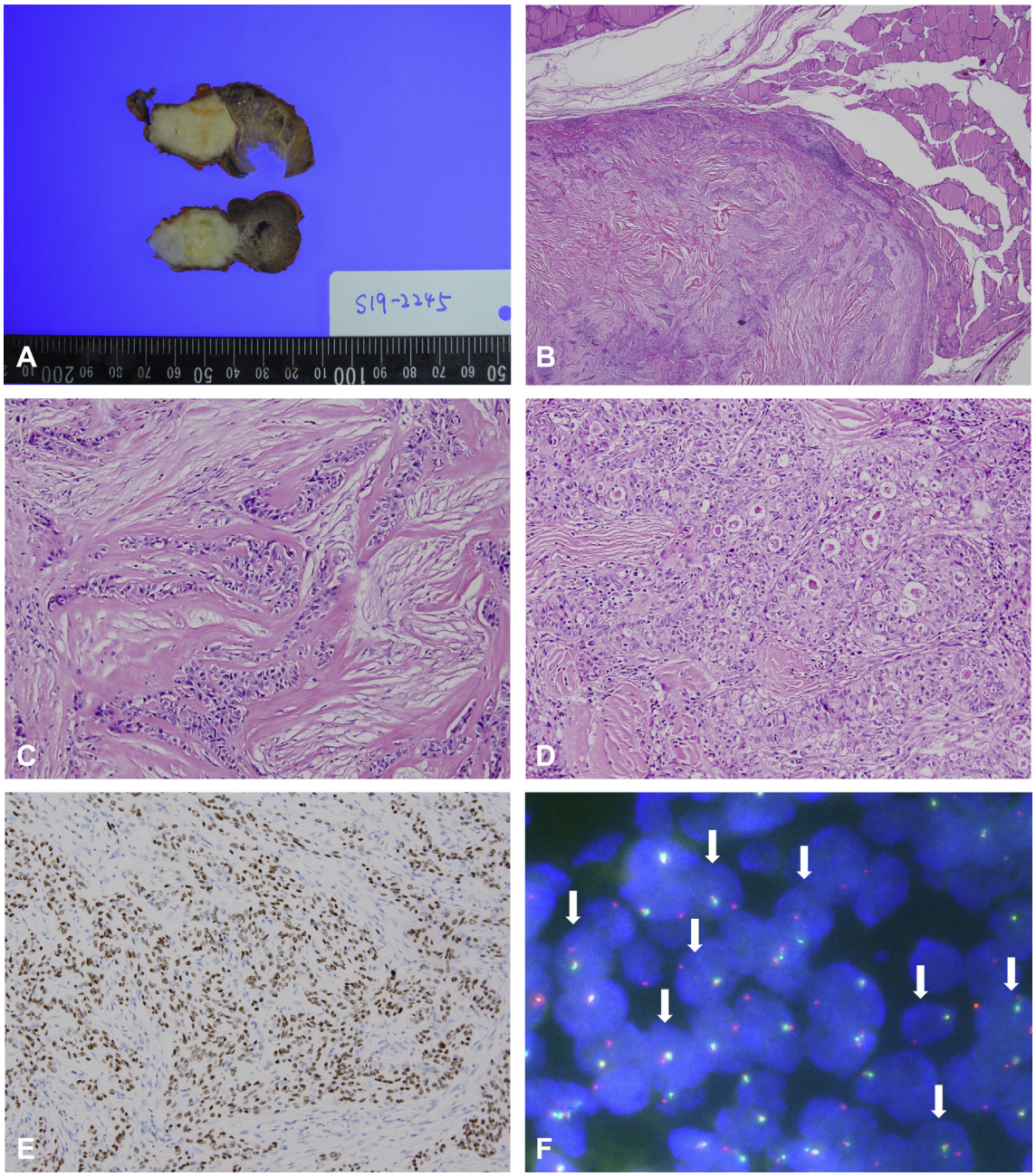


**Fig. 1** (A) Gross appearance of the resected thyroid tumour showing an elastic white solid mass; (B) the low power showing an unencapsulated nodular tumour with a well-defined border in the thyroid gland; (C) area with typical CCC showing tumour cells arranged in cords or nests associated with a dense hyalinised stroma; (D) mixed clear and eosinophilic cells forming cords and nests in a hyalinised background; (E) tumour cells showing positive p63 staining; (F) *EWSR1* rearrangement confirmed with fluorescence *in situ* hybridisation (arrows indicate most tumour cells having one fused plus one single red signals).

cavity such as tongue base or palate. CCC has also been found in the parotid gland, nasopharynx, lacrimal gland, nasal cavity, and lungs.[1–4,8,9] To the best of our knowledge, this case is the first primary thyroid CCC reported in the English literature. This thyroid CCC has similar histological and immunohistochemical features with CCC from other organs. It shows characteristic raisin-like nuclei with irregular nuclear contours, nuclear grooving, some with nuclear pseudoinclusion, and clear or pale eosinophilic cytoplasm. Most importantly, it harbours the pathognomonic *EWSR1* rearrangement, identical to its salivary gland counterpart. Our report shows that CCC, another salivary gland-type carcinoma, could also be found in the thyroid gland. The cell origin of these primary thyroid salivary gland-type neoplasms remains unknown, and the hypothesised origin includes ectopic salivary glands or metaplastic follicular cells.[5,6]

The differential diagnosis includes primary papillary thyroid carcinoma (PTC), MEC, and squamous cell carcinoma (SqCC). Morphologically, CCC and PTC have common features including irregular nuclear contours, presence of nuclear grooving, and a sclerotic background. Nevertheless, CCC does not form papillary structures with fibrovascular cores and their nuclei are less ground glass compared with those of conventional PTC. Immunohistochemical stain is a very helpful tool as TTF-1, thyroglobulin, and PAX8 are typically strongly expressed in PTC but not in CCC. The common features between CCC and MEC include mucin production, p63 expression, and small-sized

tumour cells with clear to pale eosinophilic cytoplasm mimicking the intermediate cells of MEC. Thyroid sclerosing mucoepidermoid carcinoma with eosinophilia is a unique histological variant of MEC with tumour cells arranged in nests and anastomosing cords, keratinisation, cysts lined by mucous/goblet cells, a fibrohyaline stroma with eosinophils, and negative for *MAML2* rearrangements.[7] The most reliable histological finding is that CCC lacks mucous cell-lined cysts, an important feature of thyroid MEC and thyroid sclerosing MEC with eosinophilia. SqCC and CCC have similar immunohistochemical phenotypes because both tumours are positive for p63 and negative for thyroid gland markers. However, primary thyroid SqCC is a high-grade malignancy typically associated with marked cellular pleomorphism and keratinisation. CCC shows low-grade cytological features and no keratinisation. It is important to use molecular or cytogenetic methods to demonstrate *EWSR1* rearrangement to confirm the diagnosis. A secondary tumour from a primary salivary gland CCC is a very important differential diagnosis. Since CCC is a low-grade salivary gland malignancy, distant metastasis is usually found after the operation of the primary tumour after years during follow-up.[1,4,9,10] In this case, a primary thyroid CCC is considered because the patient had no surgical history and no other lesions could be found by full-body CT scans.

Due to its rarity, the prognosis of primary thyroid CCC is not clear. Long term follow-up is needed as delayed recurrence or distant metastases have been reported in patients with primary tongue base or pulmonary CCC.[4,9,10]

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**Min-Shu Hsieh[1,2], Kuen-Yuan Chen[3], Yi-Hsuan Lee[1], Hsuan Wang[4]**

*[1]Department of Pathology, National Taiwan University Hospital, Taipei, Taiwan; [2]Graduate Institute of Pathology, National Taiwan University College of Medicine, Taipei, Taiwan; [3]Department of Surgery, National Taiwan University Hospital, Taipei, Taiwan; [4]Department of Pathology, National Taiwan University Hospital Hsin-Chu Branch, Hsin-Chu, Taiwan*

Contact Dr Hsuan Wang.
E-mail: rom721029@gmail.com

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## Histopathological evaluation of colposcopic biopsies, LLETZ and cold knife cone biopsies of the uterine cervix in post-menopausal women: considerations in the setting of the new Australian cervical HPV DNA screening program

Sir,

The Australian Renewed National Cervical Cancer Screening Program (RNCSP) commenced on 1 December 2017 after several years of thorough planning by several committees of experts, and acceptance of their recommendations by the Medical Services Advisory Committee (MSAC).[1] The RNCSP represents a quantum shift in the approach to cervical cancer screening and was predicated by the introduction in 2007 of the extremely successful Australian National HPV Vaccination Program (NHVP).[2] After the introduction of the NHVP, reduction in the incidence of precursor lesions of cervical cancer in vaccinated women has been reported,[3] and a recent publication[4] predicts that the incidence of cervical cancer in Australia will fall to less than 4 per 100,000 women by the year 2034.

A cervical screening test (CST) in the RNSCP[1] requires cervical brushings to be submitted in liquid-based cytology fixative for human papillomavirus (HPV) DNA testing for most but not all known HPV types associated with the pathogenesis of cervical cancer. The HPV DNA testing is by partial genotyping for HPV-16, HPV-18 (HPV-45 typing optional) and HPV other types (non-16/18). The RNSCP provides guidelines for pathologists reporting CST.[1] Those specimens found to be HPV DNA positive are submitted for reflex liquid-based cytological evaluation (LBC) and appropriate management of the patient is recommended in a combined HPV DNA and LBC report. Patients with 'high-risk' HPV types 16 and 18 are recommended for referral for colposcopy regardless of the LBC findings. Patients with brushings positive for HPV non-16/18 are triaged upon LBC findings. A patient with a high grade intraepithelial lesion (HSIL) or possible HSIL is recommended for referral to colposcopy, while a patient with a low grade intraepithelial