

MACROCYSTIC SEROUS CYSTADENOMA OF PANCREAS — A Case Report —

Joo Ryung Huh, M.D., Je G. Chi, M.D., Kyung Chon Jung, M.D.,
Kuk Jin Choe, M.D.* Yong Beom Yoon, M.D.**

Departments of Pathology, Surgery, Internal Medicine**
Seoul National University*

The macrocystic variant of serous cystadenomas of the pancreas has only recently been described. We present a case of a 40 year-old female, who presented with vague indigestion. The cyst was unilocular, and was lined by simple cuboidal, ciliated serous type epithelium. Fine needle aspiration, immunohistochemical, light microscopic, and electron microscopic studies are discussed.

Key Words : *Macrocystic, Serous, Cystadenoma, Pancreas*

INTRODUCTION

Since Compagno and Oertel published their landmark article in 1978 reporting 34 cases of serous cystic neoplasms of the pancreas, microcystic adenomas with their highly characteristic pathologic findings and almost uniformly benign nature, have been equated with serous cystadenomas of the pancreas (Compagno & Oertel, 1978; Saavedra-Albores et al., 1990; Cubilla & Fitzgerald, 1979; Cubilla & Fitzgerald, 1980; Cubilla & Fitzgerald, 1983; Zamora et al, 1984). The resulting nosologic connotation is that all serous adenomas of the pancreas are of microcystic type and macrocystic or unilocular serous neoplasm of the pancreas does not exist. A recently published article has described macrocystic variants of these benign serous cystadenomas (Lewandrowski et al., 1992). We present a case which was complicated by co-existing omental cysts.

REPORT OF A CASE

A 50-year old Korean female was referred to our

hospital for further evaluation of a large, cystic mass in the head of the pancreas, detected on a computerized tomogram of the abdomen (Fig. 1). She had complained of vague indigestion and constipation for two months. She denied any history of alcoholic intake or bouts of pancreatitis. No history of other tumors was obtained. No evidence of von Hippel-Lindau syndrome was present. Physical examination revealed an 11cm. long, cystic mass with smooth outline in the right upper quadrant. There was no pain or tenderness. Percutaneous needle aspiration of the cyst yielded a copious amount of brownish serous fluid containing amorphous debris. Amylase content was 104 IU/L. CEA was 1.0ng/ml. No malignant cells were noted. Preoperative differential diagnosis included pseudocyst and mucinous cystic neoplasm. At the time of surgery, the cyst was in the head of the pancreas, measured 11cm. in diameter, and was adherent to the second portion of the duodenum. Two additional cysts were found in the omentum, each measuring 3cm. and 1cm. in diameter. Intraoperative frozen sections of the pancreatic cyst showed flat cuboidal epithelium with clear cytoplasm. A diagnosis of a probably benign serous cystadenoma was rendered. Frozen sections from one omental cyst showed only fat necrosis and inflammation. Therefore, it was determined that the omental lesions did not represent metastatic foci, and the pancreatic cyst was a be-

Address for correspondence : Joo Ryung Huh M.D., Department of Pathology, Seoul National University Hosp 28 Yondan-dong, Chongno-gu, Seoul, 110-744 Korea.

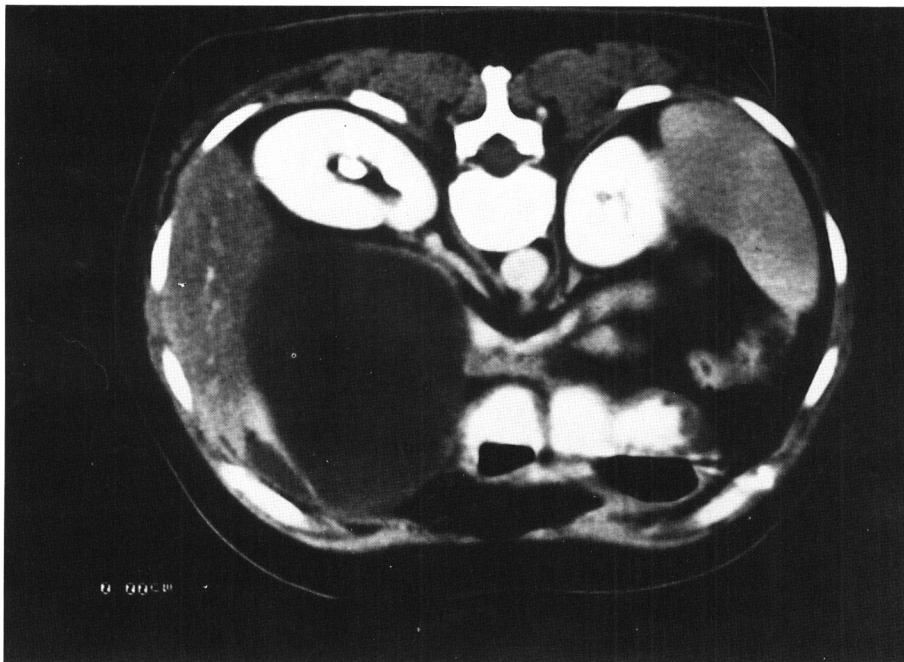


Fig. 1. Abdominal CT scan showing a unilocular cyst in the head of the Pancreas.

nign process. Enucleation of the pancreatic cyst and resection of the omentum bearing the cysts were performed. Postoperatively, the patient developed pancreatic fistula, but eventually recovered. She was well when seen at the out patient clinic two months later.

MATERIALS AND METHODS

Fine needle aspiration biopsy was performed under computed tomographic guidance. The aspirated material was smeared onto glass slides, immediately fixed in 95% alcohol and stained with the Papanicolaou method.

The tissues from the enucleated cyst were fixed in buffered formalin solution, embedded in paraffin and sectioned at 6 microns. Sections for histologic examination were stained with hematoxylin and eosin (H & E) and periodic acid-Schiff with or without diastase. Immunohistochemical stains were performed with an avidin-biotin peroxidase method using mouse monoclonal antibodies on the formalin-fixed, paraffin-embedded tissue.

For electron microscopic study, the tissue already

embedded in paraffin was recovered, minced into thin, 1-mm blocks, fixed in 2% phosphate buffered glutaraldehyde, post-fixed in 1% osmium tetroxide, dehydrated in graded alcohols, and embedded in Epon. Following examination of a 1 micrometer section with a light microscope, suitable blocks were selected for ultrathin sections. The thin sections were stained with uranyl acetate followed by lead citrate, examined and photographed with a Hitachi 500 electron microscope.

RESULT

The FNA yielded brownish watery, non-viscid, faintly cyanophilic fluid with abundant amorphous debris and numerous red blood cells (Fig. 2). The background material did not have the fine parallel fibrillary structure of mucin. Rare clusters of large cells in monolayered sheets with a honeycombing pattern, and with abundant, faintly granular to clear cytoplasm with no mucin vacuoles were present (Fig. 3). The nuclei were small and nucleoli were inconspicuous. Neither intranuclear inclusions nor nuclear grooves were present. The main problem

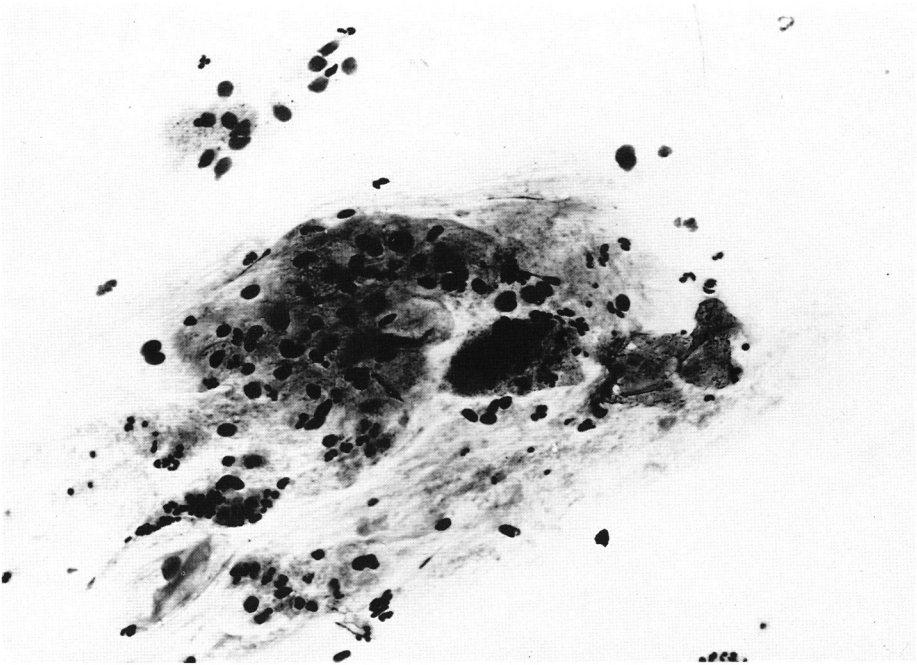


Fig. 2. Fine needle aspiration smear showing rare epithelial cell clusters in a background of amorphous debris.



Fig. 3. Fine needle aspiration smear showing honey-combed clusters of large epithelial cells with finely granular to clear cytoplasm.



Fig. 4. Gross photograph showing unilocular cyst with smooth lining.

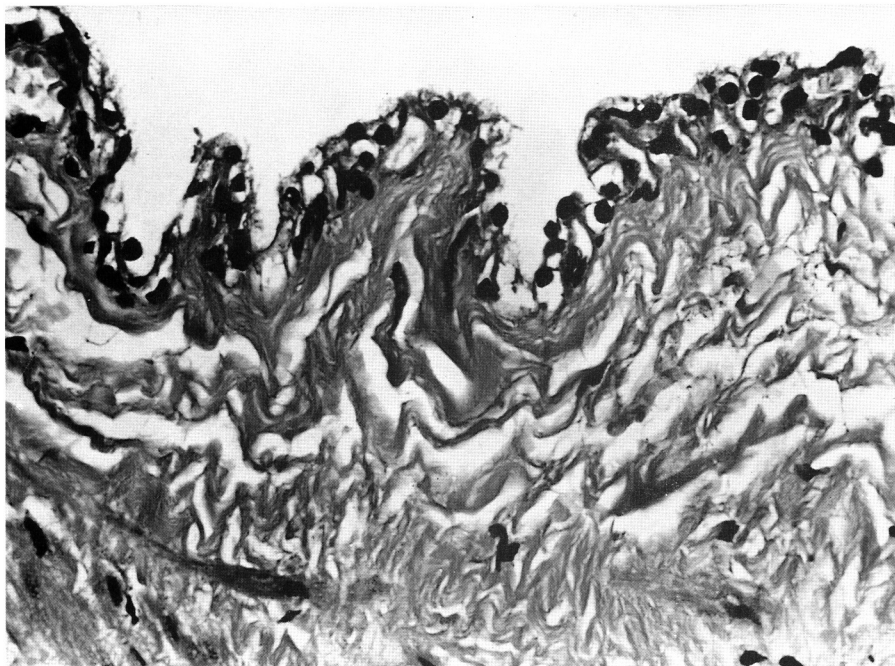


Fig. 5. H&E section showing simple, cuboidal, serous epithelium.



Fig. 6. H & E section of the omental cyst showing mesothelial lining.

was to differentiate them from the macrophages. Unlike macrophages, these cells had an epithelial arrangement and did not contain any phagocytosed material.

The gross examination of the specimen showed a well defined unilocular cyst. The external surface was irregular with attached pancreatic tissue. The cyst measured 0.1cm. in thickness. The lining of the cyst was mostly smooth but focally showed trabeculation. No communication with major ductal structures of the pancreas was noted (Fig. 4). Microscopically, the cyst was lined by simple, cuboidal serous epithelium, with small, central round to oval nuclei and clear to faintly eosinophilic cytoplasm, as typically seen in microcystic serous cystadenomas (Fig. 5). No pleomorphism, mitotic figures or prominent nucleoli was observed. No papillae or foci of mucinous epithelium was seen. Periodic acid-Schiff reaction revealed positive staining, granular material in the cytoplasm of these cells, and also diffuse staining in the luminal content, both of which were removed with diastase treatment. No myoepithelial cells were noted. Beneath the lining epithelium, loose connective tissue of variable thickness was present, while in areas, thick, hyalinized collagenous

tissue was present especially where atrophic pancreatic tissue was noted. No calcification was present. The lining was extensively denuded. In fact, only the frozen section block contained epithelium, and more than twenty sections taken after fixation revealed no lining epithelium. The omental cyst measured 2cm. and had a smooth external surface and a membranous lining, and microscopically, was lined by markedly flattened epithelium which did not show any glycogen on PAS stain, consistent with mesothelium (Fig. 6).

Immunohistochemical stains showed positive staining with epithelial membrane antigen, low molecular weight cytokeratin, but negative staining reactions with factor VIII antigen, vimentin or carcinoembryonic antigen.

Ultrastructural study showed cuboidal lining cells (Fig. 7). Short, poorly developed, irregularly spaced microvilli were present at the luminal border. The nuclei were oval to round, the chromatin pattern was rather clumped. The cytoplasmic organelles were sparse. Membrane bound dense granules as reported by Lo *et al.* (1977) were not present.

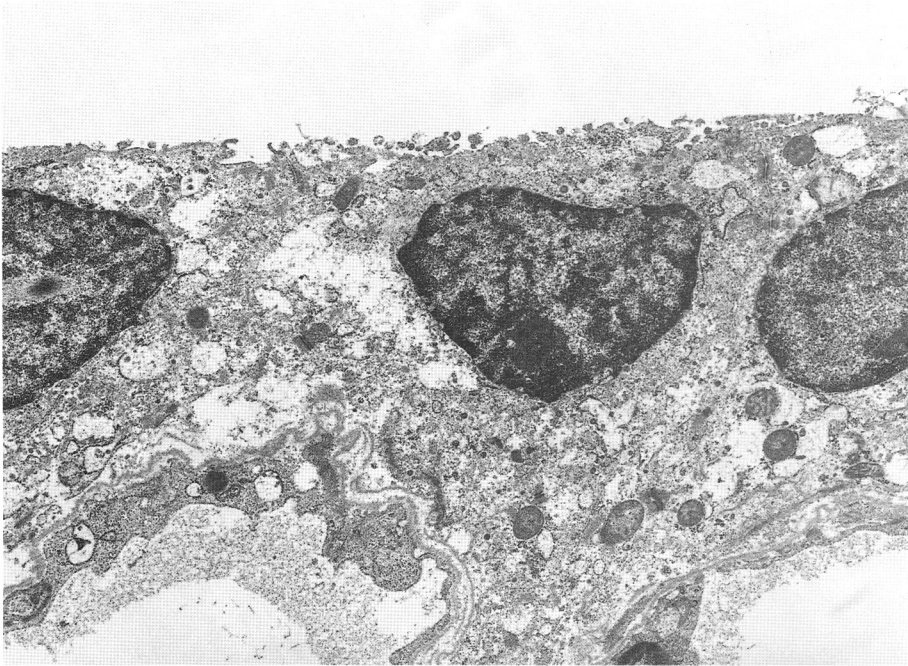


Fig. 7. Electron Micrograph showing, coarse, poorly formed microvilli, intercellular junctions and round to oval nuclei.

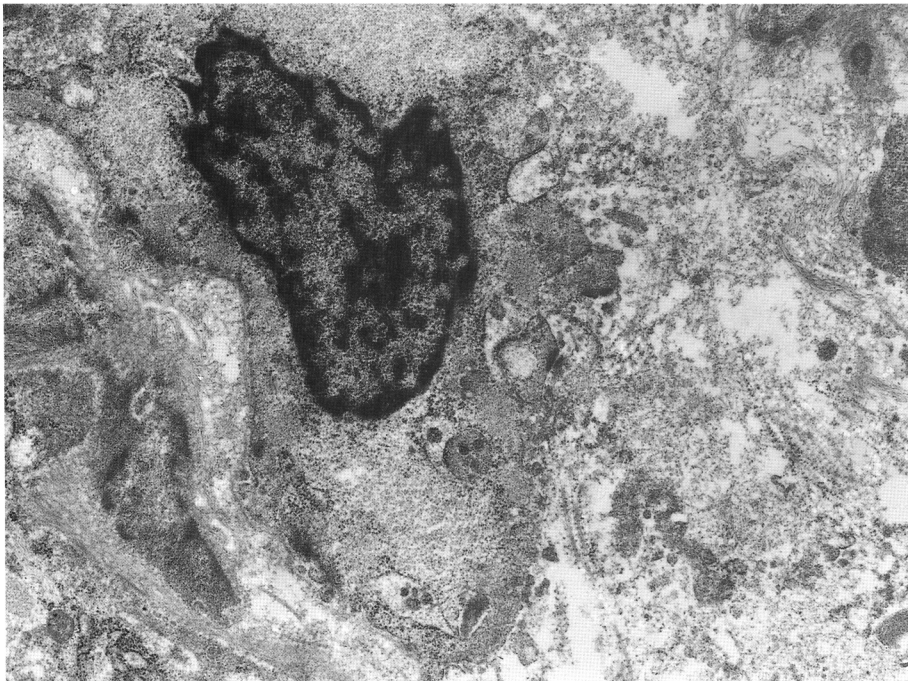


Fig. 8. Electron Micrograph showing numerous glycogen particles.

Myoepithelial cells as observed by Nyongo and Huntrakoon(1985) were not identified. Pericyte-like cells as described by Kim et al(1990) were not seen. A few desmosomes were noted between the epithelial cells. Basement membrane was present beneath these cells. Numerous glycogen granules were present in the cytoplasm(Fig. 8). The stroma consisted of many smooth muscle cells, fibroblasts, collagen fibers and capillaries. Cilia as described by Alpert et al(1988) was not seen. The omental cysts showed markedly flattened epithelium which did not contain glycogen, but possessed long stem microvilli, consistent with mesothelium.

DISCUSSION

The current case was unusual in that two smaller cysts in the omentum raised the possibility of a malignant serous cystic tumor with metastasis. However, the omental cysts were mesothelial-lined. Furthermore, nuclear atypia or glandular-like structure that might be seen in malignant counterparts was not present in the current case (Yoshimi et al., 1992). However, it should be noted that the malignant ones might be indistinguishable from benign ones, morphologically (George et al., 1989). Rare as they are, malignant serous tumors should be considered when the tumors are multi-focal or have coexisting cystic lesions, elsewhere (Yoshimi et al., 1992; George et al., 1989; Kamei et al., 1991, Kamei et al., 1992).

In their article, Lewandrowski et al.,(1992) described 5 cases of macrocystic variants of serous cystadenomas including two unilocular ones. The mode of presentation, age, gross and microscopic features and localization of the tumor in their cases are very similar to those in our case. They performed frozen sections on three of the five cases, but, the pathologic diagnosis did not alter the treatment. All five patients received complete resection, even when the diagnoses were simple cysts or pseudocysts. It was demonstrated in our case and most of theirs, that the lining tends to be extensively denuded, thereby possibly leading to the erroneous diagnosis of a pseudocyst. Indeed, in one series, discontinuity of the lining epithelium was observed in 40% of the typical microcystic tumors, and 72% of the mucinous tumors and involved an average of 40% (up to 98%) of the cyst wall area (Warshaw et al., 1990). Therefore, multiple frozen sections might be necessary before a diagnosis is reached. It is

also accepted that pre-operative distinction is not confidently made between serous tumors and mucinous neoplasms (Warshaw et al., 1990). We recommend pre-operative percutaneous needle aspiration be performed, whenever possible, since the serous tumors have a distinct morphology (Hittmair et al., 1991, Vellet et al., 1988, Young et al., 1991). The needle aspiration is very helpful, notwithstanding some limitations, when the lining cells are present or when mucin content is observed(Pyke et al., 1992). At the time of surgery, evidence for pre-existing pancreatitis should be carefully looked for. For the cystic neoplasms of the body and tail, Pyke et al. recommends distal pancreatectomy (Pyke et al., 1992). For the lesions of the head or uncinate process, they counsel against enucleation because of frequent complications and mortalities. They recommend weighing the risks and benefits of performing pancreaticoduodenectomy. In older patients with serous tumors, drainage(bypass surgery) is a good alternative, though not without complications-(Pyke et al., 1992, Corbally et al., 1989).

In conclusion, this is a case of a macrocystic(unilocular) variant of serous cystadenoma of the pancreas and we would like to re-iterate the contention of previous authors that the all-inclusive term "serous cystadenomas" encompass the spectrum of pathological findings of these benign neoplasms with glycogen-rich epithelium.

REFERENCES

- Alpert LC, Truong LD, Bossart MI, Spjut H.: *Microcystic Adenoma (Serous Cystadenoma) of pancreas. AJSP 12(4): 251-263, 1988.*
- Albores-Saavedra J, Gould EW, Angeles-Angeles A, Henson D. Cystic Tumors of Pancreas In Rosen P, Fecner R(ed): *Pathology Annual, volume 25 Norwalk, CT, Appleton & Lange, pp. 19-49, 1991.*
- Compagno J. Oertel J: *Microcystic adenomas of the pancreas (glycogen rich cystadenomas). A clinicopathologic study of 34 cases. Am J Clin Pathol 69: 289-298, 1978.*
- Corbally M, McAanena O, Urmacher C, Herman B, Shiu M: *Pancreatic cystadenoma. Arch Surg 124: 1271-1274, 1989.*
- Cubilla AL, Fitzgerald PZ.: *Classification of pancreatic cancer (non-endocrine). Mayo Clin Proc 54: 449-58, 1979.*
- Cubilla AL, Fitzgerald PJ. Surgical pathology of tumors of the exocrine Pancreas. In: *Moossa Ar, ed Tumors of the pancreas, Baltimore: Williams & Wilkins: 159-93, 1980.*

- Cubilla AL, Fitzgerald PJ. Tumors of the exocrine pancreas. In: *Atlas of Tumor pathology. Series 2 Fascicle 19. Washington DC: Armed Forces Institute of Pathology Monograph, 1983.*
- George DH, Murphy F, Michalski R, Ulmer B. *Am J Surg Pathol*; 13(1): 61-66, 1989.
- Hittmair A, Pernthaler H, Totsch M, Schmid KW: *Preoperative Fine Needle Aspiration Cytology of a Microcystic Adenoma of the Pancreas Acta Cytol*; 35(5): 546-548, 1991.
- Kamei K, Funabiki T, Ochiai M, Amano K, Kasahara M, Sakamoto T: *Multifocal pancreatic serous cystadenoma with atypical cells and focal perineural invasion. Int J Pancreatol*; 10(2): 161-72, 1991.
- Kamei K, Funabiki T, Ochiai M, Amano H, Marugami Y, Kasahara M, Sakamoto T: *Some considerations of the biology of Pancreatic Serous Cystadenoma. Int J Pancreatol*; 11(2): 97-104, 1992.
- Kim YI, Seo JW, Suh JS, Lee KU, Choe KJ: *Microcystic Adenomas of the Pancreas Am J Clin Pathol*; 94: 150-156, 1990.
- Lewandrowski K, Warshaw A, Compton C: *Macrocystic Serous Cystadenoma of the Pancrea. Hum Pathol*; 23: 871-875, 1992.
- Lo JW, Fung CKJ, Yonan TN, Martinez N: *Cystadenoma of the pancreas: an ultrastructural study. Cancer*; 39: 2470-4, 1977.
- Nyongo A, Juntrakoon A: *Microcystic Adenoma of the Pancreas with Myoepithelial cells. Am J Clin Pathol* 84: 114-120, 1985.
- Pyke CM, van Heerden JA, Colby TV, Sarr MF, Weaver AL: *The spectrum of Serous Cystadenoma of the Pancreas. Ann. Surg*; 215(2): 132-139, 1991.
- Vellet D, Leiman G, Mair S, Bilchik A: *Fine Needle Aspiration Cytology of Mucinous Cystadenocarcinoma of the Pancreas. Acta Cytol*; 32(1): 43-48, 1988.
- Warshaw AL, Compton C, Lewandrowski K, Cardenosa G, Mueller P. Cystic Tumors of the Pancreas. *Ann. Sur*: 212(4): 432-445, 1990.
- Yoshimi N, Sigeyuki S, Tanaka T, Aijin W, Bunai Y, Tate-matsu A, Okada T, Mori H: *A Rare Case of Serous Cystadenocarcinoma of the Pancreas. Cancer*; 69: 2449-2453, 1992.
- Young NA, Millani MA, Khoury P, Naryshkin S: *Differential Diagnosis of cystic Neoplasms of the Pancreas by Fine-Needle Aspiration. Arch Pathol Lab Med.* 115: 571-577, 1991.
- Zamora JL: *Cystic neoplasms of the pancreas: evolution of a concept. Am J Surg*; 149: 819-23, 1985.