REVIEW ARTICLE

Pancreatic Sarcoidosis: A Literature Review

Leila Alizadeh, Amir Houshang Mohammad Alizadeh

Research Center for Gastroenterology and Liver Diseases, Taleghani Hospital, Shaheed Beheshti University of Medical Sciences and Health Services, Tehran, Iran

ABSTRACT

Pancreatic involvement is a rare condition in the patients with systemic sarcoidosis. The incidence rate of pancreatic sarcoidosis is 1-6% of the patients with systemic disease. Symptoms related to pancreas involvement are not common and may vary from nonspecific abdominal pain or nausea and weight loss to a solid mass with obstructive jaundice. There is no specific diagnostic test for pancreatic sarcoidosis. It often is detected during surgery in the patients who are suspicious to malignant pancreatic mass and diagnosed by pathological evidences. However, Computed Tomography, magnetic resolution imaging and endoscopic ultrasound guided fine needle aspiration may be useful and safe modalities for differentiating malignant and benign pancreatic masses. There is no standard medical treatment for pancreatic sarcoidosis. Nevertheless, corticosteroid therapy may be considered for symptomatic patients. Generally, prognosis is good in the mild forms of disease and spontaneous remission rate is high.

BACKGROUND

Sarcoidosis that first was described by Hutchinson in 1877 is a chronic inflammatory disease without a definite etiology characterized by non caseous granulomas [1, 2, 3, 4]. The prevalence of this multisystemic disease is approximately 2-60 per 100000 persons and mostly affects young adults between 20-40 years. Women are affected more than men [5, 6]. Although It affects all races; however, higher rates of sarcoidosis has been reported amongst Afro-Americans, Scandinavians and Irish decent [1, 6, 7, 8]. Various risk factors such as environmental and genetic risk factors have been considered for sarcoidosis [7, 9, 10].

Although, it can involve almost any organs; but, pulmonary system is the most commonly affected site (90%) [6, 11]. Extra-thoracic involvement occurs in 30% of the patients [2, 12,]. Isolated extra pulmonary sarcoidosis account for about 10% cases [13]. In some cases multiple organ involvement can present a difficult diagnosis, because they mimic metastatic cancer [14]. The most frequent extra-thoracic sites are abdomen with a frequency of 50-70%. liver with 50-80%, spleen with 40-80%, lymph nodes with 30% and kidney are the most common intra-abdominal sites of involvement in sarcoidosis [6, 15]. Eye involvement is reported in 25% of the patients with systemic sarcoidosis. Also, skin manifestations occur in 25% of cases with sarcoidosis [16]. The main cause of mortality in systemic sarcoidosis is due to cardiopulmonary involvement [6]. Generally a, mortality rate of 1-5% has been reported for sarcoidosis [17, 18].

Gastrointestinal involvement is rare in patients with systemic sarcoidosis and may be asymptomatic; so that in 60-90% of these cases, non-caseating granuloma was detected in liver biopsy [2, 16, 19]. Liver involvement in the absence of pulmonary disease is rare and has been reported in about 13% of cases with systemic sarcoidosis [2]. Although liver involvement is mainly asymptomatic; but, it can present with hepatosplenomegaly, elevated liver enzymes, intrahepatic cholestasis, portal hypertension, and cirrhosis [20].

The first report of pancreatic involvement in a patient with systemic sarcoidosis was published in 1937 by Nickerson. He found non-caseating granulomas in autopsy of pancreas in this patient [21, 22]. In 1950, Curran and Curran presented a case of pancreatic sarcoidosis with diffuse abdominal pain who was diagnosed via exploratory laparatomy [21, 23]. In 1963, Mayock reported three cases of pancreatic involvement amongst 287 patients with systemic sarcoidosis [24]. According to a large autopsy series in Japan, the frequency rate of 2.1% was reported for pancreatic sarcoidosis. Half of these cases were asymptomatic and died of other causes [21, 25]. Noguchi in 1993 reported 14 patients with pancreatic sarcoidosis. Six had swollen pancreas with diffused nodular changes, four had enlargement of the head, and only one patient had a combination of pancreatic head mass and diffuse

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Correspondence Amir Houshang Mohammad Alizadeh
Gastroenterology and Liver Diseases Research Center
Taleghani Hospital, Parvaneh Ave., Tabnak Str., Evin
Tehran, Iran-19857
P.O.Box: 19835-178
Tel 0098-21-22432521
Fax 0098-21-22432517
E-mail ahmaliver@yahoo.com

enlargement [21, 26]. In 2006, Caceres reported 25 patients with surgically proven pancreatic sarcoidosis of which 12 cases presented with a pancreatic mass localized to the head of pancreas, and 13 cases presented with a diffusely firm nodular pancreas [17, 21]. Pancreatic sarcoidosis rarely cause symptom and it appear diffuse nodular tissue infiltration, duct obstruction or peripancreatic lymphadenopathy or pancreatic head mass that should be differentiated from pancreatic adenocarcinoma [6]. Histologic finding of pancreatic sarcoidosis reveal non – caseating granulomas with are also seen in other diseases including infectious autoimmune and neoplastic diseases [6, 13]. So that early diagnosis is warranted to avoiding unnecessary surgery [27].

In review of literatures within more than last 3 decades, we found more than 30 case reports of pancreatic sarcoidosis. In this review article we tried to summarize all about pancreatic sarcoidosis including clinical features, diagnostic methods, and treatment of this rare condition.

Clinical Manifestations

According to review literatures, incident rate of pancreatic involvement in the patients with systemic sarcoidosis is 1-6%. This involvement may be microscopic and found during autopsy as an incidental finding. In the other hand pancreatic sarcoidosis without involvement of other organs and with symptoms related only to the pancreas is extremely rare. In symptomatic cases, clinical presentations varies from nonspecific abdominal pain or acute pancreatitis with nausea and weight loss to a solid mass with obstructive jaundice. The acute symptoms were more common in younger patients (18 to 47 years) accompanied by variable hyperamylasaemia and calcaemia, while the chronic picture was more common in older age groups (25 to 67 years) suggesting the diagnosis of carcinoma. Women a slightly more than men may present with pancreatic mass. The most common site of pancreatic involvement is head of pancreas; while, involvement of tail or total pancreas is rare [1, 24, 27, 28].

In 25 cases with pancreatic sarcoidosis reported by Caceres in 2006 patients mostly presented with abdominal pain (66%), weight loss (49%), obstructive jaundice (29%) and emesis (20%), pruritus (12%), fever (8%), diarrhea (4%), abdominal distention (4%) and ascetis (4%) [17, 30]. Three cases of pancreatic sarcoidosis presented as acute pancreatitis [28, 31]. Pancreatic symptoms are mostly due to pancreas infiltration or compression by enlarged lymph nodes [1]. Sarcoidosis may rarely present as a mass in the pancreas that mimics pancreatic cancers and need to surgery for confirming diagnosis [1, 6, 21, 27, 30, 32, 33, 34, 35, 36]. Furthermore, 16% of these patients reported a history of sarcoidosis; 35% had elevated amylase; 62% had elevated Angiotensin-converting enzyme (ACE) and 26% had bilateral hilar lymphadenopathy [17].

Up to 2006, 26 cases of pancreatic sarcoidosis had been reported and summarized by Caceres *et al*. [17]. By using key word of "pancreatic sarcoidosis" in PubMed and Scopus, we found another five cases since 2006 up to now. We add these patients to Caceres findings' as following **(Table 1)**:

Amongst these patients, there are 14 female and 17 male. Average age is 47. Head of pancreas was the most common site of involvement (in 15 cases).

Diagnosis

Sarcoidosis is a multisystemic inflammatory disease of unknown origin. It is characterized by non-caseating epithelioid cell granulomas in the absence of other granulomatous diseases such as tuberculosis, fungal infections, autoimmune diseases, or delayed-type hypersensitivity reaction to foreign antigens [6, 23].

Diagnosis must be confirmed by histopathological evaluation showing non-caseating granulomas discrete well-formed non-necrotizing granulomas are the hallmark of sarcoidosis. Lesions often consist of a cluster of epitheloid and multinucleated histiocytes. There may be mild inflammation and variable fibrosis immediately surrounding the granuloma but the rest of the surrounding tissue is typically spared [55].

There is no specific laboratory test for confirming sarcoidosis as well as pancreatic sarcoidosis [56, 57]. Laboratory tests to support the diagnosis include complete blood count (CBC), electrolytes, BUN/Cr, liver enzymes, alkaline phosphatase, calcium, urinalysis including urinary calcium and creatinine, immunoglobulins and angiotensin converting enzyme (ACE). The CBC may show leukopenia, anemia, thrombocytopenia or pancytopenia. Liver enzymes, alkaline phosphatase and immunoglobulins may be elevated. Hypercalciuria is defined as urinary calcium to creatinine ratio of more than 0.2 for normal patients over the age of two years with relatively normal body mass index. Men are more likely to have difficulties with calcium homeostasis than women and an elevated urinary calcium/ Cr rat io thais more common than hypercalcemia. Elevated ACE is not diagnostic due to false-positives. However, it is found to be elevated in over 75% of cases of sarcoidosis lending further support to the diagnosis [58, 59].

Few case reports have mentioned laboratory results of pancreatic involvement in sarcoidosis. Nevertheless, laboratory findings are not specific for diagnosis of sarcoidosis. In a prospective study, 15 cases amongst 92 patients with sarcoidosis had an abnormal level of serum pancreatic amylase and 6 cases amongst 39 had an elevated serum immunorective trypsin. These findings suggest that clinical and subclinical abnormalities of pancreatic function are not uncommon in patients with sarcoidosis [60].

According to review literatures, pancreatic sarcoidosis can manifest as solid tumors; therfore, it may mimic pancreatic malignancies [33, 34, 36, 47, 49]. Varieties of differential diagnoses are considered for a pancreatic mass. For instance, pancreatic adenocarsinoma (PC), Primary pancreatic lymphoma (PPL), pancreatic neuroendocrine tumor (PNET), autoimmune pancreatitis (AIP), metastasis

Table 1. Summary of patients reported with pancreatic sarcoidosis.

S. No	Author	Age/Sex	Presentation	CXR	ACE	Amylase	Previous Sarcoidosis	Surgical Intervention	Surgical Findings	Location
1	Curran and Curran [23]	48F	Nausea/vomiting, abd. pain, weight loss	Normal	N/A	Normal	No	Exploratory laparatomy, pancreatic biopsy	Firm, nodular pancreas	Diffuse
2	Ryrie [30]	52F	Obstructive jaundice	N/A	N/A	N/A	No	Panc biopsy, biliary bypass	Mass in head of pancreas	Pancreatic head
3	Papowitz [37]	28F	Abdominal distention	Normal	N/A	N/A	No	Exploratory lapatomy,splenectomy, distal pancreatectomy	Ascitis, peritoneal granulomas, Nodular pancreas	Diffuse
4	Chaun [38]	52M	Fever, abd pain, weight loss	Normal	N/A	Normal	No	Exploratory lapatomy, pancreatic biopsy	Enlarged, nodular pancreas	Diffuse
5	Caldwell [39]	37M	Pruritis	Normal	N/A	126 IU/L	No	Cholecystectom, common duct exploration	Firm, enlarged pancreas	Diffuse
6	Tsou [40]	47F	Fatigue, weight loss, weakness	N/A	Elevated	Normal	Yes	Exploratory lapatomy for suspected uterine malignancy	Diffuse nodular pancreas	Diffuse
7	Maher [41]	59M	Abdominal pain, nausea, weight loss	Normal	N/A	Normal	No	Exploratory lapatomy, transduodenal panc biopsies	Diffusely enlarged pancreas	Diffuse
8	Friedman [42]	48F	Weight loss, abdominal pain	Bilateral hilar enlargement	Elevated	68 IU/L	No	Exploratory lapatomy, pancreatic biopsy	Enlarged nodular pancreas, peripancreatic LN	Diffuse
10	Sagalow [32]	25F	Acute abdominal pain	Normal	N/A	215 IU/L	No	Exploratory lapatomy, pancreatic biopsy	Enlarged pancreatic head, peripancreatic LN	Head of pancreas
11	Robaszkiewicz [43]	30M	Abdominal pain	Reticulonodular pattern	Elevated	Elevated	Yes	Exploratory lapatomy, pancreatic biopsy	Nodular pancreas, peripancreatic LN	Diffuse
12	Stampll [44]	47M	Abdominal pain, emesis, weight loss	Mediastinal LN	N/A	1310 IU/L	Yes	Exploratory lapatomy pancreatic biopsies	Enlarged pancreatic head, peripancreatic LN	Head of pancreas
13	Brady et al. [45]	67F	Abdominal pain	Normal	Normal	546 IU/L	No	Pancreatico-duodenectomy	Enlarged pancreatic head, peripancreatic LN	Head of pancreas
14	Toda [46]	66M	Back pain, pruritus	Normal	Normal	Slight elevation	No	Exp lap, pancreatic biopsy	Enlarged nodular pancreas, peripancreatic LN	Diffuse
15	Soyer [34]	51F	Weight loss, abdominal pain, nausea, vomiting	N/A	N/A	N/A	No	Pancreatic biopsy choledocho and gastrojejunostomy	Enlarged nodular pancreas, peripancreatic LN	Head of pancreas
16	Espinoza-Aguilar [47]	41F	Jaundice, pruritus	Normal	N/A	N/A	No	Peripancreatic node biopsy	peripancreatic lymphadenopathy	Head of pancreas
17	Garcia [48]	52F	Anemia, splenomegaly	Hilar, mediastinal adenopathy	Elevated	Normal	No	Splenectomy, distal pancreatectomy	splenomegally	Diffuse
18	Garcia [48]	34M	Severe abdominal pain	Bilateral hilar adenopathy	N/A	N/A	No	Exploratory laparatomy , peripancreatic node biopsies	Nodular pancreatic tail, enlarged peripancreatic LN	Pancreatic tail
19	Garcia [48]	33M	Fever, weight loss, abdominal pain	Bilateral hilar adenopathy	Elevated	N/A	No	Pancreatic, peripancreatic node biopsies	N/A	N/A
20	Rodriguez [49]	41F	Abdominal pain	Normal	N/A	Normal	No	Exp lap, pancreatic biopsies	Enlarged pancreatic head, peripancreatic LN	Head of pancreas
21	Snook [50]	45M	Abdominal pain, diarrhea, weight loss, jaundice	Normal	Normal	N/A	Yes	Exp lap, pancreatic biopsy	Diffusely nodular pancreas Peripancreatic LN	Diffuse
22	Siavelis et al. [28]	61M	Obstructive jaundice, weight loss	N/A	N/A	Normal	No	Pancreatico-duodenectomy	Pancreatic head mass	Head of pancreas
23	Bacal [1]	54M	Jaundice	N/A	N/A	N/A	No	Pancreatico-duodenectomy	Pancreatic head mass	Head of pancreas

24	Frank [51]	40F	Jaundice, abd pain	Normal	Normal	N/A	No	Pancreatico-duodenectomy	Pancreatic head mass	Head of pancreas
25	Frank [51]	76M	Abd pain	Normal	N/A	N/A	No	Duodenotomy, submucosal mass excision	Periampullary mass	Head of pancreas
26	Ohana [28]	54F	Abd pain, nausea, emesis, weight loss, jaundice	Normal	N/A	Normal	No	Pancreatico-duodenectomy	Pancreatic head mass and peripancreatic LN	Head of pancreas
27	Caceres [17]	60M	Abdominal pain, weight loss	Normal	Normal	Normal	No	Pancreatico-duodenectomy	N/A	N/A
28	Wijkstrom [35]		biliary obstruction mimicking pancreatic malignancy	N/A	N/A	N/A	No	N/A	N/A	N/A
29	Cook [52]	60M	No symptom , only elevated CA19-9	N/A	N/A	N/A	No	Intraoperative frozen section	peripancreatic lymphadenopathy	Head of pancreas
30	Yamaguchi [53]	80F	Back pain	N/A	N/A	N/A	No	distal pancreatectomy and splenectomy	hard mass in the pancreas body	Body pf pancreas
31	Mayne [33]	52M	Weight loss obsteructive jaundi	N/A	N/A	N/A	No	Whipple's procedure	mass was deemed unresectable due to invasion of the superior mesenteric vein	Head of pancreas
32	Zhang [54]	47M	idiopathic epigastric abdominal pain	N/A	N/A	N/A	No	N/A	N/A	Head of pancreas

*Some part of this table is obtained from Caceres study in 2006 [17]

from other primary sites, and rare diseases such as pancreatic tuberculosis or pancreatic sarcoidosis. All of these conditions can mimic pancreatic adenocarcinoma [61]. Isolated metastatic cancers to the pancreas can be occur most commonly in melanoma, renal cell, lung, colon, gastric, breast, and ovarian cancers and rarely in prostate cancer [62, 63].

Although previous history of sarcoidosis can be helpful for diagnosing pancreatic involvement in a patients with pancreas related signs and symptoms, but only 16% of patients mention history of systemic sarcoidosis before presenting symptoms that led to detection of pancreatic involvement [2].

So far, there is no specific diagnostic imaging for pancreatic sarcoidosis. Although CT is a useful modality for detecting pancreatic masses but it is not specific for diagnosing pancreatic sarcoidosis. Essentially, an ill-defined pancreatic head mass, narrowing and dilatation of the common bile duct with or without pancreatic duct dilatation, and enlarged lymph nodes are the most common CT findings reported in the literatures [1, 28, 33, 34, 64, 65, 66]. **Figure 1** shows Computer tomography (CT) scan findings in a case of pancreatic sarcoidosis. It reveals a smooth shaped lesion involving the pancreatic head, measuring 3.6 cm at its greatest diameter [52].

Pancreatic sarcoidosis should be considered in the differential diagnosis of multiple pancreatic masses on MRI with low signal intensity on T1- weighted images, mild high signal intensity on T2- weighted images, and decreased enhancement compared to the normal pancreas after administration of gadolinium [64].

MRI findings in pancreatic sarcoidosis have been described in the literature in the last decade. For instance, in Baroni study, MRI findings of a patient with pancreatic sarcoidosis revealed multiple masses within the body and tail of the pancreas, with slight hyperintensity on T2-weighted images and delayed progressive enhancement after administration of gadolinium, becoming isointense to the rest of the pancreas on the portal venous and delayed venous phases **(Figure 2)** [64, 6]. Although, these findings are unusual in primary pancreatic adenocarcinoma, but some other differential diagnoses are strongly considered including

Figure 1: Computer tomography (CT) scan findings in a patient with pancreatic sarcoidosis.

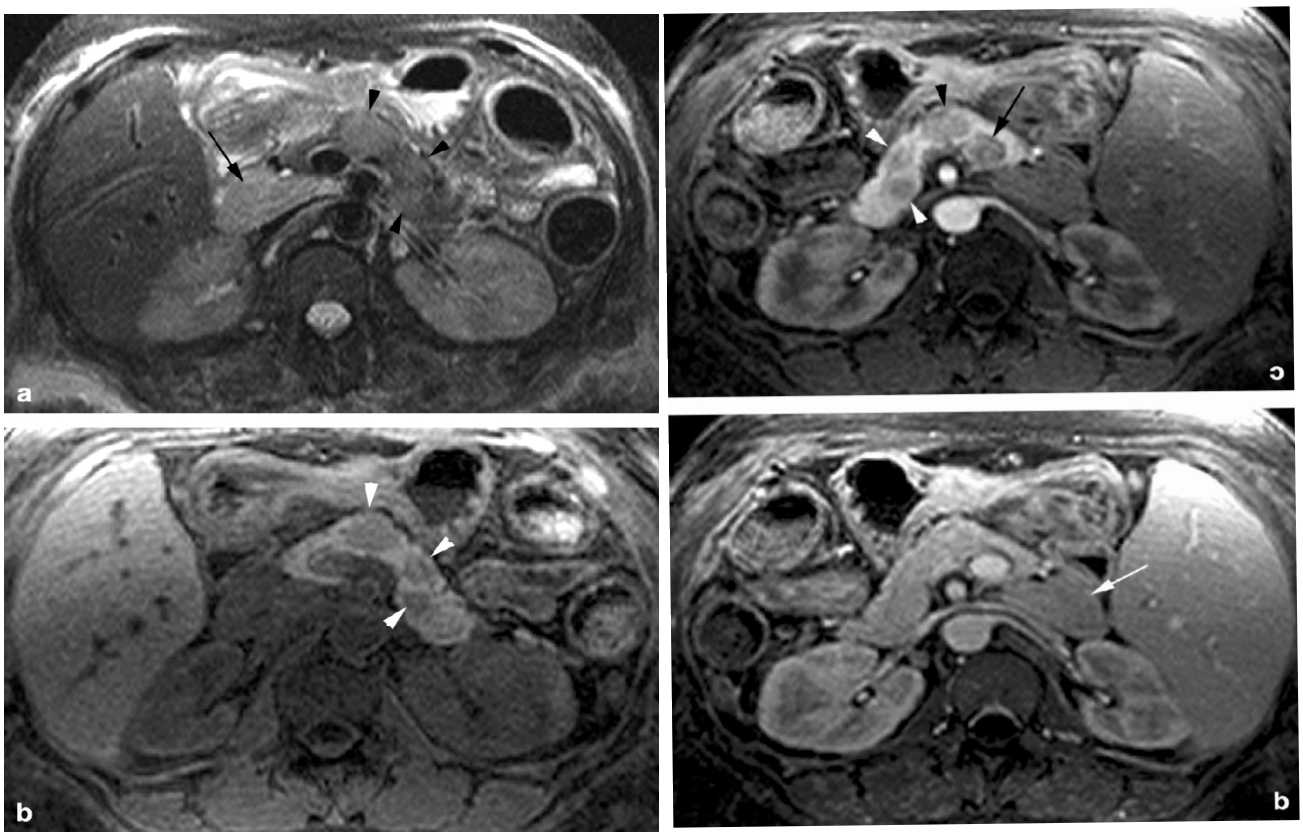

Figure 2. MRI finding in a patient with pancreatic sarcoidosis. **(a).** Axial T2-weighted showing three poorly defined masses in the pancreatic body and tail [arrowheads]. **(b).** Axial non-contrast-enhanced three-dimensional fat-saturated T1-weighted.The pancreatic masses within the pancreas are more conspicuous (arrowheads). **(c).** Axial three-dimensional fat-saturated T1-weighted that demonstrates decreased enhancement of the pancreatic masses [arrowheads]. **(d).** Axial three-dimensional fat-saturated T1-weighted the pancreatic masses are imperceptible because they have become isointense to the normal pancreatic parenchyma. Note the enlarged enhancing peripancreatic lymph node (arrow).

non-hyperfunctioning neuroendocrine tumors, pancreatic metastases, lymphoma, and granulomatous infection [64].

Neuroendocrine tumors can be multiple and usually present as discrete nodules with low signal on T1-weighted images, and high signal on T2-weighted images. However, the majority of them will enhance to a greater degree than the normal pancreatic parenchyma during the arterial phase after administration of gadolinium [20]. Pancreatic metastases will present as multiple parenchymal masses in only 5–10% of cases, and their imaging aspects may resemble those of the distant primary neoplastic source (the most common being renal cell carcinoma)[25].

Endoscopic ultrasound (EUS) is a high sensitive and less aggressive modality for diagnosis small pancreatic tumors [67]. Several studies has compared CT, MRI and EUS for diagnosing, differentiating pancreatic mass. Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) is a safe procedure for diagnosing pancreatic mass with obtaining tissue samples for pathologic evaluation [68]. Fine-needle aspiration (FNA) cytology and fluid analysis together with morphological characteristics helps differentiate malignant lesions from benign masses [69]. The reported sensitivity and specificity of EUS-FNA for various solid lesions in pancreas are as high as 97% [70]. This modality is useful for differentiating other causes of pancreatic involvement such as pancreatic tuberculosis [71, 72, 73]. Thus, it may be a helpful procedure for diagnosing pancreatic sarcoidosis.

Treatment

So far, there is no standard medical treatment for pancreatic sarcoidosis. Although the prognosis is variable; but, the prognosis of mild pancreatic involvement is good, and spontaneous remission rate is high [2, 21, 48]. Generally, corticosteroids are drug of choice for treatment of sarcoidosis. It is recommended for management of more severe forms of sarcoidosis such as cardio pulmonary, ocular and central nervous system involvement as well as patients with malignant hypercalcemia and constitutional symptoms [21, 31, 75]. Corticosteroids control disease by suppressing the pro-inflammatory cytokines and chemokines involved in cell mediated immune response and granuloma formation [76].

There is no agreement on optimal dose and duration of corticosteroid therapy [76]. Long time corticosteroid therapy can be associated with complications such as hypertension, cushingoid effects, psychosis, osteoporosis, glaucoma, cataracts, hypokalemia, glucose intolerance, telangiectasis, acne, and gastropathy. Due to the serious effects of chronic corticosteroid pharmacotherapy, it should be used only after careful estimation of its risks and benefits. After discontinuing corticosteroids, the recurrence rate of pancreatic sarcoidosis in severe symptomatic cases is 100% [31].

It is proposed that corticosteroids may alleviate abdominal pain and reduce elevated serum level of amylase and lipase [77]. In the literatures, 18 patients

with pancreatic sarcoidosis were followed up. Six patients improved without any treatment; whereas, 10 improved with corticosteroids [2, 17].

As alternative therapeutic methods, other non-steroidal drugs may be used in treatment of some refractory life-threatening forms of sarcoidosis such as azathioperin, methotroxate and hydroxyl chlroquine [4, 76, 78, 79]. In a case with pancreatic sarcoidosis presented with pancreatitis, mycophenolate mofetile was used successfully [80]. In recent years, numerous reports have been published about effectiveness of retuximab and infliximab in treatment of severe forms of sarcoidosis such as pulmonary and ocular sarcoidosis [79, 81, 82, 83, 84, 85].

Conflicting Interest

The authors had no conflicts of interest.

References

1. Bacal D, Hoshal Jr VL, Schaldenbrand JD, Lampman RM. Sarcoidosis of the pancreas: case report and review of the literature. Am Surg 2000; 66:675-8. [PMID: 10917480]

2. Harder H, Büchler MW, Fröhlich B, Ströbel P, Bergmann F, Neff W, et al. Extrapulmonary sarcoidosis of liver and pancreas: a case report and review of literature. World journal of gastroenterology: World J Gastroenterol 2007; 13:2504-9. [PMID: 17552036]

3. Agostini C, Semenzato G, James DG. Immunological, clinical and molecular aspects of sarcoidosis. Mol Aspects Med 1997; 18:91-165. [PMID: 9220446]

4. Costabel U, Hunninghake GW. ATS/ERS/WASOG statement on sarcoidosis. Sarcoidosis Statement Committee. American Thoracic Society. European Respiratory Society. World Association for Sarcoidosis and Other Granulomatous Disorders. Eur Respir J 1999; 14:735-7. [PMID: 10573213]

5. Rybicki BA, Major M, Popovich J, Maliank MJ. Racial differences in sarcoidosis incidence: a 5-year study in a health maintenance organization. Am J Epidemiol 1997; 145:234-41. [PMID: 9012596]

6. Gezer NS, Başara I, Altay C, Harman M, Rocher L, Karabulut N, Seçil M. Abdominal sarcoidosis: cross-sectional imaging findings. Diagn Interv Radiol 2015; 21:111-7. [PMID: 25512071]

7. James D. Epidemiology of sarcoidosis. Sarcoidosis 1992; 9:79-87. [PMID: 1344062]

8. Newman LS, Rose CS, Bresnitz EA, Rossman MD, Barnard J, Frederick M, Terrin ML, et al. A case control etiologic study of sarcoidosis: environmental and occupational risk factors. Am J Respir Crit Care Med 2004; 170:1324-30. [PMID: 15347561]

9. Rybicki BA, Iannuzzi MC. Epidemiology of sarcoidosis: recent advances and future prospects. Semin Respir Crit Care Med 2007; 28:22-35. [PMID: 17330190]

10. Rybicki B, Maliarik M, Major M, Popovich Jr J, Iannuzzi MC. Epidemiology, demographics, and genetics of sarcoidosis. Semin Respir Infect 1998; 13: 166-73. [PMID: 9764947]

11. MacArthur KL, Forouhar F, Wu GY-H. Intra-abdominal complications of sarcoidosis. J Formos Med Assoc 2010; 109:484-92. [PMID: 20654787]

12. Vardhanabhuti V, Venkatanarasimha N, Bhatnagar G, Maviki M, Iyengar S, Adams WM, Suresh P. Extra-pulmonary manifestations of sarcoidosis. Clinical radiology 2012; 67:263-76. [PMID: 22094184]

13. Tu C, Lin Q, Zhu J, Shao C, Zhang K, Jiang C, Ding Z, et al. Isolated sarcoidosis of accessory spleen in the greater omentum: A case report. Exp Ther Med 2016; 11:2379-2384. [PMID: 27284324]

14. Hammen I, Sherson DL, Davidsen JR. Systemic sarcoidosis mimicking malignant metastatic disease. Eur Clin Respir J 2015; 2:26761. [PMID: 26672956]

15. Panasci DJ, Gordon DH, Sadovsky R. Sarcoidosis of the liver: evaluation with multiple imaging modalities. Comput Med Imaging Graph 1992; 16:55-8. [PMID: 1555184]

16. Sharma OP. Sarcoidosis: clinical, laboratory, and immunologic aspects. Semin Roentgenol 1985; 20:340-55. [PMID: 3906901]

17. Caceres M, Sabbaghian MS, Braud R, Wilks S, Boyle M. Pancreatic sarcoidosis: unusual presentation resembling a periampullary malignancy. Curr Surg 2006; 63:179-85. [PMID: 16757369]

18. Committee AEW. Statement on sarcoidosis. Am J Respir Crit Care Med 1999; 160:736-55. [PMID: 10430755]

19. Tang S-j, Wu R, Bhaijee F. Gastrointestinal Sarcoidosis and Gastric Melanosis. Video journal & encyclopedia GI endoscopy 2014.

20. Owen N, Sohaib S, Peppercorn P, Monson J, Grossman A, Besser G, Reznek RH. MRI of pancreatic neuroendocrine tumours. Br J Radiol 2001; 74:968-73. [PMID: 11675319]

21. Shukla M, Hassan MF, Toor V, Kaur J, Solomon C, Cohen H. Symptomatic pancreatic sarcoidosis. Case report and review of literature. JOP 2007; 8:770-4. [PMID: 17993729]

22. Nickerson D. Boeck's Sarcoid: Report of Six Cases in which Autopsies Were Done. Arch Path 1937; 24:19.

23. Curran Jr J, Curran Sr J. Boeck's sarcoid of the pancreas. Surgery 1950; 28:574. [PMID: 14776666]

24. Mayock RL, Bertrand P, Morrison CE, Scott JH. Manifestations of sarcoidosis: analysis of 145 patients, with a review of nine series selected from the literature. Am J Med 1963; 35:67-89. [PMID: 14046006]

25. Scatarige JC, Horton KM, Sheth S, Fishman EK. Pancreatic parenchymal metastases: observations on helical CT. AJR Am J Roentgenol 2001; 176:695-9. [PMID: 11222207]

26. Noguchi H, Hirai K, Seo A, Yoshitake M, Sakai T, Abe H, Hidaka R, et al. Sarcoidosis accompanied by pancreatic impairment. Intern Med 1993; 32:15-20. [PMID: 8495038]

27. Thermann P, Dollinger MM. Extrapulmonary sarcoidosis: gastrointestinal involvement -case report and review of literature. Z Gastroenterol 2016; 54:238-44. [PMID: 27043887]

28. Ohana G, Melki Y, Rosenblat Y, Kravarusic D, Weil R. Pancreatic sarcoidosis mimicking a malignant tumour. Eur J Surg 2002; 168:513-5. [PMID: 12549696]

29. Siavelis HA, Herrmann ME, Aranha GV, Garcia G, Eubanks T, Reyes CV. Sarcoidosis and the pancreas. Surgery 1999; 125:456-61. [PMID: 10216537]

30. Ryrie D. Sarcoidosis with obstructive jaundice. Proc R Soc Med 1954; 47:879. [PMID: 13215528]

31. McCormick P, Malone D, FitzGerald M, FitzGerald O. Pancreatitis in sarcoidosis. Br Med J (Clin Res Ed) 1985; 290:1472. [PMID: 3922537]

32. Sagalow BR, Miller CL, Wechsler RJ. Pancreatic sarcoidosis mimicking pancreatic cancer. J Clin Ultrasound 1988; 16:131-4. [PMID: 3130406]

33. Mayne AIW, Ahmad J, Loughrey M, Taylor MA. Sarcoidosis of the pancreas mimicking adenocarcinoma. BMJ Case Rep 2013; 2013:bcr2013009118. [PMID: 23784760]

34. Soyer P, Gottlieb L, Bluemke DA, Fishman E. Sarcoidosis of the pancreas mimicking pancreatic cancer: CT features. Eur J Radiol 1994; 19:32-3. [PMID: 7859757]

35. Wijkstrom M, Bechara RI, Sarmiento JM. A rare nonmalignant mass of the pancreas: case report and review of pancreatic sarcoidosis. Am Surg 2010; 76:79-84. [PMID: 20135945]

36. Okoro N, Moldovanyi C, Wehbi M, Obideen K. Sarcoidosis masquerading as pancreatic cancer. Pract Gastroenterol 2006; 30:83.

37. Papowitz AJ, Li JK. Abdominal sarcoidosis with ascites. Chest Journal 1971; 59:692-5. [PMID: 5087945]

38. Chaun H, King D, Gofton J, Sutherland W, Bogoch A. Sarcoidosis of the pancreas. Am J Dig Dis 1972; 17:725-30. [PMID: 5065301]

39. Caldwell JH, Evans WE. Granuloma (sarcoid?) of the pancreas. A case report. Am J Gastroenterol 1978; 69:320-2. [PMID: 665651]

40. Tsou E, Romano M, Kerwin D, Soteropoulos G, Katz S. Sarcoidosis of anterior mediastinal nodes, pancreas, and uterine cervix: three unusual sites in the same patient. Am Rev Respir Dis 1980;122:333-8. [PMID: 7416610]

41. Sarcoidosis P, Maher L, Choi H, Dodds WJ. Noncaseating Granulomas of the Pancreas. Probable sarcoidosis. Am J Gastroenterol 1981;75:222-225. [PMID: 7234846]

42. Friedman HZ, Weinstein RA. Sarcoidosis of the pancreas. Arch Intern Med 1983;143:2182-2183. [PMID: 6639240]

43. Robaszkiewicz M, Cauvin J, Nousbaum J, Geier B, Volant A, Gouerou H. [Pancreatic sarcoidosis]. Gastroenterol Clin Biol 1989;13:302-304. [PMID: 2659419]

44. Stampfl DA, Grimm IS, Barbot DJ, Rosato FE, Gordon SJ. Sarcoidosis causing duodenal obstruction. Dig Dis Sci 1990;35:526-532. [PMID: 2180656]

45. Brady MS, Garfein CF, Klimstra D, Brenann MF. Sarcoidosis of the pancreas. Journal of surgical oncology. 1993;54(2):132-7.

46. Toda K, Souda S, Yoshikawa Y, Momiyama T, Ohshima M. Narrowing of the distal common bile duct and the portal vein secondary to pancreatic sarcoidosis. Am J Gastroenterol 1994;89:1259-1261. [PMID: 8053449]

47. Espinoza-Aguilar E, Alcala T, Fuentes Q, Sanchez-Vizcaino S, Aguilar-Tablada C, Galvan T. Sarcoidosis simulado carcinoma de cabeza de pancreas. Rev Esp Enferm Dig 1996;88:221-222. [PMID: 8645518]

48. Garcia C, Kumar V, Sharma O. Pancreatic sarcoidosis. Sarcoidosis Vasc Diffuse Lung Dis 1996;13: 28-32. [PMID: 8865406]

49. Rodriguez J, Dyck W. An unusual case of sarcoidosis presenting as a pancreatic mass. The Am J Gastroenterol 1996;91: 2253-2254. [PMID: 8855773]

50. Snook B, Duggan M, Birkett D. Sarcoidosis of the pancreas: a case report. Am Surg 1996;62:947-948. [PMID: 8895719]

51. Frank JL, Goldman M, Nathanson I, Pierangelo D, Kaufman JL, Freeman JK, Reed WP. Surgical management of pancreatic sarcoid. Eur J Surg 2001;167:68-72. [PMID: 11213826]

52. Cook J, Spees T, Telefus P, Ranaudo JM, Carryl S, Xiao P. Pancreatic sarcoidosis discovered during Whipple procedure. J Surg Case Rep 2013;2013:rjt016. [PMID: 24964428]

53. Yamaguchi K, Sato N, Minagawa N, Matsumura M, Mori Y, Tamura T, Shibao K, et al. Sarcoidosis in a patient with a circumportal pancreas with a retroportal main pancreatic duct: a case report. Pancreas 2013;42:1197-1199. [PMID:24048464]

54. Zhang L-N, Xue Q-L, Wang J-X. Mimicking pancreatic malignancy: a systemic sarcoidosis. Ann Saudi Med 2013;34:70-74. [PMID:24658558]

55. Myers J, Tazelaar H. Challenges in pulmonary fibrosis: 6• Problematic granulomatous lung disease. Thorax 2008;63:78-84. [PMID: 18156572]

56. Judson MA. The diagnosis of sarcoidosis. Clin Chest Med 2008;29:415-427. [PMID: 18539235]

57. Judson MA, Thompson BW, Rabin DL, Steimel J, Knattereud GL, Lackland DT, Rose C, et al. The diagnostic pathway to sarcoidosis. Chest 2003;123:406-12. [PMID: 12576358]

58. Heinle R, Chang C. Diagnostic criteria for sarcoidosis. Autoimmun Rev 2014;13:383-387. [PMID: 24424172]

59. Baughman RP, Culver DA. Sarcoidosis. Lacet 2003; 36:xv [PMID: 26593148]

60. McCormick P, O'Donnell M, McGeeney K, FitzGerald O, McCormick D, FitzGerald M. Sarcoidosis and the pancreas. Ir J Med Sci 1988;157:181-183. [PMID: 2460419]

61. Atwal T, Gleeson FC. Solid Pancreatic Masses: Not Always Adenocarcinoma. Gastroenterol Hepatol (N Y) 2012;8: 853-854. [PMID: 24693277]

62. Merkle E, Boaz T, Kolokythas O, Haaga J, Lewin J, Brambs H. Metastases to the pancreas. Br J Radiol 1998;71:1208-1214. [PMID: 10434919]

63. Jarufe N, McMaster P, Mayer A, Mirza D, Buckels J, Orug T, Tekin K et al. Surgical treatment of metastases to the pancreas. Surgeon 2005;3:79-83. [PMID: 15861941]

64. Baroni RH, Pedrosa I, Tavernaraki E, Goldsmith J, Rofsky NM. Pancreatic sarcoidosis: MRI features. J Magn Reson Imaging 2004;20:889-893. [PMID: 15503350]

65. ErichHübner NPA. CT in the differentiation of pancreatic neoplasms–progress report. Dig Dis 2004;22:6-17. [PMID: 15292690]

66. Salavati A, Promteangtrong C, Torigian D, Alavi A. The evolving role of PET/CT and PET/MRI in the management of sarcoidosis. Society of Nuclear Medicine Annual Meeting Abstracts; 2014: Soc Nuclear Med.

67. Palaniappan S, Arvind M, Dinesh J, Melpakam S, Vijaya S, Venkataraman J, Rela M. Role of endoscopic ultrasound-guided fine-needle aspiration in the diagnosis of space occupying lesions of the pancreas. J Gastrointest Endosc 2014; 5:110.

68. Michael H, Ho S, Pollack B, Gupta M, Gress F. Diagnosis of intra-abdominal and mediastinal sarcoidosis with EUS-guided FNA. Gastrointest Endosc 2008;67:28-34. [PMID: 18155422]

69. Tian MC, Guo W, Lei S. Evaluation of endoscopic ultrasound-guided fine needle aspiration of space-occupying lesion of the pancreas. Endoscopy 2011; 43:A17.

70. Basturk O, Coban I, Adsay NV. Pancreatic cysts: pathologic classification, differential diagnosis, and clinical implications. Arch Pathol Lab Med 2009;133:423-438. [PMID: 19260748]

71. Puri R, Thandassery RB, Eloubeidi MA, Sud R. Diagnosis of isolated pancreatic tuberculosis: the role of EUS-guided FNA cytology. Gastrointest Endosc 2012;75:900-9004. [PMID: 22440205]

72. Puri R, Mangla R, Eloubeidi M, Vilmann P, Thandassery R, Sud R. Diagnostic yield of EUS-guided FNA and cytology in suspected tubercular intra-abdominal lymphadenopathy. Gastrointest Endosc 2012;75:1005-1010. [PMID: 22421494]

73. Gupta P, Guleria S, Agarwal S. Role of endoscopic ultrasound guided FNAC in diagnosis of pancreatic TB presenting as mass lesion: A case report and review of literature. Indian J Tuberc 2011;58:120-124. [PMID:21941951]

74. Sharma V, Rana SS, Bhasin DK. Endoscopic ultrasound guided fine needle aspiration for diagnosis of pancreatic tuberculosis. JOP 2013;14:521. [PMID: 24018601]

75. Huffdtutter J, Huffstutter J. Hypercalcemia from sarcoidosis successfully treated with infliximab. Sarcoidosis Vasc Diffuse Lung Dis 2012;29:151-52. [PMID: 23311123]

76. Grutters J, van Den Bosch J. Corticosteroid treatment in sarcoidosis. Eur Respir J 2006;28:627-636. [PMID: 16946094]

77. Eklund A, Bois R. Approaches to the treatment of some of the troublesome manifestations of sarcoidosis. J Intern Med 2014;275:335-349. [PMID: 24433397]

78. Lynch 3rd J, McCune WJ. Immunosuppressive and cytotoxic pharmacotherapy for pulmonary disorders. Am J Respir Crit Care Med 1997;155:395-420. [PMID: 9032171]

79. Ayyala US, Padilla ML. Diagnosis and treatment of hepatic sarcoidosis. Curr Treat Options Gastroenterol 2006;9:475-483. [PMID: 17081481]

80. O'Connor AS, Navab F, Germain MJ, Freeman JK, Mulhern JG, O'Shea MH, Lipkowitz GS, et al. Pancreatitis and Duodenitis from Sarcoidosis: Successful Therapy with Mycophenolate Mofetil. Digestive diseases and sciences. 2003;48:2191-2195. [PMID: 14705827]

81. Vorselaars AD, Verwoerd A, van Moorsel CH, Keijsers RG, Rijkers GT, Grutters JC. Prediction of relapse after discontinuation of infliximab therapy in severe sarcoidosis. Eur Respir J 2014;43:602-609. [PMID: 23988768]

82. Lower EE, Baughman RP, Kaufman AH. Rituximab for refractory granulomatous eye disease. Clin Ophthalmol 2012;6:1613-1618. [PMID: 23055686]

83. Baughman R, Sweiss N. Rituximab for refractory pulmonary sarcoidosis. Am J Respir Crit Care Med 2012;185:A3640.

84. Sweiss NJ, Lower EE, Mirsaeidi M, Dudek S, Garcia JG, Perkins D, Finn PW, et al. Rituximab in the treatment of refractory pulmonary sarcoidosis. Eur Respir J 2014;43:1525-1528. [PMID: 24488568]

85. Abdullah RR, Wells AU, Renzoni EA, Morar N, Maher TM, Keir GJ. Infliximab: An effective rescue therapy in refractory extra-pulmonary sarcoidosis. Eur Respir J 2013; 42:P3792.