Eruptive Xanthoma in Acute Pancreatitis: A Systematic Review of Case Reports

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ABSTRACT

Background: *Eruptive xanthoma is a skin lesion caused by localized lipid deposits in the dermis, characterized by an eruption of yellow papules typically present on the buttocks, shoulders, and extensor skin surfaces of the extremities. Eruptive xanthoma is associated with acute pancreatitis as a result of hypertriglyceridemia or other lipid disorders. This study aims to discuss several case reports of patients with eruptive xanthomas and acute pancreatitis to provide descriptions and similarities between cases.*

Methods: *This systematic review was conducted using Preferred Reporting Items for Systematic Reviews and Meta-analysis guidelines. Case reports about eruptive xanthoma and acute pancreatitis are included in this systematic review. The literature search was done using PubMed, EBSCOHost, ProQuest, and Google Scholar. Critical evaluation for case reports by Joanna Briggs Institute is used for risk of bias assessment.*

Results: *A literature search identified 6 case reports after eliminating irrelevant and duplicated studies. All assessed case reports reported similar dermatologic manifestations of eruptive xanthoma. Majority of patients reported severe acute abdominal pain as the main symptom of acute pancreatitis. All studies showed an increased level of lipid profiles, and other diagnostic workups support the diagnosis of eruptive xanthoma and acute pancreatitis. Risk of bias in case reports included was acceptable.*

Conclusion: *Eruptive xanthomas can be found in patients with acute pancreatitis with correlation to hypertriglyceridemia and lipid disorders. Proper recognition, diagnosis, and treatment for eruptive xanthoma and acute pancreatitis should be kept in mind for practitioners.*

Keywords: *Eruptive xanthoma, acute pancreatitis, systematic review*

ABSTRAK

Latar Belakang: *Eruptive xanthoma merupakan lesi kulit akibat deposit lipid terlokalisir pada dermis, dengan karakteristik erupsi papul kekuningan biasanya muncul pada bokong, bahu, dan ekstensor ekstremitas. Eruptive xanthoma dihubungkan dengan pankreatitis akut sebagai hasil dari hipertrigliseridemia dan gangguan lipid lainnya. Tujuan dari studi ini adalah membahas beberapa laporan kasus pasien dengan eruptive xanthoma dan pankreatitis akut untuk memberikan deskripsi dan persamaan antar kasus.*

Metode: *Tinjauan sistematis ini dibuat menggunakan pedoman PRISMA. Laporan kasus mengenai pasien dengan eruptive xanthoma dan pankreatitis akut dimasukkan dalam studi. Pencarian literatur menggunakan database PubMed, EBSCOHost, ProQuest, dan Google Scholar. Daftar penilaian evaluasi kritis untuk laporan kasus yang dibuat oleh JBI digunakan untuk penilaian risiko bias.*

Hasil : *Pencarian literatur mendapatkan 6 laporan kasus setelah mengeliminasi studi yang tidak relevan dan duplikat. Semua laporan kasus melaporkan manifestasi dermatologis yang sesuai dengan eruptive xanthoma. Sebagian besar pasien melaporkan gejala nyeri perut akut berat sebagai gejala utama pankreatitis akut. Semua studi menunjukan peningkatan profil lipid dan hasil pemeriksaan lain mendukung diagnosis dari eruptive xanthoma dan pankreatitis akut. Risiko bias dari laporan kasus yang digunakan dinilai dapat diterima untuk dijadikan sebagai bagian dari telaah sistematis.*

Kesimpulan : *Eruptive xanthoma dapat ditemukan pada pasien dengan pankreatitis akut dengan adanya korelasi terhadap hipertrigliseridemia dan gangguan profil lipid. Pengenalan akan gejala, diagnosis, dan tatalaksana yang baik untuk eruptive xanthoma dan pankreatitis akut perlu diketahui oleh para dokter.*

Kata Kunci : *Eruptive xanthoma, pankreatitis akut, telaah sistematis*

INTRODUCTION

Eruptive xanthoma is one of the clinical features of xanthoma.[1] Xanthomas are isolated lipid deposits in the skin dermis, and the typical skin lesions are associated with hypertriglyceridemia and other primary or secondary lipid metabolism disorders.[2] Eruptive xanthoma is marked by an eruption of yellowish papules, surrounded by an erythematous halo, which typically appears on the buttocks, shoulders, and extensor surfaces of the extremities.[3] The development of eruptive xanthoma is associated with acute pancreatitis as a result of hypertriglyceridemia. The estimated prevalence of eruptive xanthomas is 18 occurrences per 100,000 individuals with hypertriglyceridemia, and the third most common cause of acute pancreatitis is hypertriglyceridemia.[4] The prevalence of hypertriglyceridemia-induced pancreatitis reported to be as high as 22%.[5]

Acute pancreatitis involves the acute inflammation of the pancreas.[6] One of the typical signs is abdominal pain, which usually begins in the epigastric and radiates to the back. It is characterized as a very intense, acute pain and is linked to nausea and vomiting. The severity of acute pancreatitis can range significantly, from mild cases requiring conservative treatment to severe and complex conditions.[7]

As mentioned before, eruptive xanthomas are correlated with acute pancreatitis from the complication of lipid disorder. Therefore, it is important to know eruptive xanthomas as a clinical sign of hypertriglyceridemia as one of the common etiologies of acute pancreatitis. This review discussed several case reports of patients with eruptive xanthomas and acute pancreatitis to provide descriptions and similarities between cases.

METHODS

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement. The protocol for this review is registered with PROSPERO (CRD42024531794). The literature search was done using four databases: PubMed, ProQuest, EBSCO, and Google Scholar, using "eruptive xanthoma" and "acute pancreatitis" as the main keywords. Additional hand-searching was conducted to identify any available unpublished studies. No time restriction is applied. The result of the search was imported to EndNoteX9 and the duplicates were removed.

The inclusion criteria of the study were case reports about patients with eruptive xanthoma and acute pancreatitis at any time published and written in English. The exclusion criteria were articles that did not provide full-text, literature review, and systematic review methods and were not in English. All case report outcomes were assessed for risk of bias using the critical evaluation checklist for case reports by Joanna Briggs Institute (JBI). Each appraisal criterion could be marked as "Yes," "No," "Unclear," or "Not Applicable." Each item was scored as 1 (Yes) or 0 (No/Unclear/Not Applicable), resulting in a total score out of 8. The case report was considered acceptable and included in the systematic review if it met 5 of the 8 appraisal criteria.

Results that meet the inclusion criteria were independently reviewed by at least 2 reviewers. The reviewers selected literacy according to the inclusion criteria for this study. Disagreements arising from the process of the evaluation were all resolved by discussion among the review team. Reviewers identified potential studies by screening abstracts and journal articles for inclusion, assessing the full text for eligibility criteria, and then including the relevant studies.

RESULT

Literature was searched and 70 articles were found, with no unpublished studies identified. Thirty five articles were screened after removing the duplications, and excluded 28 articles. Six case reports on eruptive xanthoma in acute pancreatitis were selected after assessing full text as per eligibility criteria. The process for establishing search criteria, selecting studies, and determining exclusions is illustrated in **Figure 1.**

All cases originated from different countries including Turkey, Japan, Spain, United States, India, and Poland. All patients were male with ages ranging from 26 to 54 years.

Patient Clinical Manifestations

All cases reported severe acute abdominal pain as the main symptom of acute pancreatitis, with one exception case from Innue-nishimoto, et al. since no clinical manifestation stated for acute pancreatitis symptoms.[9] The locations of pain reported were in the upper abdomen, specifically epigastric, left hypochondrium, with some radiates to the back. All cases reported the same complaints of multiple yellow bumps or papules before they complained of acute abdominal pain. The majority of lesions reported were on the extremities, with some reported on the trunk and buttocks. One case from Innue-nishimoto, et al. reported the skin lesion is also pruritic.[9] Further information about patient clinical manifestations in selected case reports is provided in Table 1.

Dermatologic Status

The dermatologic manifestations in all assessed case reports reported multiple yellow papules, some colored brown and erythematous, with size reported ranging from 3 to 6 mm, located mostly in extremities, with some on the shoulders, chest, abdomen, and buttocks. A case by Bujny et al. found a skin lesion with raised domes and pink envelope which was initially misdiagnosed as molluscum contagiosum.[13] Full description of dermatologic manifestations in selected case reports is written in Table 1.

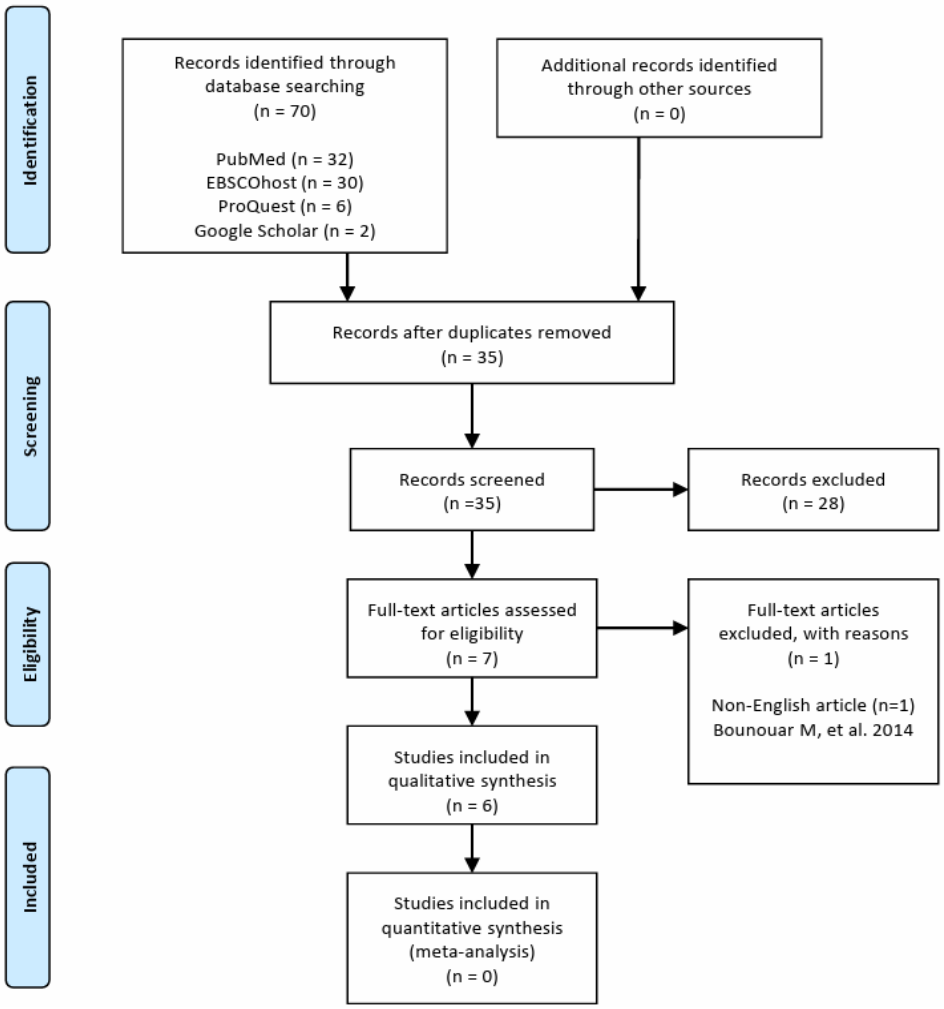

Figure 1. Flow diagram of identification and selection of studies

Table 1. Description of the patient's characteristics

Author, year, and title	Patient	Clinical Manifestations	Dermatologic manifestations	Investigations done	Interventions	Results
Duzayak et al. 2017.[8] Acute pancreatitis with eruptive xanthoma.	Age : 27 years Gender : Male Place : Turkey	Multiple yellowish-brown bumps on arms and legs for 6 months. Severe abdominal pain 6 days later on the second admission.	Multiple yellowish papules ranging 3-6 mm in arms, elbows, and thighs.	Laboratories (TGA, TC, HDL, LDL, AST, ALT, FBG, HbA1c), HP, IHC, Leukocyte count, CRP, amylase, Abdominal US, Abdominal CT scan.	Gemfibrozil, Metformin, TPE with FFP, and albumin via double membrane filtration.	Eruptive xanthoma completely disappeared after 6 months.
Innue-nishimoto et al. 2016.[9] Eruptive Xanthoma with Acute Pancreatitis in a Patient with Hypertriglyceridemia and Diabetes.	Age : 41 years Gender : Male Place : Japan Comorbidities : DM, hyperlipidemia, hypertriglyceridemia	Pruritic, erythematous papules for 2 weeks. Diagnosed with acute pancreatitis on the admission with no clinical manifestations stated.	Multiple yellowish, erythematous papules approximately 5-mm, on the trunk and extensor surfaces of the extremities.	Laboratories (Leukocyte count, ALP, CRP, HbA1c, amylase, lipase, TGA, TC, HDL, LDL, Apo A-I, Apo A-II, Apo B, Apo E, Apo C-II, Apo C-III), HP.	Fasting, nafamostat mesilate, ulinastatin, bezafibrate.	Improvement of acute pancreatitis after 16 days. Eruptive xanthoma, Serum triglyceride and total cholesterol values within normal range after 1.5 months.
Martinez et al. 2008.[10] Eruptive xanthomas and acute pancreatitis in a patient with hypertriglyceridemia	Age : 33 years Gender : Male Place : Spain	Acute pain in the left hypochondrium and vomiting. Papular dermatosis and diabetic symptoms 10 days prior admission.	Multiple white-yellowish papules on the lower limbs, buttocks and thorax.	Laboratories (Leukocyte count, CRP, urinary glucose and ketone, RBG, amylase, lipase, bilirubin, TGA), HP, Abdominal CT.	Saline solution, intravenous insulin and analgesia, fibrates.	Pain and hyperglycemic symptoms were controlled rapidly. No further follow-ups about xanthomas progression stated.
Makdsi et al. 2010.[11] Acute Pancreatitis with Eruptive Xanthomas.	Age : 54 years Gender : Male Place : United States Comorbidities : Type 2 DM	One day history of epigastric abdominal pain with 1 month history of tender nonpruritic rash on right elbow, abdomen, buttocks, posterior thighs, and knees.	Multiple yellow waxy papules on the extensor surfaces of arms, abdomen, thighs, knees, and buttocks.	Laboratories (Lipase, TGA, HbA1c), Abdominal CT scan.	Dietary and pharmacologic. No specific interventions stated.	Improvements at outpatient follow-up 2 weeks later.
Rohith et al. 2021.[12] Hypertriglyceridemic pancreatitis with eruptive xanthomas.	Age: 26 years Gender: Male Place: India	Two day history of severe upper abdominal pain radiating to the back with fever, low blood pressure, and tachycardia.	Multiple yellowish papular lesions over the extensor surface of bilateral forearms, arms, and dorsum of hands.	Laboratories (leukocyte count, amylase, lipase, TGA, TC, HDL), Abdominal CT scan.	Fasting, aggressive intravenous fluid resuscitation, intravenous heparin and insulin, followed by oral.	Hemodynamically stabilized and no further episodes after 1-year follow-up.
Bujny et al. 2014.[13] Skin lesion in the form of eruptive xanthomasas - a first manifestation of severe hyperlipidemia complicated by acute pancreatitis in a patient with newly diagnosed type 2 diabetes.	Age: 40 years Gender: Male Place: Poland	Severe pain in upper abdomen and radiating to the back with deterioration after meal, Increased thirst, polyuria, sleepiness, numerous follicular changes in skin of arm.	Multiple follicular changes of light brown and yellow with pink envelope and raised domes without skin irritation on the shoulders, arms, elbows, buttocks and knees.	Laboratories (TC, TGA, serum amylase, urinary amylase, CRP, RBG, full blood count, liver function, kidney function), Abdominal US, Chest X-ray, ECG, Abdominal CT scan.	Painkillers, fat-restricted diet, fluid therapy, fenofibrate, simvastatin, insulin, metformin, omega 3	Patient was discharged home with instruction. Improvements in lipid profile and skin lesion within a month.

Abbreviations. TGA: Triglycerides; TC: Total Cholesterol; HDL: High-density Lipoprotein Level; LDL: Low-density Lipoprotein Level; AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase; FBG: Fasting Blood Glucose; RBG: Random Blood Glucose; ALP: alkaline phosphatase; CRP: C-Reactive Protein; Apo: Apolipoprotein; HP: Histopathology; IHC: Immunohistochemistry; US: Ultrasound; CT: Computed Tomography; TPE: Therapeutic plasma Exchange; FFP: Fresh Frozen Plasma.

Comorbidity

Most of the case reports showed the symptoms that are associated with type 2 Diabetes Mellitus as one of comorbidities that arise from these patients. Only one case report stated that the patient had no history of diabetes mellitus from Rohith et al..[12] Furthermore, two patients presented in these cases were obese in cases from Bujny et al. and Duzayak et al..[8,13] High lipid profiles such as hypertriglyceridemia or hyperlipidemia were also found in all cases.

Further Workups

All cases included in this review used laboratories as further workups for the diagnosis of eruptive xanthomas and acute pancreatitis. Lipid profiles were checked in all studies, specifically as triglycerides (TGA) in all studies, high-density lipoprotein (HDL) in 3 studies,[8,9,12] low-density lipoprotein (LDL) in 2 studies,[8,9] total cholesterol (TC) in 4 studies,[8,9,12,13] and apolipoproteins in 1 case by Innue-nishimoto et al.[9] All studies showed an increased level of lipid profiles. Detailed information about the laboratory results is summarized in Table 2.

Serum amylase and lipase were checked in 3 studies for laboratory diagnosis of acute pancreatitis.[8,9,12] In other cases, Makdsi et al. only checked serum lipase alone,[11] and serum amylase alone was performed in Duzayak et al. and Bujny et al..[8,13] All studies revealed an increased levels of serum amylase and lipase, except for serum amylase levels in Bujny et al..[13] However, urinary amylase and abdominal ultrasonography (US) were also performed by Bujny et al., with the result of high amylase concentration (1,180 mg/dL) and non-diagnostic for the ultrasound. [13] Five studies included abdominal computed tomography (CT) scans for imaging investigation. All CT results had similar results of thickening or enlarged pancreatic size. [8,10-13] Detailed CT scan results in case reports included are reported in Table 3.

In three cases, the patient underwent histopathology for definitive diagnosis of eruptive xanthoma.[8-10] All histopathology results showed foam cells distributed in the dermis. The result from Duzayak et al. revealed vacuolar cytoplasmic histiocytes and lymphocytes infiltration that distributed in the collagen fibres in the middle and upper dermis.[8] Inuoe-nishimoto et al. also revealed foamy cells that infiltrated the dermis with extracellular lipids.[9] Martinez et al. showed a similar appearance of a group of histiocytes with froth-like cytoplasm.[10] Detailed information of histopathology results is available in Table 3. Duzayak et al. also added Immunohistochemistry with the results of histiocytes stained positively with Cluster of Differentiation 68 (CD68).[8]

Additional workups for the diagnosis of Diabetes Mellitus in patients include fasting blood glucose (FBG), random blood glucose (RBG), and glycated hemoglobin (HbA1c). RBG was obtained in study from Martinez et al. and Bujny et al.,[10,13] while Duzayak et al. used FBG.[8] HbA1c was obtained in 3 cases by Martinez et al., Innue-nishimoto et al., and Makdsi et al.[9-11] In addition, Martinez et al. also added urinary glucose and ketone.[10] All studies showed marked increase in blood glucose level and HbA1c. Detailed laboratory results are available in Table 2.

Other workups in the cases mentioned were complete blood count (in Bujny et al.[13]) and leukocyte count in 4 studies,[8-10,12] C-reactive protein (CRP) level in 4 studies, [8-10,13] and alkaline phosphatase (ALP) in 1 study by Innue-nishimoto et al.[9] Liver functions (aspartate aminotransferase or AST, alanine aminotransferase or ALT) were tested in 2 studies.[8,13] Additionally, Duzayak et al. also used Abdominal US for liver imaging.[8] Bujny et al. added other workups including kidney functions, Chest x-ray and electrocardiography (ECG).[13]

Treatment

Several treatments were provided, both pharmacological and non-pharmacological. Most pharmacological drugs were given such as fibrates, lipid-lowering therapy, and antidiabetic drugs. Some of the case reports reported the other medicines that had been given besides those drugs mentioned earlier, such as painkillers, omega 3, anticoagulants, and other anti-inflammatory drugs like ulinastatin in Nishimoto et al..[9] Three studies reported intravenous fluid therapy or saline solution as another pharmacological treatment for those patients.[10,12,13] At first, the patients were given an intravenous route of fluid therapy, as the conditions improved, they were given fluid via oral route. Another study also reported pharmacological therapy with Therapeutic Plasma Exchange (TPE) with albumin and fresh frozen plasma with double membrane filtration according to Duzayak et al..[8]

Some studies like Nishimoto et al. and Rohith et al. suggested that the patient did fasting.[8,12] A study by Bujny et al. suggested the patient did the fat-restriction diet to control lipid profile, triglyceride, and blood glucose.[13]

Results and Follow-ups

The results were remarkable, with all studies reported the treatment brought success with resolution of symptoms and disappearance of eruptive xanthoma within a variable period. Study by Makdsi et al. reported that symptoms of acute pancreatitis and dermatological lesion were improved after 14 days while Nishimoto et al. reported that the symptoms of acute pancreatitis improved after 16 days and eruptive xanthoma disappeared within 1,5 months.[9,11] Bujny et al. also reported that the skin lesion improved and the lipid profile normalized in one month.[13] Studies from Duzayak et al. and Rohith et al. stated that the eruptive xanthoma disappeared within 6 months and 1 year, respectively.[8,12]

Risk of Bias Assessment

Table 4 displays the bias risk evaluated with Critical Appraisal Checklist for Case Reports. All of the studies included information for the patient demographic criteria and clear description of the patient's history. Five of six studies clearly described the patient's present clinical condition. All studies clearly described diagnostic tests or assessment methods and results. Four studies had given a solid explanation of intervention and therapy processes. All studies had given detailed information of post-intervention clinical conditions, but none of them explained adverse or unanticipated events in the study. Lastly, half of the studies provided takeaway lessons from the case. Overall, most case reports adequately detailed the patient's demographics, clinical history with timeline, current condition at presentation, diagnostic procedures, and outcomes. Following the criteria, all six case reports were deemed acceptable and included in this systematic review.

Table 2. Laboratory results in patients included

Study ID	TGA	TC	HDL	LDL	serum Amylase	Serum Lipase	RBG	FBG	HbA1c
Duzayak et al. 2017. [8]	105 (0.25-5) mmol/L	11.5 (2.8-5) mmol/L	3.8 mmol/L	0.3 mmol/L	110 (28-100) U/L	N/A	N/A	4.3 (1.8-2.5) mmol/L	54.1 (20-42 mmol/mol)
Innue-nishimoto et al. 2016. [9]	6784 (30-150) mzg/dL	803 (130-219) mg/dL	12 (42-74) mg/dL	23 (70-140) mg/dL	340 (40-130) U/L	960 (11-53) U/L	N/A	N/A	9.2 (4.6-6.2)%
Martinez et al. 2008.[10]	2350 mg/dL	N/A	N/A	N/A	Increased	Increased	310 mg/ dL	N/A	N/A
Makdsi et al. 2010. [11]	6200 mg/dL	N/A	N/A	N/A	N/A	852 (8-78) mcg/L	N/A	N/A	12.7%
Rohith et al. 2021. [12]	2928 mg/dL	601 mg/dL	105 mg/ dL	N/A	546 mg/dL	346 mg/ dL	N/A	N/A	N/A
Bujny et al. 2014. [13]	3755 mg%	694 mg%	45 mg%	N/A	28 mg/dL	N/A	140 mg/dL	N/A	N/A

N/A: not available; Reported normal values are within the brackets

Table 3. Histopathology of skin lesion and Abdominal CT scan results performed in selected cases

Study ID	Skin Lesion Histopathology	Abdominal CT scan
Duzayak et al. 2017. [8]	Vacuolar cytoplasmic histiocytes (foam cells) and lymphocytic infiltration that distributed in the collagen fibers on the upper and middle dermis.	Thick hypodense pancreatic tail, dirty infiltrate, minimal local fluid on peripancreatic fatty planes.
Innue-nishimoto et al. 2016. [9]	foamy cells that infiltrated the dermis with extracellular lipids.	Not performed.
Martinez et al. 2008.[10]	Clusters of histiocytes with froth-like cytoplasm.	Edematous pancreatitis without necrotic areas, abscesses, hemorrhages, or pseudocysts, and fluid accumulation in the pararenal region.
Makdsi et al. 2010. [11]	Not performed.	Extensive inflammatory changes surrounding the head of the pancreas.
Rohith et al. 2021. [12]	Not performed.	Bulky pancreas with multiple intrapancreatic and peripancreatic collections. No signs of necrosis, abscess, or pseudocyst detected.
Bujny et al. 2014. [13]	Not performed.	Enlarged pancreatic head, body, and tail with irregular shape.

Table 4. Critical appraisal of case reports included

Study ID	1. Were patient's demographic characteristics clearly described?	2. Was the patient's history clearly described and presented as a timeline?	3. Was the current clinical condition of the patient on presentation clearly described?	4. Were diagnostic tests or assessment methods and the results clearly described?	5. Was the intervention(s) or treatment procedure(s) clearly described?	6. Was the post-intervention clinical condition clearly described?	7. Were adverse events (harms) or unanticipated events identified and described?	8. Does the case report provide takeaway lessons?	Overall appraisal:
Duzayak et al. 2017. [8]	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Include
Innue-nishimoto et al. 2016. [9]	Yes	Yes	No	Yes	No	Yes	No	No	Include
Martinez et al. 2008. [10]	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Include
Makdsi et al. 2010. [11]	Yes	Yes	Yes	Yes	No	Yes	No	No	Include
Rohith et al. 2021. [12]	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Include
Bujny et al. 2014. [13]	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Include

DISCUSSION

Eruptive xanthomas are skin lesions that occur from local storage of lipids.[14] Eruptive xanthomas represent sudden eruptions of yellow skin papules with an erythematous halo, which typically emerge on the shoulders, butt, and extensor surfaces of the extremities.[15] All cases had a similar manifestation of multiple yellow papules on the extremities, trunk, and buttocks. Majority of cases reported patients were asymptomatic from the lesion except one reported pruritic, which correlates with eruptive xanthomas that majority of lesions are often asymptomatic, but itching and tenderness may also be seen.[14] All patients with eruptive xanthoma in this review also reported hypertriglyceridemia, consistently with the cause of xanthoma. The formation of xanthoma results from accumulations of serum lipoproteins that eventually deposit within the skin. Histopathology of skin lesions reported in several cases showed foamy cells, which are histopathologically characteristic for xanthomas, and several variations of cells and surrounding materials associated with eruptive xanthoma.[1] These findings are consistent with skin deposition of triglycerides or lipids in the eruptive xanthomas.[16] The characteristic appearance of the skin lesion is presented in **Figure 2.**

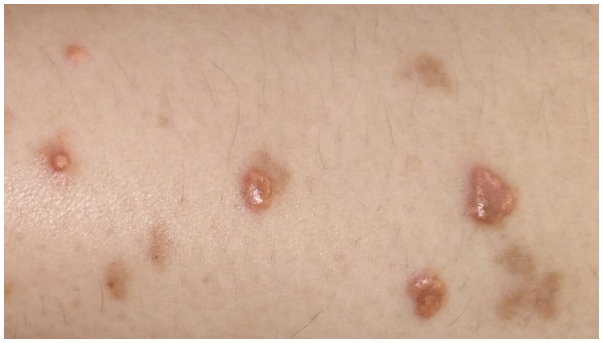

Figure 2. Eruptive xanthoma lesionsImage source: personal documentation

The most common presenting symptom of acute pancreatitis is abdominal pain, with the location in epigastric and often radiation to the back.[5] In this review, all reported cases had severe acute upper abdominal pain with some radiating to the back. Diagnosis of acute pancreatitis other than clinical symptoms includes rise of serum amylase or lipase three times above the upper limit of normal range and pancreatic findings on CT scan or magnetic resonance imaging (MRI). All patients included in this review reported an increase in serum amylase and lipase up to three or more times of normal value. One patient from Bujny et al. had a normal serum amylase but a significant increase of amylase activity in urine. CT scan results reported in cases included are consistent with the morphology classification of acute pancreatitis, with an enlargement of pancreas, pancreatic tissue enhancement, and inflammatory changes of peripancreatic fat, without or with collection of peripancreatic fluid.[5,17] Hypertriglyceridemia can cause acute pancreatitis if the level >1000 mg/dL, which is consistent with the TGA results in all reported cases.

Xanthomas can be found at any age, but mostly occur around 20 years old In people with familial hypercholesterolemia.[18] However in this review, all patients were male with age ranging from 26 to 54 years. Many studies included in this article stated that the patient had an eruptive xanthoma ranging from several days like 10 days until several months like 6 months before admission in which the patient complained of severe acute abdominal pain. This shows that eruptive xanthoma is an early complication of hypertriglyceridemia. This also can be the first sign that appears before developing into acute pancreatitis. The clinician can also be more vigilant about the incidence of acute pancreatitis if the patient

has developed eruptive xanthoma. A study reported characteristics of patients with acute pancreatitis caused by hypertriglyceridemia were predominantly male with 14:7 ratio.[19]

Patients included in this review had a comorbidity of diabetes mellitus and two patients had obesity. Inadequate insulin levels play a significant role in elevating endogenous lipoproteins, such as very low-density lipoprotein (VLDL) and chylomicrons, as well as in the development of xanthomas and atherosclerotic plaques. Diabetes mellitus and obesity further exacerbate insulin deficiency in tissues beyond adipose, stemming from reduced sensitivity due to various factors like lipotoxicity, changes in adipokines, increased proinflammatory cytokines, hexosamine flux, and activation of endoplasmic reticulum signaling. Insulin insufficiency also diminishes the activity of lipoprotein lipase by activating angiopoietin-like protein 3 (ANGPTL3). Heightened ANGPTL3 levels in individuals with hyperglycemia or obesity can lead to elevated serum levels of remnant lipoproteins, chylomicrons, LDL, and VLDL. Also, their overproduction can be induced by lipolysis-derived fatty acid and glycerol. Macrophages can recognize and engulf the infiltrating remnants in the vessel walls or skin. Then it can form foam cells after phagocytosis and are deposited into the skin and vessel walls, which leads to atherosclerosis and eruptive xanthoma.[2]

Treatment of eruptive xanthoma is directed to the underlying causes, which in this case is to decrease the serum triglyceride content, and its regression may take months.[1] In patients with hypertriglyceridemia, treatment should be started with pharmacological interventions using fibrates to reduce triglyceride levels, as used in several cases in this review.[15] Statins also can be used to lower lipid levels, and in emergency situations, TPE is an effective method for rapid recovery.[20] Management of patients with acute pancreatitis is fluid resuscitation to maintain tissue perfusion from depletion of intravascular volume due to fluid retention in pancreatic, peripancreatic, and systemic edema. Isotonic crystalloid formulations are preferred. Fasting to prevent exacerbation of pancreatitis must not be prolonged and should initiate enteral feeding within 24 to 72 hours.[17] Insulin and oral medications are used to treat hyperglycemia and diabetes mellitus in patients as needed.[21]

The study's findings reveal significant correlations between patient demographics, clinical manifestations, dermatological status, comorbidity, further workups, treatment response, and follow-up outcomes. For instance, demographic data (Table 1) highlight patients with acute pancreatitis presenting with eruptive xanthoma have elevated levels of triglycerides (TGA), abnormal lipid profiles, and high serum pancreatic enzyme levels, as shown in Table 2. Histopathological and CT-scan findings across various case reports further support this association. In these patients, histopathology frequently reveals foam-like histiocytic infiltration in skin biopsies, while CT-scan imaging demonstrates inflammatory changes in the pancreas, as summarized in Table 3. Based on the conclusions of the various tables, patients with eruptive xanthoma can develop acute pancreatitis. From our perspective, the findings of our study are consistent with prior literature showing an association between acute pancreatitis and the occurrence of eruptive xanthoma.

Several limitations should be taken into account. Firstly, all studies are case reports, therefore the results presented could have been altered by many biases in the methodology. The sample size in all cases is relatively low. Hence, more case reports related to this review are needed. Additionally, the study does not include non-english case reports, which might limit the comprehensiveness of the study. Lastly, not all studies are uniform or consistent. For example, not all studies performed skin lesion biopsies for the definitive diagnosis of eruptive xanthoma, although eruptive xanthoma can be diagnosed clinically without the use of histopathology.

CONCLUSION

Synthesis and analysis of case reports on eruptive xanthoma in acute pancreatitis are performed in this review. Eruptive xanthomas can be found early before developing symptoms of acute pancreatitis in correlation with hypertriglyceridemia and lipid disorders as the main etiology. Comorbidities such as diabetes mellitus and obesity are related to this case. Proper recognition, diagnosis, and treatment for eruptive xanthoma and acute pancreatitis should be kept in mind for practitioners.

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