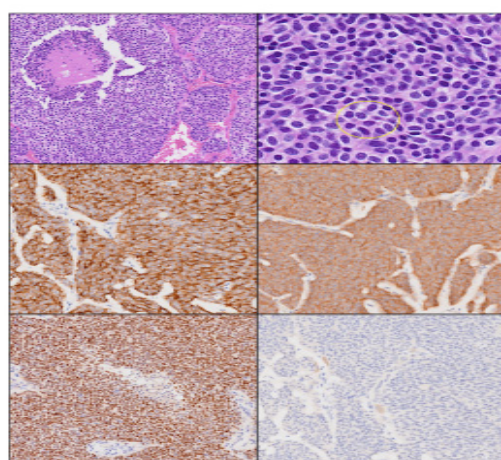


Case reports of atypical thymic carcinoid next gene sequencing analysis

고려대학교 구로병원 내과¹, 고려대학교 구로병원 흉부외과², 고려대학교 구로병원 병리과³안중진¹, 최주환¹, 이준희², 김세희³, 김현구², *이승룡¹

Atypical Thymic Carcinoid (ATC) is a rare thymic neuroendocrine tumor derived from the neuroendocrine system. The incidence of ATC is 0.18 per 1, 000, 000 population, and the total number of ATC throughout the world is little over 100. Patients with ATC were diagnosed while undergoing regular medical checkup. Approximately half of the patients exhibit symptoms of chest pain, dyspnea etc. While the disease tends to be asymptomatic, ATC tends to be undergoing aggressive clinical courses. However, due to low incidence of the disease, information with regards to ATC, such as cause or genetic information, has not been fully understood. The WHO classifies thymic neuroendocrine tumors into low-grade typical carcinoids, intermediate-grade atypical carcinoids, and two high-grade malignancies, large cell neuroendocrine carcinoma and small cell carcinoma. ATCs are well differentiated neuroendocrine carcinomas with increased mitotic count (usually within 2-10 mitotic count per HPF) and presence of necrosis. While the WHO classifies Thymic carcinomas based on such criteria, Dinter et al have shown that such criteria needs to be revised. (Dinter et al. 2019) According to the research, large cell neuroendocrine carcinoma tends to have exceeding mitotic count accepted for ATCs while having carcinoid morphology. This unique characteristic of large cell neuroendocrine carcinomas makes difficult to distinguish it from other types of thymic endocrine tumors. Dinter et al. suggested that including molecular features such as gene copy number variation could help to better distinguish thymic neuroendocrine tumors. Recent study raised the possibility of ATCs progressing into high grade malignant tumors, it is important to investigate the genetic features of the ATCs. However, for its low incidence, little is known about the genetic features of ATCs. In this article, we would like to present 5 cases of patients who have been diagnosed with atypical thymic carcinoids. We also investigated the genetic component of the tumors via conducting Next generation sequencing to better understand the nature of Atypical thymic carcinoids.



Tumor cells are uniform and polygonal and show solid and insular growth pattern (A). Tumor cells have relatively small and round nuclei with finely granular chromatin, inconspicuous nucleoli, and moderate eosinophilic cytoplasm (B). Tumor has foci of comedonecrosis (A, asterisk) and up to 6 mitoses /2mm² (B, yellow circle). Tumor cells are positive for neuroendocrine markers including chromogranin (C), Synaptophysin (D) and INSM-1 (E) but negative for TTF-1 (F). (bar = 50µm)

(A)Comedonecrosis
(B)Mitosis (6/2mm²)
(C)Chromogranin
(D)Synaptophysin
(E)INSM-1
(F)TTF-1

Table 1.

	Age	Sex	Clinical manifestation	Presence of necrosis on biopsy sample	Immunohistochemical pattern	Mitotic count (/10HPF)	Surgical procedure	Chemotherapy regimen	Radiotherapy	Progress Free Survival
Case 1	34	M	none	Present	CD56, Synaptophysin, Chromogranin	2	Thymectomy	Adj Etopo-Cis 4C	Adj RT 60Gy	No recurrence after 2 years of surgery
Case 2	47	M	Shoulder and chest pain	Present	CK, Vimentin, CD56, Synaptophysin, Chromogranin	1	Thymectomy	Adj Etopo-Cis 4C	none	No recurrence after 2 years of surgery
Case 3	60	M	none		CD56, Synaptophysin, Chromogranin	2	Thymectomy	Did not receive CTx	Adj RT 50Gy	No recurrence after 4 years of surgery
Case 4	72	F	none		INSM-1, Synaptophysin, CK, c-kit (focal), Ki-67 index 15%	6	Thymectomy	Adj Etopo-Cis 4C	Adj RT 60Gy	No recurrence after 1 year of surgery
Case 5	60	M	none		CD56, Synaptophysin, Chromogranin	2	Thymectomy		Adj RT 54Gy	Treatment in progress