IMAGING IN THORACIC CANCER

Unique case of combined stage Ia atypical carcinoid, large cell neuroendocrine carcinoma and adenocarcinoma of the lung

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Although the 2004 World Health Organization classification[1] attempted to clarify the role of combined neuroendocrine tumors of the lung, these are yet to be clearly defined. Problems concerning clinical behavior are a result of unclear pathophysiology, the limited number of published cases, and the heterogeneity of histotypes involved.[2] The aggressiveness of these lesions is related to prevailing histopathology and grading (Table 1).

We herein report a singular case of a stage IA combined atypical carcinoid with a large cell neuroendocrine and a lung scar cancer, its clinico-pathological workup, and its correlation with existing data in the literature.

During a diagnostic workup after a car accident in a 65-year-old male smoker (R.T.), a 1.2 cm solitary pulmonary nodule of the right upper lobe was accidentally discovered. The patient had a co-morbidity history of diabetes type 2, cardiovascular diseases, and reported an episode of right-sided pneumonia during his youth. The pre-operative whole body positron emission tomography (PET) scan (Fig. 1A1 and 1A2) showed significant metabolic activity of the primary lesion (SUV 5.3, arrow) in the right upper lobe of the lung, as well as of the multiple rib fractures (SUV 5.5, asterisk). While the computed tomography (CT) guided biopsy was positive for a well-differentiated neuroendocrine tumor, the study of the 1.2 cm lesion (Fig. 1B, 12.5x) from the surgical lung specimen clearly defined a unique combination of three different malignancies. The tumor, partially encased in scar tissue and studied with a panel of immunohistochemical markers (Table 2), showed 60% positivity for atypical carcinoid (AC), 10% for large cell neuro-endocrine carcinoma (LCNEC), and 30% for adenocarcinoma (ADC). The labeling index as determined by hematoxylin-eosin, and Ki67 (MIB1 clone) was for each histotype: AC up to three mitoses per 2 mm^2 and low Ki-67 index (1%); LCNEC large number of mitoses and 70% of Ki-67 index; and the ADC component had an acinar and papillary pattern with a Ki-67 index up to 30%. The systematic nodal dissection performed was negative for metastatic disease (pT1aN0Mx, Stage IA).

The post-operative whole body PET scan (Fig. 1C1 and 1C2) performed seven months later was negative for any radiometabolic tracer uptake at the previous thoracic sites. At the 24 month follow-up from surgery the patient is alive with no evidence of local and/or distant metastases.

Finding three different combined histotypes – two neuroendocrine tumors associated with a NSCLC – is very rare,[3,4] and is usually found in sizeable lesions (Table 1), occasionally represented in a pulmonary scar carcinoma.[5] In this case, we were able to successfully diagnose and treat a unique case of combined aggressive neuroendocrine and NSCLC tumors.

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Disclosure

The authors have no conflicts of interest to disclose.

Table 1 A review of the literature of carcinoid tumor of the lung combined with other malignant tumor

	Author (Year of publication)	Journal	Sex	Age	Smoke	Site	Size mm max	Histotypes	Metastases YES or NO (site, type of tumor)	IHC	Follow-up (months)
1.	Rainosek et Coll. [1994]	Am J Clin Pathol 102:360–64	F	52	YES	LUL	80	AC, RMS	YES (hilar node RMS)	Ker, CEA, Vim, Desm, Myg, CgA	3 NED
2.	Filiz S et Coll. [1998]	Lung Cancer 21:53–58	M	60	YES	LLL (S6)	20	70% AC, 30% ADC	YES (hilar node, ADC)	NSE, CAM 5.2, Syn, Leu-7, CgA	12 NED
3.	Cavazza et Coll. [2001]	Pathologica 93(3):216–20	M	71	YES	RLL(S6)	25	TC, ADC	YES (hilar node, ADC)	CgA, Syn	n/a
4.	Freeman et Coll. [2001]	Int J Surg Pathol 9(2):169–73	F	69	NO	LLL	30	TC, GNB	n/a	CKs, CgA, NF, Leu-7, Syn, S-100P, PP, SOM, GFAP, ACTH	n/a
5.	Rodriguez et Coll. [2003]	Human Pathology 34(10):1061–65	M	70	n/a	RLL	40	TC, ACT	n/a	Try, α-1-aCTry, Amy, CgA, Syn, LIP	n/a
6.	Sano A et Coll. [2011]	Interact Cardiovasc Thorac Surg 12(2);311–2	F	55	YES	RUL(S3)	13	TC, ACT	NO	n/a	31 NED
7.	Owens et Coll. [2011]	Int J Surg Pathol 19(2); 273–5	F	71	YES	LMB	50(*)	TC, SQCC	YES (hilar node, SQCC)	Syn, Ki-67	n/a

AC, atypical carcinoid; ACT, acinar cell tumor; ACTH, adrenocorticotropic hormone; ADC, adenocarcinoma; Amy, amylase; CgA, chromogranin A; CK, cytokeratin; F, female; GFAP, glial fibrillary acid protein; GNB, ganglioneuroblastoma; IHC, Immunohistochemistry; LIP, lipase; LLL, left lower lobe; LMB, left main bronchus; M, male; n/a, not available; NF, neurofilament; NSE, neuron-specific enolase; PP, pancreatic polypeptide; RLL, right lower lobe; RMS, rhabdomyosarcoma; RUL, right upper lobe; SOM, somatostatin; SQCC, squamous cell carcinoma; Syn, synaptophysin; S-100p, S-100 protein; TC, typical carcinoid; Try, trypsin; α-1-aCTry, alpha-1-antichymotrypsin. *(7) the size was evaluated at clinical staging and the patient did not undergo surgery for N3 positive.

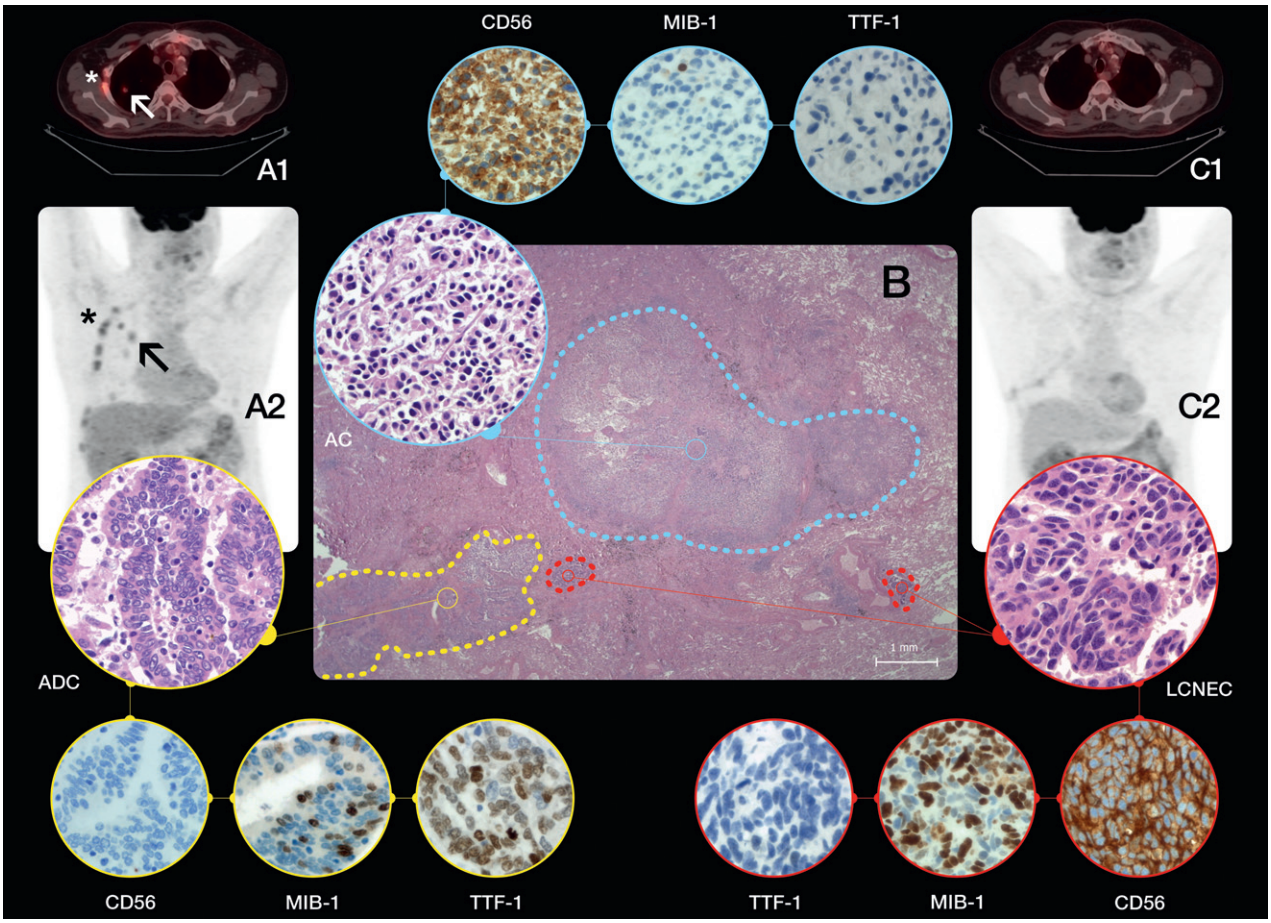

Figure 1 Pre-operative (A1 and A2) and post-operative (C1 and C2) whole body positron emission tomography (PET) scan. Histological study (B) of the 1.2 cm lesion.

Table 2 Antibody panel used in the study

Antibodies	Clone	AC	LCNEC	ADC
Cytokeratin pool	AE1/AE3	+	+	+
Thyroid transcription factor 1	8G7G3/1	–	–	+
CD56	MOC-1	+	+	–
Synaptophysin	SY38	+	+	–
Chromogranin A	LK2H10	+	+	–

AC, atypical carcinoid; ADC, adenocarcinoma; CD, cluster of differentiation; LCNEC, large cell neuroendocrine carcinoma.

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