PANCREATIC ASTHENIA AS A POST-OPERATIVE COMPLICATION IN PATIENTS WITH LESIONS OF THE PANCREAS*

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Certain symptoms have been recognized for many years as occurring in pancreatic disease. These are asthenia, anorexia, nausea and vomiting, a tendency to hemorrhage, ptyalism, abnormal stools, epigastric pain and tenderness and rapid emaciation. One or more of these symptoms are mentioned by the numerous investigators in their discussions of the clinical picture of inflammatory and neoplastic lesions of the pancreas. But so far as the writer has been able to determine in a review of the literature a group of these symptoms has not been described as a syndrome appearing as a post-operative complication in the surgical therapy of the biliary tract and pancreas. In discussing the subject with several of the members of this Association, it is evident that this symptom complex has been noted by many of them and is considered a puzzling and difficult problem in the post-operative therapy of their biliary cases.

I desire to present an analysis of 18 cases with this complication from the Surgical Service of the Presbyterian Hospital, New York City. Seventeen of these patients were under my care, the eighteenth was recently operated upon by Dr. F. B. St. John and is included in this series with his kind permission.

In a series of 230 consecutive unselected cases of diseases of the biliary tract and pancreas operated upon by the writer, special attention has been paid to the pathology, symptoms, complications and results as related to the pancreas. Of these 230 cases 40 showed definite pancreatic lesions. The cases with questionable or moderate thickening of the pancreatic tissue about the common duct are not included. (See Table I.) Eighteen of these cases presented the complication which because of its most striking and constant symptom, asthenia, has been named pancreatic asthenia. At the Presbyterian Hospital we regard it as an entity. It is characterized by extreme asthenia, anorexia—in some cases a very loathing for all food, apathy, nausea and vomiting, a marked drop in blood-pressure, rapid loss of weight. In some cases there has been noted in addition a tendency to hemorrhage, with and without jaundice or biliary fistula, ptyalism, pain and tenderness over the pancreas, obstipation and diarrhœa. (See Table II.)

Pancreatic asthenia has appeared in our cases at intervals after operation varying from the second to the ninth day, and has lasted for periods varying

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TABLE I

Pathology of the 40 Cases with Pancreatic Lesions

Acute Inflammatory Lesions.		7
Hemorrhagic pancreatitis	2	
Suppurative pancreatitis with fat necrosis	4	
Abscess of the pancreas	1	
Chronic inflammatory lesions		17
Chronic pancreatitis without cholecystitis or cholelithiasis	4	
Chronic pancreatitis with cholecystitis and cholelithiasis	7	
Pancreatic lymphangitis involving the entire head with cholecystitis and cholelithiasis	6	
Diabetes mellitus with cholecystitis and cholelithiasis		5
Carcinoma of the pancreas		11
Primary carcinoma of the pancreas	8	
Primary carcinoma of the gall-bladder with metastases to the pancreas	2	
Primary carcinoma of the stomach with metastasis to the pancreas	1	

TABLE II

Analysis of Symptoms in 18 Cases of Pancreatic Asthenia

Asthenia was present in 18 cases.
Anorexia was present in 18 cases.
Apathy was present in 15 cases.
Nausea and vomiting was present in 18 cases.
Loss of weight was present in 18 cases.
Marked and continued fall in blood pressure was found in all of the last 7 cases on whom daily determinations were made.
Tendency to hemorrhage present in 6 cases.
Ptyalism present in 2 cases.
Pain and tenderness over the pancreas present in 3 cases.
Jaundice appeared after operation, present in 5 cases.
Obstipation was present in 2 cases.
Diarrhœa was present in 2 cases.

from two to thirty days, the average period being twelve days. The symptoms appear, as a rule, after the patient has recovered from the shock of the operation, when he is apparently doing well. In the patients recovering from this condition the change for the better is often surprisingly abrupt, appearing with a sudden return of appetite and relish for food. It differs from the cholemic state that one sees in cases with long-standing biliary obstruction and damaged liver. These patients with pancreatic asthenia are never comatose. They maintain a clear sensorium, are never delirious. Languor and apathy are pronounced. Weakness is their chief complaint. Asthenia, anorexia, nausea, drop in blood-pressure have been the first symptoms to appear. The asthenia is as marked in some cases as it is in Addison's disease. It is a subjective symptom causing the patient real concern. It is objectively manifested by the muscular relaxation, the mask-like facial expression, the feeble drawling voice, the weakened grip. All effort is avoided. Treatments are dreaded and exhausting. Oser, in his monograph on pancreatic disease, described this asthenia, but not in the post-operative

period. In discussing Chronic Indurative Pancreatitis he says:[1] "It is a well-known fact that many patients suffering from gall-stone, even without permanent jaundice, become so very weak and rapidly emaciated that the development of cancer is suspected, and yet after a long time patients wholly recover." Again in discussing asthenia in carcinoma of the pancreas, he remarks: "One peculiarity especially is frequently pronounced and manifest in the cachexia caused by pancreatic cancer, namely, the great weakness and prostration which cannot be explained by the inanition alone. The sensation of weakness may be too great for words—the patient avoids expression of suffering because it is worse to bear than the violent pain. The patients lie quiet and apathetic."[2] Apathy and languor have been noted in all of our cases, and is considered a result of the asthenia.

Anorexia is a constant symptom. In several of our patients there has been an aversion for all food, even fluids. This has been noted as independent of the nausea. Oser,[3] in speaking of anorexia in pancreatic disease, mentions "a loathing for food, especially for meats." Nausea and vomiting may be very marked; it has been present in all of our cases and has complicated the maintaining of fluid intake.

Blood-pressure studies have been carried out in our last seven cases. There has been a constant finding of marked drop in blood-pressure readings during the pancreatic asthenia as compared to the pre-operative readings. In one patient with a pressure of 215/130 before operation readings of 110/80 to 120/80 were noted during the course of her asthenia which lasted three weeks. Subsequent to her leaving the hospital her pressure rose to 200/120. In another patient pre-operative readings showed 110/70. During the most marked manifestations of his asthenia his systolic pressure fell to 50 with an imperceptible diastolic. No other observations on low blood-pressure in pancreatic disease after operation have been found in the literature.

A tendency to hemorrhage has been noted in two of our cases without jaundice, in four with jaundice. Prolonged bleeding and clotting time was a serious complication in these six cases. Jaundice appeared for a few days during the period of asthenia in four of our cases in whom stones were not found in gall-bladder or ducts at time of operation. In one of these patients jaundice continued for almost two years after the onset of the pancreatic complication. Ptyalism or excessive salivation was present in two of our cases during the pancreatic asthenia. This symptom is one of the earliest attributed to pancreatic disease. Schmackpfeffer,[4] in 1817, first called attention to it. Battersby,[5] in 1844, noted ptyalism in a case of pancreatic cyst, as did Ludolf,[6] in 1890. Halzmann,[7] in 1894, Caparelli,[8] in 1892, Guidiceandra,[9] in 1896, discussed this symptom in cases of pancreatic calculus. Friedrich,[10] in 1878, considered it a result of stomach involvement. Oser[11] explains it on the basis of associated nausea. A low sugar tolerance was determined in one of the eighteen cases after the asthenia disappeared. Pancreatic asthenia did not occur, however, in any of the five diabetics operated upon for gall-stone disease.

TABLE III

Analysis of Pathological Findings in 18 Cases of Pancreatic Asthenia

Case	Operative findings and operation	Result	Autopsy findings
1	Abscess in head of pancreas. Drainage of abscess.	Recovery 24 mos.	
2	Chronic pancreatitis involving the entire pancreas. Gall-bladder full of calculi. Cholecystectomy, choledochostomy.	Died	Hemorrhage in the interlobular septa. Ducts dilated. Acute interstitial pancreatitis.
3	Fat necrosis in omentum. Head of pancreas hard, nodular œdematous, gall-stones in the gall-bladder and common duct, cholecystectomy, choledochostomy.	Recovery 19 mos.	
4	Chronic cholecystitis. No calculi were found in gall-bladder or ducts. Lymph-nodes were enlarged along cystic and common ducts. Lymphangitis of the head of the pancreas. Cholecystectomy, appendicectomy.		She developed jaundice with asthenia and loss of weight. Lived 26 months. Died of chronic pancreatitis. Autopsy not obtained.
5	Chronic cholecystitis, calculi in gall-bladder and common duct. Entire pancreas was markedly enlarged, œdematous, indurated. Nodes were enlarged along the duct and over the head of the pancreas. Cholecystectomy, choledochostomy.	Died 20th day	Pancreas firm, nodular, enlarged, considerable increase in the interlobular connective tissue, especially in the body and tail.
6	Chronic cholecystitis, calculi in gall-bladder, one in common duct. The entire pancreas was hard, nodular, enlarged throughout. Cholecystectomy, choledochostomy.	Recovery 17 mos.	
7	Hydrops of gall-bladder. No calculi, common duct dilated, no calculi, pancreas showed a large, hard, nodular head with a cyst in its upper aspect. Cholecystduodenostomy.	Died	Patient recovered after her pancreatic asthenia. Tumor mass which had been palpable before operation disappeared in epigastrium for several months. Symptoms of asthenia recurred at end of 18 months and she died one month later. Autopsy not obtained as she died in a small suburb.

Case	Operative findings and operation	Result	Autopsy findings
8	Acute and chronic cholecystitis. Chronic cholangitis (B. coli communis). Calculi in gall-bladder and common duct. Enlarged nodes along common duct and over head of pancreas. Lymphangitis of entire head of pancreas. Cholecystectomy, choledochostomy.	Recovery 42 mos.	
9	Walls of gall-bladder calcareous gall-stone 5 x 4 x 4 cm. occupied the shrunken gall-bladder and compressed the common duct. Lymphangitis of the head of pancreas. She had been jaundiced eight months. Liver markedly enlarged. Cholecystostomy.	Recovery 56 mos.	
10	Chronic cholecystitis. Calculi in gall-bladder and common duct, lymphangitis of entire head of the pancreas. Cholecystectomy, choledochostomy.		
11	Chronic cholecystitis. Chronic pancreatitis, entire head and tail hard, nodular and enlarged. Cholecystectomy, choledochostomy.	Recovered 21 mos.	
12	Chronic cholecystitis. Single cholesterin stone in gall-bladder, 2 months pregnancy. Cholecystectomy.	Died 28th day	Developed pancreatic asthenia with jaundice on 2nd day. This persisted until 26th day. She then had very severe epigastric pain, developed hemorrhage and went into collapse. Autopsy.—Acute diffuse cholangitis hæmatoma in submucosa of the duodenum, closing lumen of the bowel. Hemorrhages into the retroperitoneal tissues. Fat necrosis. Sclerosis of pancreas with hemorrhage in it.
13	Gall-bladder distended, acutely inflamed. No calculi found in gall-bladder or ducts. Head of pancreas very hard, nodular, common duct dilated. Diagnosis: Acute cholecystitis carcinoma of pancreas. Cholecystectomy, choledochostomy.	Died 14th day	She showed hemorrhages into bowel and subcutaneous tissues.

Case	Operative findings and operation	Result	Autopsy findings
14	Carcinoma of gall-bladder. Chronic cholecystitis. Calculi in gall-bladder. Chronic pancreatitis. Cholecystectomy, transduodenal. Choledochostomy.	Died 19th day	*Autopsy.* Chronic pancreatitis, acute pancreatitis. Necrosis and liquefaction of periduodenal tissue and duct of Wirsung. Carcinoma of pancreas, liver, ovary and adrenal.
15	Carcinoma of body of pancreas. Exploratory celiotomy.	Died 15th day	
16	Carcinoma of pancreas. Cholecystgastrostomy.	Died 2nd day	
17	Carcinoma of gall-bladder. Carcinoma of common duct. Calculi in gall-bladder. Cholecystectomy, choledochostomy.		She developed typical pancreatic asthènia on 2nd day. These symptoms continued for 16 days, when she was taken to her home by her family. She died 2 mos. later. Whether or not the pancreas was involved in this case not determined, as autopsy was not obtainable.
18	Carcinoma of pancreas, cholecystostomy.	Died 20th day	

Course of the Complication.—The symptoms showed a duration of 2 to 30 days, the average period being 12 days. Save in carcinoma cases the syndrome cleared abruptly with the return of appetite. In several of the cases this change was striking. The request for bizarre dishes is often the first indication of subjective improvement. Thus Case I, after three weeks of refusing all food, even the simplest fluids, one morning informed us she was hungry and desired a dish of tripe. When this was prepared by her daughter she ate it with gusto and proceeded to an uninterrupted recovery. Case VI, after eleven days of complete anorexia, asked for a piece of juicy steak. He recovered progressively thereafter. The rapid gain in weight and sense of well-being have in several of our cases been as striking as was the loss of weight, asthenia and apathy during the course of the complication.

Pathology.—The pathological findings in these eighteen cases as determined at operation or post-mortem have been variable and in several of the cases very puzzling. Speculation as to the pathological findings in a given case of pancreatic disease is as hazardous to-day as in Fitz's time, who after 27 years of investigating, in his masterly way, the pathology of the pancreas remarked [12] in 1903 that "morbid changes in the pancreas are found frequently after death without symptoms having been observed during life to

indicate their presence. On the other hand, the diagnosis of probable pancreatic disease, perhaps of the gravest sort, has been made from the recognition of one or more symptoms or signs which at times have been associated with alterations of the pancreas and the patient has recovered or the gland when exposed has presented no abnormal appearance." Yet it will be seen from the analysis of the pathological findings in Table III that definite pathology was found in the pancreas in all but Case XVII. Whether or not the carcinoma of the common duct in this case, found near the lower end of the duct, extended into the pancreas was not determined at the operation. The patient died at home two months after leaving the hospital and autopsy was not obtained.

Treatment.—This is largely directed to the relief of fluid depletion. Continual vomiting and disinclination to take fluids results in low urine output and nitrogen retention. Glucose infusions in 5 to 10 per cent. solutions have been well taken without glycosuria. This would indicate that the islands of Langerhans are not involved in these pancreatic lesions. Blood transfusion has tided over several of our cases during the critical period of asthenia, especially those in whom it has persisted for more than 10 days. Lavage of the stomach, with hot saline solution or tap water, has not controlled the vomiting as effectively as in other abdominal cases where ileus or gastric dilatation is a factor. For the tendency to hemorrhage we have

TABLE IV

Mortality Statistics in 18 Cases of Pancreatic Asthenia

Case 2	Died 14 day	Acute pancreatitis found at autopsy.
Case 5	Died 20 day	Chronic pancreatitis found at autopsy.
Case 12	Died 28 day	Acute pancreatitis found at autopsy. Acute ileus.
Case 13	Died 14 day	Carcinoma of pancreas found at operation. Hemorrhages into bowel, and subcutaneous tissue.
Case 14	Died 19 day	Carcinoma of gall-bladder found at autopsy. Chronic pancreatitis.
Case 15	Died 15 day	Carcinoma of body of pancreas found at operation.
Case 16	Died 2 day	Carcinoma of pancreas found at operation.
Case 18	Died	Carcinoma of pancreas found at operation.

Post-operative results in the 10 cases leaving the hospital

Case 1	24 mos.
Case 3	19 mos.
Case 4	Died at end of 26 months of a chronic pancreatitis.
Case 6	14 mos. 244 Has weakness in the scar.
Case 7	18 mos. after operation tender mass reappeared in the epigastrium with jaundice and asthenia. Died one month later.
Case 8	42 mos.
Case 9	56 mos.
Case 10	12 mos.
Case 11	24 mos.
Case 17	Died 2 mos. after leaving the hospital of carcinoma.

found [18] intravenous infusions of calcium lactate in 0.2 to 0.5 per cent. solution shortened the bleeding and clotting time and has controlled the hemorrhage in all but three cases, all of whom showed carcinoma of the pancreas.

Epigastric pain and tenderness is best relieved with poultices. Tympanites responds to hot colon irrigations in some, to medicated enemas in others. We have found digitalis in the form of digitan given by rectum in 10 c.c. doses, has improved the general vasomotor and intestinal tone in a number of our cases.

Results.—It will be seen from Table IV that of 18 patients showing this syndrome 8 died while in the hospital, 5 showing carcinoma; 3 died after leaving the hospital in from 2 to 26 months. All of the surviving 7 patients show a symptomatic 4, relief from all symptoms, from 12 to 56 months after operation. From Table V it is evident that the lesions of the pancreas increase to a marked degree the hazard of the surgery of the biliary tract. In the entire series of 230 cases analyzed there were 25 deaths in the hospital, of these 25 fatal cases 15, or 60 per cent., showed pancreatic involvement. (See Table V.) Of 172 cholecystectomies, however, with the pathology limited to the gall-bladder at time of operation, there was but one death—Case XII reported in the series with pancreatic asthenia—the result of an acute pancreatitis developing after operation.

TABLE V

Death Analysis in 25 post-operative deaths in a series of 230 patients operated upon for Disease of the Biliary Tract and Pancreas.

15 of these cases showed pancreatic involvement.
11 showed carcinoma of the pancreas.
2 showed acute pancreatitis.
2 showed chronic pancreatitis.
Of the remaining 10 cases,
- 1 showed carcinoma of the cystic duct.
- 1 died of sepsis with B. coli chronic cholangitis.
- 3 died of cholemia with long standing biliary cirrhosis and common duct stone obstruction.
- 1 died of uremia following secondary cholecystectomy for common duct stone.
- 1 died of Welch bacillus cholecystitis and cellulitis.
- 1 died of vibrion septique cholangitis and cellulitis.
- 1 died of B. coli bacteria and acute endocarditis.
- 1 died of multiple liver abscess.

In 172 cholecystectomies for inflammatory disease or calculus limited to the gall-bladder there was but one death, the result of an acute pancreatitis developing after operation.

CONCLUSIONS

1. There is a group of symptoms appearing as a post-operative complication in patients with pancreatic lesions, characterized by asthenia, anorexia, nausea and vomiting, low blood-pressure and rapid loss of weight.

2. In a series of 18 cases reported definite pathology of the pancreas was determined in 17 either at operation or post-mortem.

3. The asthenia, anorexia, low blood-pressure and loss of weight is not dependent upon malignancy, inasmuch as 12 of the 18 cases reported showed pancreatitis rather than carcinoma.

4. The involvement of the pancreas increases to a marked degree the hazard of biliary surgery.

5. The inflammatory lesions and calculus formation limited to the gall-bladder should be treated surgically before the process of inflammation extends to the pancreas.

REFERENCES

[1] Oser, L.: Diseases of the Pancreas. Nottnagels Practice. Diseases of the Pancreas, Adrenal and Liver, p. 147.
[2] *Loc. cit.*, p. 162.
[3] *Loc. cit.*, p. 154.
[4] Diss. Inaug. de quibusd. Pancreatis Morbis, 1817, 26.
[5] Battersby, F.: Gazette Médicale de Paris, 1844, vol. xxxix, p. 617.
[6] Ludolf: Dissert., 1890.
[7] Halzmann, M.: Munsch. Med. Woch., 1894, No. 20, p. 389.
[8] Caparelli.
[9] Guidiceandra.
[10] Friedrich.
[11] *Loc. cit.*
[12] Fitz, Reginald H.: Transactions of the Congress of Am. Phys. and Surg., 1903, p. 36.
[13] Whipple, A. O.: Annals of Surgery.