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CASE REPORT

Acinar cystic transformation in the pancreatic tail

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Abstract
Pancreatic acinar cystic transformation (ACT) is a rare non-neoplastic cystic lesion that is predominantly located at the pancreatic head in females. Preoperative definitive diagnosis of ACT remains challenging despite advances in radiologic imaging methods. A 25-year-old male patient presented with abdominal discomfort and a 50-mm cystic lesion in the pancreatic tail. The patient underwent laparoscopic distal pancreatectomy, because branch duct intraductal papillary mucinous neoplasm cannot be ruled out and the presence of abdominal symptoms. The resected specimen revealed a collection of small and large cysts lined by a single cuboidal epithelium layer with scattered pancreatic tissue exhibiting fibrosis in the septal wall. The cystic lesion was epithelial, trypsin-positive, B cell lymphoma 10-positive, cytokeratin 19-positive, mucin 1-positive, and MUC6-negative with a differentiated lobular central conduit causing to an adeno-cystic cell, thereby supporting the ACT diagnosis. Distinguishing ACT from other pancreatic cystic tumors remains a diagnostic challenge despite improvements in radiologic imaging methods. Surgical resection may be justified when other cystic neoplasms cannot be excluded because of its heterogeneous nature, although the ACT is a non-neoplastic lesion, and cases of malignant transformation have never been reported to date.

Keywords Acinar cystic transformation · Pancreatic cystic tumors · Pancreatectomy · Immunohistochemical staining

Introduction

The common pancreatic cystic neoplasms comprise intraductal papillary neoplasm (IPMN), mucinous cystic neoplasm (MCN), and serous cystic neoplasm (SCN). Pancreatic acinar cystic transformation (ACT) is a rare non-neoplastic cystic lesion that is difficult to differentiate from the aforementioned neoplastic cystic lesions. The exact etiology of ACT remains unclear. A case was originally reported as "acinar cell cystadenoma (ACA)" in 2002 [1], and the term gradually evolved to ACT due to its non-neoplastic nature. The 2010 World Health Organization classification categorized ACA as a benign lesion, and the 2019 fifth edition reclassified ACT as a non-neoplastic cystic lesion. Several case reports have been published since then, all of which reported no neoplastic features during follow-up, suggesting ACT as not a benign counterpart of acinar cell cystadenocarcinoma [2]. ACT is desirable to diagnose using radiological or ultrasound imaging, because it is non-neoplastic, but imaging diagnosis is challenging [3]. Recent advancements in radiologic imaging technology have improved the detection rate of pancreatic cysts, highlighting the importance of correctly identifying rare diseases, such as ACT. Understanding the clinicopathologic features of ACT is crucial for appropriate clinical and surgical management and follow-up. Typically, surgical resection is performed to alleviate symptoms or to exclude other cystic neoplasms associated with malignancy, and diagnosis is made on a pathology specimen. Pathological features, such as positive periodic acid stain (PAS), KRT7, KRT19, trypsin, cytokeratin 19 (CK19), and B cell lymphoma (BCL)10, among others, are essential for diagnosis [2, 4]. Recent studies using next-generation sequencing have revealed ACT as a heterogeneous entity that may encompass a spectrum of lesions with different etiopathogenesis [5]. The surveillance of ACT continues to

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be controversial, and careful examination of each case is important. Here, we present a case of a male patient with a large cystic lesion in the pancreatic tail diagnosed as ACT after pancreatic resection. Distinguishing between the various types of pancreatic cystic lesions has important prognostic and therapeutic implications.

Case report

A 25-year-old male patient without any significant medical history presented with abdominal distension and upper abdominal pain. A cystic lesion measuring approximately 50 mm in size was identified in the pancreatic tail upon referral to our hospital, raising suspicions of either IPMN or solid pseudo-papillary neoplasm. Subsequent contrast-enhanced computed tomography (CT) scans revealed the presence of a cystic lesion larger than 50 mm in size at the pancreatic tail, with no discernible mural nodule (Fig. 1). Further examination with magnetic resonance imaging (MRI) revealed the presence of a limited number of dilated lumens in the pancreatic tail, as opposed to a multifocal cyst. Notably, cyst wall enhancement or main pancreatic duct dilation was not observed. T1-weighted and diffusion-weighted images exhibited low signal intensity, while T2-weighted images showed high signal intensity, with no detectable enhancement component (Fig. 2). Endoscopic ultrasound (EUS) revealed the presence of a multifocal cyst measuring approximately 50 mm in the pancreatic tail, with no apparent septal wall thickening or pancreatic duct communication. The cysts varied in size, and main pancreatic duct communication or dilation was not detected during EUS (Fig. 3). Fluorodeoxyglucose–positron emission tomography scans revealed no significant lesion accumulation and no suspicious findings of metastasis. Cytology or biopsy was not performed because of the risk of seeding from puncturing cystic lesions. Imaging studies did not reveal any microcyst-like structures suggestive of SCN, and the lesion was deemed to have the morphology of a limited number of dilated lumens, leading to a primary suspicion of branched IPMN, although the absence of obvious pancreatic duct communication was atypical.

Surgical resection was recommended for this patient due to his age and the tumor size, if it was considered branch duct IPMN, based on the pancreatic IPMN management guidelines [6]. Hence, we proposed surgical resection, and written informed consent was obtained from the patient.

The patient underwent laparoscopic distal pancreatectomy and splenectomy. Intraoperative ultrasonography was used to determine the cut line, which revealed no evidence of mural nodules. The postoperative course was uneventful, and the patient was discharged on postoperative day 13. The patient's abdominal discomfort was resolved postoperatively.

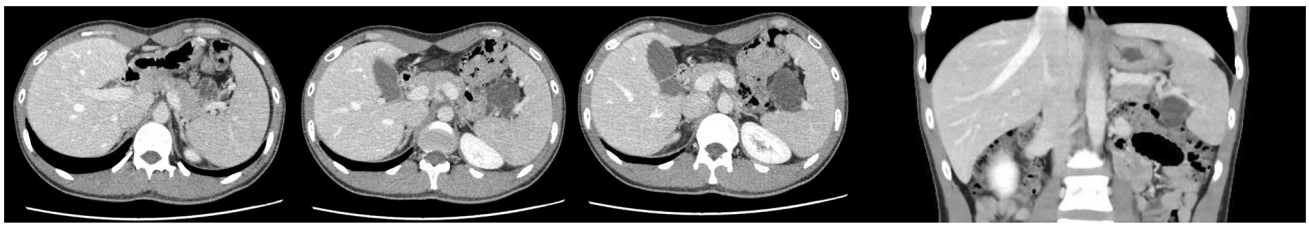

Fig. 1 Contrast-enhanced computed tomography (CT) revealed a cystic lesion larger than 50 mm in size at the pancreatic tail, without any noticeable mural nodules

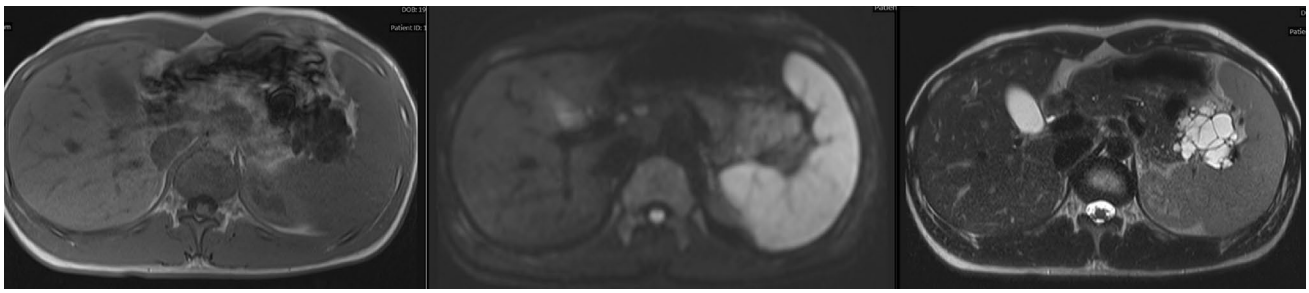

Fig. 2 Magnetic resonance imaging (MRI) revealed a few dilated lumens within the pancreatic tail, as well as cysts of various sizes located within a larger cyst. Enhancement was not observed in the cyst wall, and dilation of the main pancreatic duct was not detected. TI-weighted and diffusion-weighted images revealed a low signal, whereas T2-weighted images revealed a high signal, with no detectable enhancement component

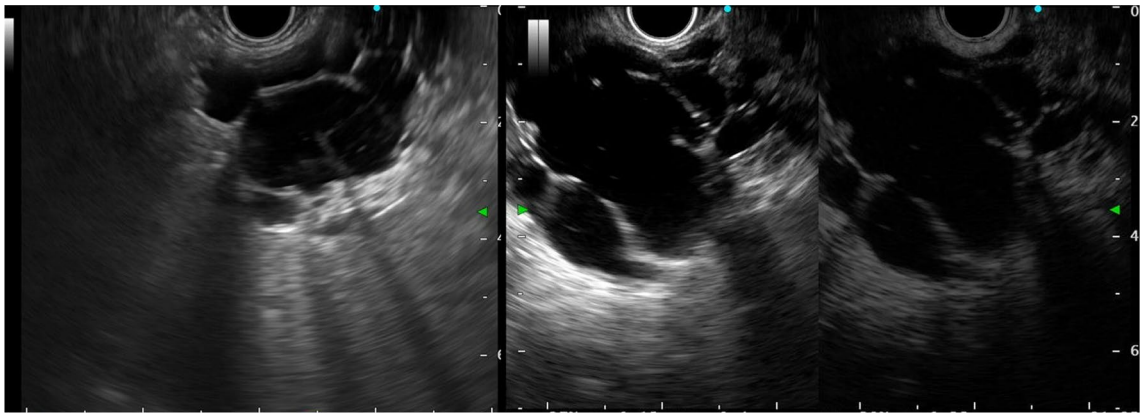

Fig. 3 Endoscopic ultrasound (EUS) revealed a multi-sized, multifocal cyst of approximately 50 mm in the pancreatic tail. The septal wall did not display any thickening, and the cysts varied in size. Furthermore, there was no main pancreatic duct communication or dilation

Gross examination of the resected specimen revealed multiple cysts up to 30 mm in diameter in the pancreatic tail, filled with pale yellow serous fluid (Fig. 4). Microscopic examination revealed a collection of small and large cysts lined by a single cuboidal epithelium layer with minimal atypia. In addition, pancreatic tissue with fibrosis was scattered in the septal wall (Fig. 5). Immunohistochemical analysis demonstrated trypsin, BCL10, CK19, and MUC1 positive lesions (Fig. 6). Conversely, alpha-inhibin, MUC6, MUC5AC, PgR, and GLUT-1 were negative. The lesion was identified as an epithelioid cystic lesion, demonstrating the differentiation from a lobular central conduit to an adenocyst. ACT was diagnosed based on a comprehensive evaluation.

One year has passed since resection, and no tumor recurrence or symptoms have been observed.

Discussion

ACT, which was previously referred to as ACA, represents a scarce cystic pancreatic lesion. Consequently, a limited number of case series have been documented, and their fundamental characteristics remain obscure. The most comprehensive literature review available revealed ACT as commonly observed in the female gender (female to male ratio: 2.4:1), with an average age of 44.8 years (range: 9–68 years), and is typically located in the pancreatic head in 50% of cases [2]. The current case showed an ACT in the pancreatic tail of a

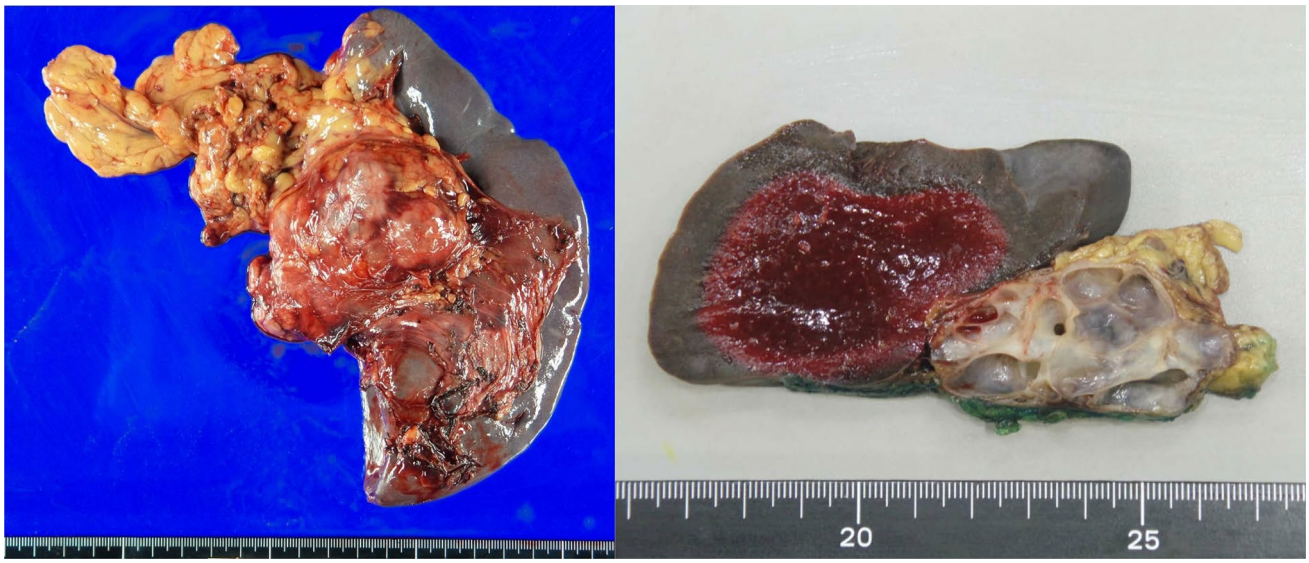

Fig. 4 Gross examination of the resected pancreatic tail revealed multilocular cysts, with diameters of up to 30 mm, filled with pale yellow transparent serous fluid

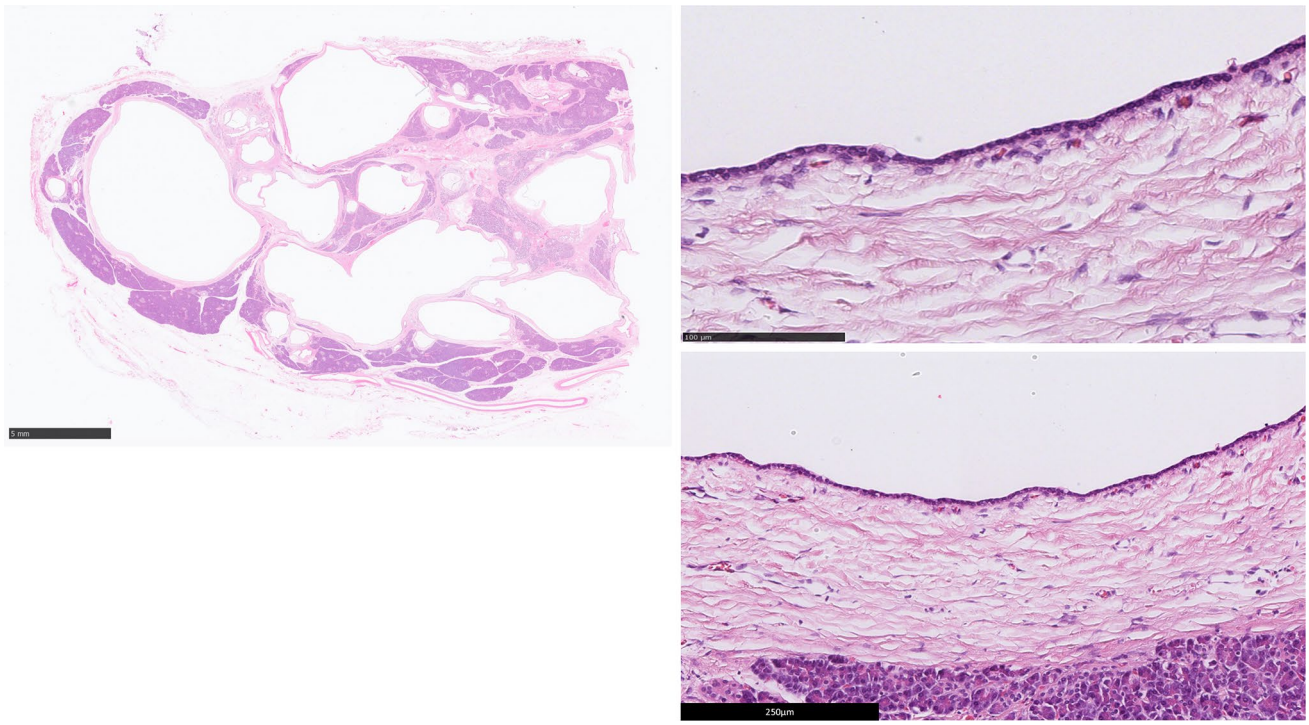

Fig. 5 Microscopic examination revealed that the cystic wall was lined with a monolayer of cuboidal epithelium that exhibited poor atypia and no mucus accumulation. Pancreatic tissue with fibrosis was scattered throughout the septal wall. Scale bar 5 µm, 100 µm, and 250 µm

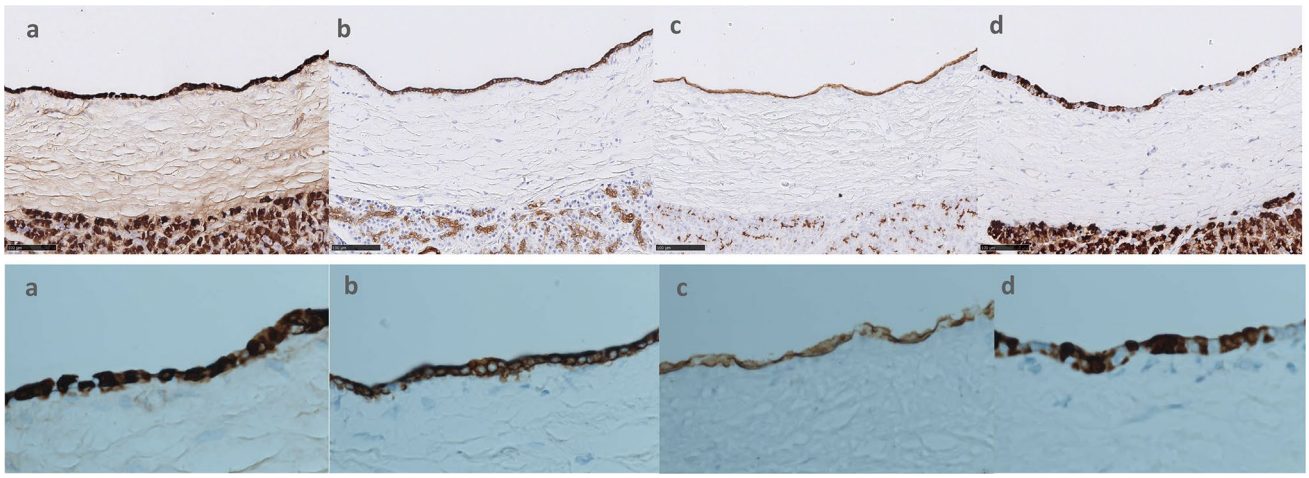

Fig. 6 Immunohistochemically, the lesion exhibited positive results for trypsin (**a**), BCL10 (**b**), CK19 (**c**), and MUC1 (**d**). Scale bar 100 µm

youthful male, which is a comparatively infrequent occurrence. Abdominal discomfort has been identified as the most commonly reported symptom. Cysts are typically discovered at the pancreatic head. Their dimensions usually range from 5 to 197 mm, with an average size of approximately 50 mm. In addition, primary pancreatic duct communication was observed in only 16% of instances. Gross examination identified ACT as multilocular in 59% and unilocular in 41% of cases [2]. The radiologic characteristics are delineated as follows: US exhibits multilocular cystic lesion without any mural nodule or solid component; CT reveals analogous cystic lesions, frequently lacking contrast effect; MRI demonstrates low signal intensity on T1-weighted images and high signal intensity on T2-weighted images. Pancreatic cystic ailments, such as pseudocysts, IPMN, MCN, and SCN, are among the differential diagnoses, but preoperative diagnosis remains arduous. Delavaud C et al. aimed to distinguish between ACA and BD–IPMN by employing CT and

Table 1 Immunohistochemical staining of the pancreatic cystic tumors

Targeted differential cells	Staining	Our case (ACT)	IPMN	SCN	MCN
Acinar cells	Trypsin	+	−	−	−
Acinar cells	BCL10	+	−	−	−
Pancreatic duct epithelium	CK19	+	−	−	−
Pancreatic acinar central cells	MUC1	+	+	−	−
Gastric pyloric grand	MUC6	−	+	+	+
Gastric orbital epithelial cells	MUC5AC	−	+	−	−
Gonad-associated cells	Alpha-inhibin	−	−	+	+
Gonad-associated cells	PgR	−	−	−	+

MRI regarding branch duct (BD)–IPMN, which necessitates the most meticulous discrimination in ACT diagnosis [3]. Four radiological criteria enable the differentiation of ACA from IPMN: the presence of five or more cysts, clustered peripheral small cysts, cyst calcifications, and the absence of communication with the main pancreatic duct. The presence of at least two or three of these imaging criteria confers a strong diagnostic value for ACC. Attempts at biopsy or cytology are infrequent because of the cystic nature of the lesion. However, a cyst wall biopsy was performed using Moray® micro forceps in one successful preoperative diagnosis case [7]. Preoperative attempts to achieve a conclusive diagnosis are rare, and a definitive diagnosis is commonly established through surgical specimens. The other three criteria proposed by Delavaud C et al. were satisfied in our case, which could raise suspicion for ACT, although there was an absence of cyst calcification. However, eliminating other cystic tumors remained challenging, thereby rendering the decision to forego surgery a daunting task.

Microscopically, ACT is defined by numerous cysts of diverse sizes. These findings are recognized as non-neoplastic pathologies, because the cysts are coated by segments of acinar and ductal epithelium, yet they do not exhibit cytologic atypia, mitoses, necrosis, or infiltrative growth [8]. Immunohistochemical staining proves as a valuable tool in distinguishing ACT from other neoplastic cystic lesions, such as IPMN, SCN, and MCN. The acinar component stains positively for trypsin or chymotrypsin. Meanwhile, BCL10, CK19, and MUC1 are predominantly positive in ACT, whereas α-inhibin and neuron-specific enolase (NSE) yielded negative results [2, 4]. MUC5AC, MUC2, MUC6, CDX2, and MUC1 are valuable in distinguishing between IPMN and ACT subtypes [2]. Keratins (KRT 7, 8, 18, and 19), α-inhibin, MUC6, and typically, NSE exhibit a positive staining pattern, whereas trypsin is consistently negative in cases of SCN [4]. Table 1 delineates the differential diagnosis, based on immunostaining, between the pancreatic cystic disease under study and other comparable entities.

Previous literature indicated that ACT has no potential for malignant transformation [9–11], thus caution should be exercised regarding surgical indications. However, surgical treatment and definitive diagnosis may be acceptable because of the diagnosis difficulty based on biopsy, the large cyst diameter and their symptomatic nature, and the difficulty in differentiating them from other cystic neoplasms. A recent study by Luchini et al. demonstrated an intriguing histomorphological and molecular analysis, aimed at elucidating the true nature of ACT. The researchers used next-generation sequencing techniques, revealing the presence of two pathogenic/likely pathogenic mutations in two distinct cases—one with ductal-like epithelium and the other with pancreatic intraepithelial neoplasia. These findings suggest that ACTs are benign in nature and may originate from a heterogeneous array of conditions/backgrounds, including acinar microcysts, malformations, obstructive/inflammatory settings, genetic predispositions, and potentially neoplastic origins [5]. ACT can undergo neoplastic transformation due to the presence of driver mutations. long-term follow-up may be necessary and further studies involving the accumulation of cases are warranted until the true nature of ACT is fully elucidated.

In summary, the ACT is benign lesions that should be considered in the differential diagnosis of pancreatic cystic lesions. Immunohistochemical stains can help distinguish ACTs from malignant lesions. However, preoperative diagnosis is essential to avoid unnecessary surgical treatment. Accurate diagnosis is crucial for appropriate treatment planning, and establishing criteria for surgical indications based on the accumulation of cases would be advantageous.

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Declarations

Conflict of interest The authors declare no conflicts of interest.

Ethical approval We conducted our study in accordance with the Declaration of Helsinki.

Informed consent Written informed consent was obtained from the patient for the publication of this manuscript. All identifying informa-

tion, aside from age and sex, was removed, and the images provided were anonymized to protect patient confidentiality.

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