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Adenocarcinoma arising in an ectopic mediastinal pancreas

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Abstract Pancreatic ectopia in the mediastinum is rare, and there are no reports that it has ever given rise to malignancy. Here we report a case of adenocarcinoma arising in ectopic pancreatic tissue in the mediastinum of a 66-year-old woman. The tumor arose in a partially cystic and partially solid ectopic pancreas containing both exocrine and endocrine components. Thorough clinical examination and clinical follow-up did not reveal other primary sites. The tumor was partially resected but metastasized to the anterior sternum 6 months later and was re-excised. No other similar cases of primary mediastinal pancreatic adenocarcinoma are on record in medical literature.

Keywords: Adenocarcinoma; Ectopic pancreas; Mediastinum

1. Introduction

Pancreatic ectopia in the gastrointestinal tract may be present in 2% of autopsies [1]. However, ectopic pancreatic tissue in the mediastinum is much less common, and fewer than 20 cases have been reported since the original description by Shillitoe in 1957 [2]. In all these cases, the mediastinal pancreatic tissue was composed of normal exocrine and/or endocrine pancreatic elements. No malignant transformation was reported in these cases. However, adenocarcinomas arising from ectopic pancreas along the gastrointestinal tract have been reported [3,4]. We report here a case of primary adenocarcinoma arising in an ectopic mediastinal pancreas. To our knowledge, this is the first case description of adenocarcinoma arising from an ectopic mediastinal pancreas. We discuss the clinicopathologic features of this case and also present a literature review on the previous reports of ectopic pancreas in the anterior mediastinum.

2. Case report

A 66-year-old healthy nonsmoking woman presented in June 2006 with worsening chest pain over the past 6 to 8 months. An outside computed tomographic scan was reviewed to reveal a mass expanding the anterior mediastinum. A provisional diagnosis of thymoma was made and the patient was scheduled for median sternotomy in order to resect the tumor. Intraoperatively, it was noted that the tumor grossly eroded through the posterior aspect of the sternomanubrial junction and involved the pericardium, left phrenic nerve, left mammary artery, and left innominate vein. It was evident that the patient had metastatic carcinomatosis with implants on the pericardium and pleura. These were biopsied, and frozen section was diagnosed as "metastatic adenocarcinoma." Although complete resection was not possible, a debulking procedure was performed due to the local mass effects and compression of surrounding structures. Chemotherapy targeting pancreatic cancer was recommended and administered at an outside institution. Six months later, a new painful sternal mass developed on the anterior aspect of the sternum inferior to the original sternotomy incision. This mass was excised ten months after the original surgery. Grossly, the lesion appeared nodular and necrotic with erosion into the anterior aspect of the sternum. Microscopic examination confirmed that it was an adenocarcinoma similar to the mediastinal primary. This was felt to represent a metastasis due to its location and the fact that it had not been observed in association with the original tumor during the first operation. Thorough clinical

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examination did not reveal a primary pancreatic lesion or any other primary tumor sites. The patient was lost for further follow up at our institution after the resection of the second lesion, and died of unknown causes in September 2007, 15 months after initial presentation.

3. Pathology

Grossly, the tumor appeared red-tan with a smooth glistening surface and was composed of 2 pieces measuring 7.8 × 4.6 × 2.7 cm and 10.8 × 9.1 × 3.7 cm, respectively. The cut surface was partially cystic and partially solid. The cysts contained a brown-tan mucinous material, whereas the cut surface was firm and yellow-tan with associated nodules and adipose tissue. Microscopically the cyst was lined by cuboidal to columnar mixed serous and mucinous cells. Pancreatic islets and exocrine ducts were located within the cyst wall (Fig. 1A). The presence of islet cells was confirmed by strong diffusely positive immunohistochemical staining for chromogranin, neuron specific enolase, and insulin. Areas of dysplastic pancreatic ducts were identified (Fig. 1B). The solid areas contained areas of normal pancreas and extensive areas of infiltrating mucinous adenocarcinoma (Fig. 1C). Immunohistochemical stains showed that the tumor cells were positive for cytokeratins CK7 and CK20 and negative for TTF-1, CA125, and CD5. Thymus was identified in the resected specimen and was focally invaded by the adenocarcinoma (Fig. 1D). The tumor was sampled extensively to rule out the diagnosis of teratoma. Based on the above histologic findings and the fact that the patient did not have a pancreatic mass or other primary tumor sites, the final pathologic diagnosis was “Invasive mucinous adenocarcinoma, arising in a pancreatic cyst of the mediastinum.” One lymph node was

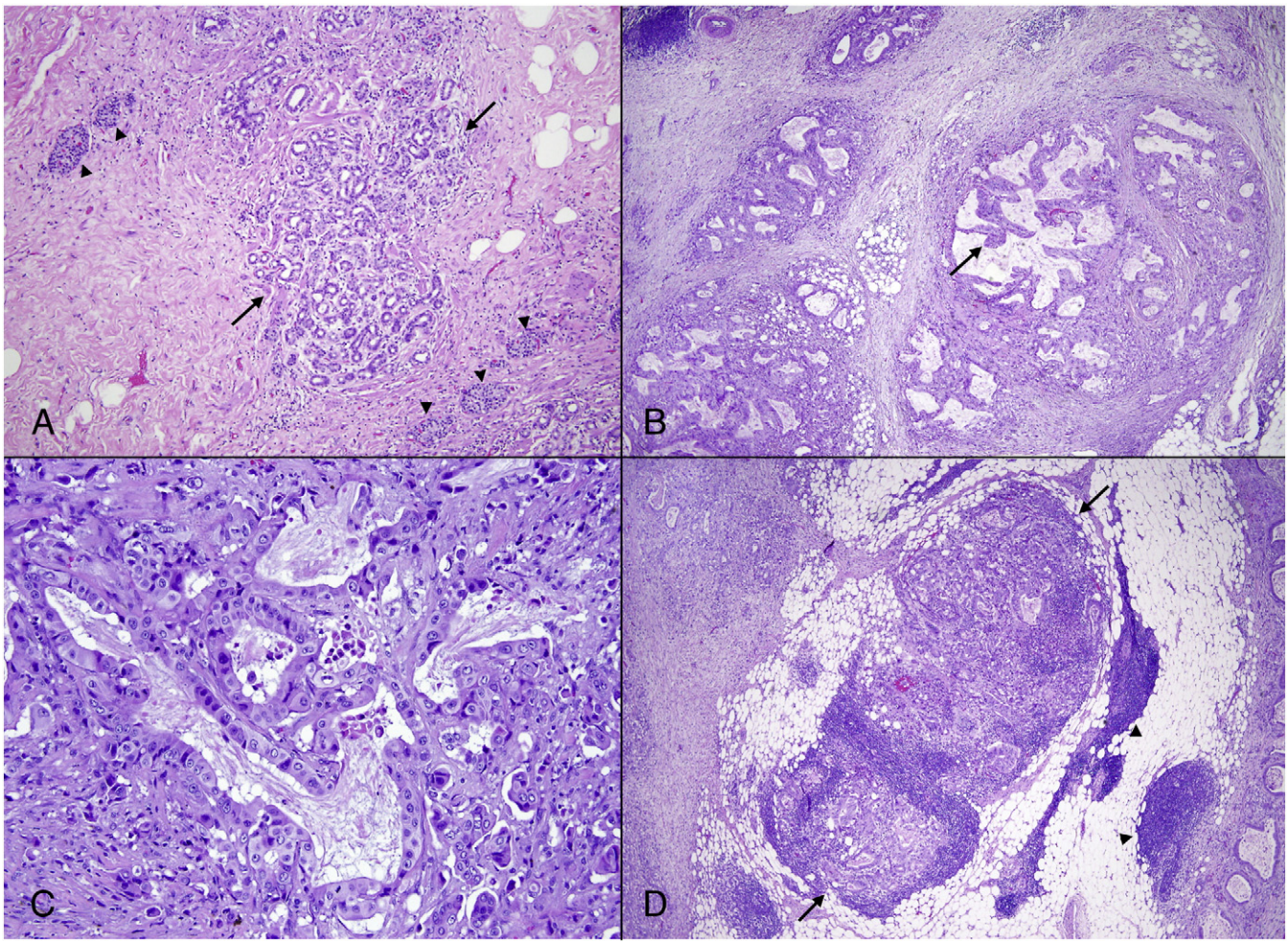

Fig. 1. Pancreatic carcinoma arising in a cystic ectopic pancreas. A, Normal pancreas. Normal pancreatic exocrine ducts are shown at center (arrows), flanked by clusters of pancreatic islets (arrowheads) (hematoxylin and eosin; original magnification ×100). B, Dysplastic exocrine ducts. Ducts are still arranged in nodules but show considerable variation in size and shape with papillary projections into the lumen of a large mucous-filled duct (arrow) (hematoxylin and eosin; original magnification ×100). C, Mucinous adenocarcinoma with hyperchromatic nuclei, apoptosis, necrosis, and profound architectural atypia (hematoxylin and eosin; original magnification ×200). D, Thymus invaded by adenocarcinoma. Areas of fat and normal thymic tissue (arrowheads) near a large focus of invasive adenocarcinoma, which is replacing most of the thymic tissue in this field (arrows) (hematoxylin and eosin; original magnification ×100).

received and was negative for malignancy. The metastatic tumor showed similar morphology.

4. Discussion

Ectopic pancreas in the anterior mediastinum is a unique entity that has been reported fewer than 20 times in the literature since the first acknowledged case described by Shillitoe et al in 1957[2] (Table 1). Several clinical and pathologic conclusions can be derived from those previously reported cases: (1) Clinical presentation is highly variable and usually nonspecific, ranging from heart murmur due to compression of the heart and great vessels by the tumor to lobar pneumonia and shortness of breath, presumably from bronchial obstruction. One emergent case presented with pericardial tamponade due to cyst rupture. (2) The mediastinal lesions are anteriorly located and typically large (>10 cm) and cystic. This most commonly leads to a provisional diagnosis of cystic teratoma; other differentials include cystic thymoma, echinococcosis, ectopic thyroid, abscess, and pericardial cyst. (3) Involvement of adjacent organs (thymus [2,5-7], lung [2,6,8], vasculature [2,9], pericardium [7,10], phrenic nerve [2,11]) is common even in benign cases and should not be interpreted as evidence of a malignant tumor in absence of microscopic evidence of malignancy. (4) The treatment of choice is surgical resection, which usually results in a relief of symptoms and generally excellent outcome.

The histogenesis of pancreatic tissue in the mediastinum is unclear, and several theories have been proposed to explain this phenomenon. (1) One theory is that of heteroplasia—multipotent cells in the ventral wall of the primitive foregut develop into pancreatic endocrine and exocrine elements in response to unknown signals [6,7,12]. (2) Alternatively, it has been suggested that these lesions are variants of enteric (duplication) cysts. Enteric cysts are thought to develop from abnormalities of the notochord and are often associated with vertebral abnormalities. Classically, enteric cysts are lined by gastric mucosa and covered by a muscular wall, and frequently have a patent connection to the stomach or other region of the gastrointestinal tract. The cyst extends to the mediastinum through a natural hiatus (esophageal or aortic) in the diaphragm, and thus, the cyst is usually located posteriorly, not anteriorly, in the mediastinum [10]. (3) It has been suggested that faulty migration of ventral pancreas during development results in ectopically located pancreatic cells in the mediastinum that then proliferate into a cystic mass [12]. In a sense, this would be an analogous situation to an enteric cyst that has lost its patent connection to the foregut, and is arising from the pancreas rather than the stomach. (4) In the present case, we sampled the tumor extensively and saw no evidence of teratomatous elements. Nevertheless, based on the anterior location and the observation that mature teratomas may be composed of a single tissue type (eg, thyroid in struma ovarii or skin elements in a dermoid cyst) it has been suggested that these pancreatic cysts in fact represent unilateral differentiation of a teratoma into pancreatic tissues [6]. We favor the theory of heteroplasia over that of an enteric cyst or displaced ventral pancreatic bud because of the anterior location. In addition, were teratomas the origin, we would hope to see a spectrum of

Table 1
Clinical features of 16 cases of ectopic mediastinal pancreas (including present case)

Reference, y	Age	M/F	Symptom	Size (cm)	Treatment	Follow up
Shillitoe [2], 1957.	15	F	SOB, joint pains, night sweats, fatigue	5.5 at least (fragmented)	Surgery	No recurrence
Carr [6], 1977	57	F	none	10	Surgery	–
von Schweinitz [7], 1990	5	M	Chronic pneumonia	3 × 3 × 3	Surgery	No recurrence
Perez-Ordonez [1], 1996.	16	F	Heart murmur	12	Surgery	No recurrence (2 y)
Gong [15], 1997.	26	F	Chest pain, cough	20 × 15	Surgery	–
Gong [15], 1997	26	F	Chest pain	4.3 × 1.5	Surgery	–
Wu [16], 1998	60	F	Chest pain	10 × 5	Surgery	–
Cagirici [9], 2001	45	F	Cough, chest pain, headache	10	Surgery	No recurrence (2 y)
Iglesias Sentis [10], 2004	44	M	sudden epigastric and chest pain, SOB	10 × 8 × 7.5	Surgery	No recurrence
Tamura [8], 2005	39	M	Chest pain	10 × 8	Surgery	No recurrence (8 years)
Al-Salam [5], 2006	40	M	Fever, neck swelling, dyspnea	8 × 6 × 6	Surgery	–
Wang [17], 2007	17	F	Chest pain, SOB	12.5 × 12.0 × 4.5	Surgery	–
Wang [17], 2007	24	F	Chest pain, SOB	10.0 × 8.0 × 4.0	Surgery	–
Chen [12], 2009	32	F	None	16.0 × 13.0 × 8.0	Surgery	No recurrence (3 mo)
Ehricht [11], 2009	25	M	Lobar pneumonia	15 × 15	Surgery	No recurrence (6 mo)
Present case	66	F	Chest pain	10.8 × 9.1 × 3.7 and 7.8 × 4.6 × 2.7	Surgery	Metastatic adenocarcinoma 6 months after resection, died 15 months after resection

M indicates male; F, female; SOB, shortness of breath.

lesions with other elements in progression to this fully differentiated state (ie, 50% pancreas, 50% teratoma; or 90% pancreas, 10% teratoma). Nevertheless, further study is necessary to elucidate the histogenesis of these lesions.

Adenocarcinoma of the anterior mediastinum is most commonly due to metastasis; common primary tumor sites include lung, kidney, and gastrointestinal tract. Primary mediastinal mucinous adenocarcinomas are rare, and the only documented examples are case reports of thymic carcinomas or malignant teratomas [13,14]. We publish this case to document an unreported entity of primary adenocarcinoma arising from mediastinal ectopic pancreas. The histologic findings demonstrate benign mucinous epithelium and dysplastic epithelium in the cystic exocrine part of the ectopic pancreas admixed with endocrine islets, in transition to solid areas of invasive mucinous adenocarcinoma. Tumor cells are positive for CK7 and CK20, resembling the keratin expression pattern of primary pancreatic adenocarcinoma. We feel that the diagnosis of primary adenocarcinoma arising from ectopic pancreas should follow the same criteria as for primary thymic carcinomas in the mediastinum [13] and include (1) main tumor mass located in anterior mediastinum and (2) no evidence of a possible primary tumor elsewhere.

In summary, we have discussed a unique case among unique cases, in which ectopic pancreas in the anterior mediastinum gave rise to pancreatic adenocarcinoma which metastasized to the anterior sternum 6 months after surgical resection of the primary tumor. Ectopic pancreas in the anterior mediastinum is a unique entity that is important to recognize because of the possibly severe consequences that result (pneumonia, pericardial tamponade, adenocarcinoma), the recurrence of effusions, shortness of breath, pneumonia after aspiration due to exocrine pancreas activity, and the fact that prognosis is extremely favorable when managed surgically. Clinical, laboratory, and imaging studies are nonspecific and histopathological analysis following resection is required to distinguish the pancreatic origin of the lesion from other possibilities such as a cystic thymoma or cystic teratoma and make a definitive diagnosis. Being aware of the rare occurrence of primary mucinous adenocarcinoma in anterior mediastinum from ectopic pancreas may help avoid misdiagnosis, patient over-stage and unnecessary extensive clinical workup.

References

[1] Perez-Ordonez B, Wesson DE, Smith CR, et al. A pancreatic cyst of the anterior mediastinum. Modern Pathol 1996;9:210-4.

[2] Shillitoe AJ, Wilson JE. Enterogenous cyst of thorax with pancreatic tissue as a constituent. J Thorac Surg 1957;34:810-4.

[3] Goodarzi M, Rashid A, Maru D. Invasive ductal adenocarcinoma arising from pancreatic heterotopia in rectum: case report and review of literature. Hum Pathol 2010;41:1809-13.

[4] Guillou L, Nordback P, Gerber C, et al. Ductal adenocarcinoma arising in a heterotopic pancreas situated in a hiatal hernia. Arch Pathol Lab Med 1994;118:568-71.

[5] Al-Salam S, Al Ashari M. Ectopic pancreatic tissue in the anterior mediastinum. Virchows Arch 2006;448:661-3.

[6] Carr MJT, Deiraniya AK, Judd PA. Mediastinal cyst containing mural pancreatic tissue. Thorax 1977;32:512-6.

[7] von Schweinitz D, Wittekind C, Freihorst J. Mediastinaler sequester mit ektopem Pankreasgewebe [Mediastinal sequestration with ectopic pancreas]. Z Kinderchir 1990;45:249-50 [German].

[8] Tamura Y, Takahama M, Kushibe K, et al. Ectopic pancreas in the anterior mediastinum. Jpn J Thorac Cardiovasc Surg 2005;53:498-501.

[9] Cagirici U, Ozbaran M, Veral A, et al. Ectopic mediastinal pancreas. Eur J Cardio-Thorac 2001;19:514-5.

[10] Sentis MI, Sanchis JB, Garolera JMG, et al. Mediastinal enteric cyst: unusual clinical presentation and histopathology. Arch Bronconeumol 2004;40:185-7 [Spanish].

[11] Ehricht A, Putzschler F, Weissmann K, et al. Ektopes Pankreasgewebe in einer Mediastinalzyste - eine seltene klinische Manifestation. [Ectopic pancreatic tissue within a mediastinal cyst—a rare clinical manifestation]. Zentralbl Chir 2009;134:178-81 [German].

[12] Chen ZH, Yu RS, Dong F, et al. CT findings of an ectopic pancreas in the anterior mediastinum. Korean J Radiol 2009;10:527-30.

[13] Ra SH, Fishbein MC, Baruch-Oren T, et al. Mucinous adenocarcinomas of the thymus: report of 2 cases and review of the literature. Am J Surg Pathol 2007;31:1330-6.

[14] Weidner N. Germ-cell tumors of the mediastinum. Semin Diagn Pathol 1999;16:42-50.

[15] Gong N, Fang G. Ectopic pancreas in within thorax: two cases reports. Chin J Thorac Cardiovasc Surg 1997;13:308 [Chinese].

[16] Wu J, Chen Y, Ni X. Ectopic pancreas in anterior mediastinal with pseudo-cyst: one case report. Chin J Thorac Cardiovasc Surg 1998;14:214 [Chinese].

[17] Wang W, Li KC, Qin W, et al. Ectopic pancreas in mediastinum—report of 2 cases and review of the literature. J Thorac Imag 2007;22:256-8.