Case Report

Emphysematous pancreatitis predisposed by Olanzapine

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ABSTRACT

A 32-year-old male presented to our intensive care unit with severe abdominal pain and was diagnosed as acute pancreatitis after 2 months of olanzapine therapy for bipolar disorder. His serum lipase was 900 u/L, serum triglyceride 560 mg/dL, and blood sugar, fasting and postprandial were 230 and 478 mg/dL, respectively on admission. Contrast enhanced computed tomography (CECT) of abdomen was suggestive of acute pancreatitis. Repeat CECT showed gas inside pancreas and collection in peripancreatic area and patient underwent percutaneous drainage and antibiotics irrigation through the drain into pancreas. We describe the rare case of emphysematous pancreatitis due to development of diabetes, hypertriglyceridemia and immunosuppression predisposed by short duration olanzapine therapy.

Key words: Emphysematous pancreatitis, local metronidazole application, olanzapine

INTRODUCTION

Emphysematous pancreatitis (EP) is a rare life-threatening condition of the pancreas, associated with gas-forming bacteria wherein there is gas formation within or around the pancreas,[1] identified by abdominal computed tomography (CT) scan. Although no definite predisposing factors have been identified, it is seen to be commonly occurring in patients with diabetes mellitus, which predisposes to gas gangrene[2] and tuberculosis (TB) with HIV infection. Until date, only few discrete cases have been reported. Olanzapine is an atypical antipsychotic drug used either alone or in combinations for various psychiatric conditions, e.g., schizophrenia, bipolar disorder or depressive episodes associated with it, treatment of acute resistant depression in adults etc., Besides prominent central nervous system side-effects, some important gastrointestinal/endocrine adverse effects are increased appetite and weight gain, hyperglycaemia, hypertriglyceridemia (HTG) etc., none of which is directly related to EP. Few cases of olanzapine induced oedematous, mild pancreatitis are reported in literature.[3] In our case, the patient developed severe necrotising EP without any of the proposed predisposing factors except intake of olanzapine. To the best of our knowledge, EP triggered by short duration olanzapine has never been reported before. Patient gave written informed consent for reporting this for publication.

CASE REPORT

A 32-year-old male patient, weighing 86 kg (body mass index 30 kg/m^2) diagnosed as a case of bipolar disorder 5 months ago was started on lithium 400 mg daily initially. Even with an incremental dose of lithium over 2 months, he had not improved. Therefore, olanzapine (Oleanz®, SUN Pharmaceutical Industries Ltd., Mumbai, India) 5 mg twice daily was added to his regimen. He had no other co-morbidities and no previous medication history. He was non-alcoholic and non-smoker. He was also complaining of weight gain. After 2 months of starting olanzapine, he developed nausea, vomiting, and severe epigastric pain without any history of haematemesis, melaena and jaundice. There was no previous history of pancreatitis and

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gall stone disease. Family history for diabetes was negative. On examination, he had a heart rate of 105-115/min with blood pressure 110/56 mm Hg and respiratory rate of 24-28/min and was febrile. Abdominal examination demonstrated epigastric tenderness with guarding including normal liver dullness on percussion and absent bowel sound. Ultrasonography (USG) showed bulky pancreas with pancreatic oedema with no peripancreatic collection. Upper gastrointestinal (GI) endoscopy showed no abnormality. His pain was increasing in intensity and referred to back. On the 10th day of pain abdomen, he developed breathlessness and admitted to intensive care unit in view of low arterial O_2 saturation and dyspnoea. All drugs he was on were stopped. Blood investigation showed serum lipase 900 U/L (normal level 10-140 U/L), serum triglyceride 560 mg/dL (normal level <150 mg/dL) and blood sugar (fasting and postprandial) were 230 and 478 mg/dL, respectively with normal serum calcium level. Mild derangement in liver function tests was noticed. His HIV serology status was nonreactive. The patient was put on mask oxygen, later on intubated as arterial blood gas was unfavourable and kept on mechanical ventilation with lung protective strategy. Chest X-ray showed left sided pleural effusion [Figure 1]. Contrast enhanced computed tomography scan abdomen (CECT) on 13th day showed pancreatic necrosis (15%) with oedema and peripancreatic collection, no cholelithiasis or choledocholithiasis with a large pelvic fluid collection[Figure 2]. Pleural effusion was managed with left sided percutaneous drain and pelvic collection with USG guided percutaneous drainage. Inotropic and vasopressor support were continued for 7 days. Repeat CECT on 21th day showed pancreatic necrosis (40-50%) with gas formation in pancreas and peripancreatic areas, suggesting CT severity index 6-7/10 [Figure 3]. The diagnosis of EP was made. Sepsis was managed with appropriate antibiotics. Peripancreatic drain was inserted and culture report from drained fluid showed anaerobic enteric organisms. Intravenous imipenem and clindamycin were administered initially. Later on peripancreatic region was irrigated with metronidazole through percutaneous drain for few days. The patient required sustained low efficiency dialysis on alternate days for acute kidney injury. Hyperglycaemia was controlled with regular insulin infusion. He was extubated after 13 days of mechanical ventilation. Enteral feeding (nasojejunal) was started gradually. On stabilisation, the patient was discharged from the hospital on the 48th day with drug and life style advice for correcting dysglycaemia, dyslipidaemia and increased body weight. Olanzapine was replaced by other drugs.

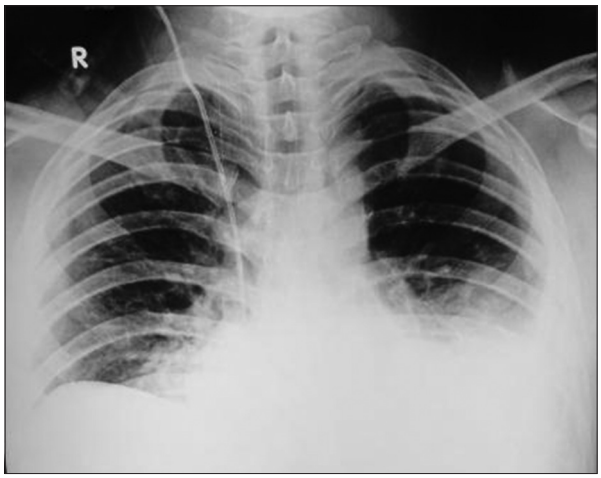

Figure 1: Chest X-ray showing left sided pleural effusion

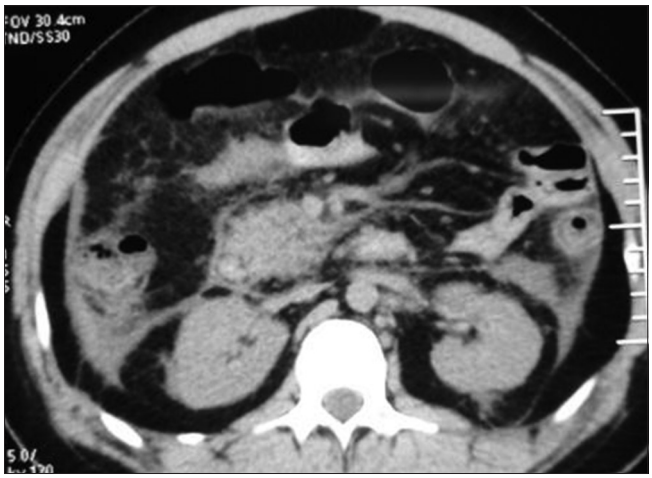

Figure 2: Computed tomography scan abdomen showing oedematous pancreatitis on day 13 of pancreatitis

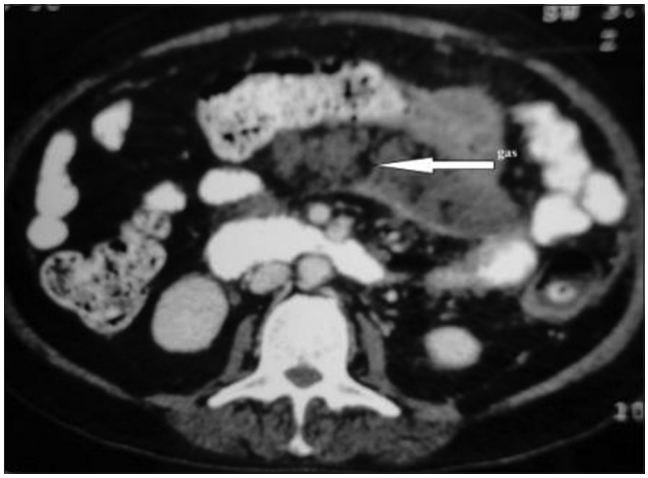

Figure 3: Computed tomography scan of abdomen showing gas formation in pancreas on day 21 of pancreatitis

Subsequently, the patient lost about 15 kg body weight and did not develop symptoms/signs of pancreatitis.

DISCUSSION

Emphysematous pancreatitis is a rare form of acute pancreatitis with gas formation within the pancreas, which occurs mostly in patients with diabetes, compromised immunity due to HIV infection etc., Most commonly implicated organism is *Escherichia coli*.[4] Other organisms are klebsiella, pseudomonas, enterobacter,[5] Clostridium perfringenes[4] and rarely TB. Only few cases have been reported until date.

Olanzapine, an atypical antipsychotic, although has no direct role in the causation of EP can predispose to hyperglycaemia, HTG, diabetes, metabolic syndrome and weight gain. These effects have been attributed/hypothesized to be because of various mechanisms as below: olanzapine promotes fat deposition by directly affecting adipocyte function[6]; it may increase triglyceride levels[7]: it may cause body weight gain and hyperphagia by altering appetite signalling in the brain and periphery.[8]; it disturbs the metabolism by making the body take preferentially its energy from fat (instead of privileging carbohydrates). Due to high residual carbohydrate, insulin resistance develops.[9]; it also alters pancreatic insulin secretion by inhibiting M_3 muscarinic receptors[10] and causes hyperglycaemia.

Solanki *et al*. in their study have reported a role for insulin resistance and hyperglycaemia in predisposing diabetics to acute pancreatitis.[11] Ultimately, hyperglycaemia leads to diabetes, immunosuppression and obesity which can predispose to pancreatitis. HTG is one of the leading causes of acute pancreatitis. Though serum levels >1000 mg/dL predispose to pancreatitis,[12] the moderate HTG probably increased susceptibility in our patient. All these factors might have predisposed to EP. Incidence of drug induced acute pancreatitis is about 0.1-2% of all cases[13] and it is usually reversible when the causative drug is stopped. Drug induced pancreatitis has some common features like temporal association and, known response pattern. Peripancreatic local application of metronidazole is a new approach to increase drug delivery to target site with minimum systemic adverse effects.[14] Though pancreatic penetration of metronidazole after intravenous injection has been found to be highest (99%) in the necrotic tissue,[15] it can also induce pancreatitis in 2% cases.[16] Our patient was already suffering from another drug induced pancreatitis. Additive effect of two drugs causing higher risk of pancreatitis had been reported with olanzapine and lisinopril.[17] Hence, local irrigation with metronidazole is justified here. The patient improved and survived from severe pancreatitis after stoppage of offending drug and conservative management including minimally invasive intervention.

CONCLUSIONS

We have described a rare case of EP in young male due to development of diabetes, HTG and immunosuppression predisposed by olanzapine. This drug should be used cautiously in individuals with increased risk of developing pancreatitis. In patients with this drug prescription for long duration, a high index for clinical suspicion of pancreatitis should be kept in mind with monitoring for hyperglycaemia and HTG. Local application of metronidazole may be effective in intr-abdominal or retroperitoneal anaerobic infection.

REFERENCES

1. Birgisson H, Stefánsson T, Andresdóttir A, Möller PH. Emphysematous pancreatitis. Eur J Surg 2001;167:918-20.
2. Grayson DE, Abbott RM, Levy AD, Sherman PM. Emphysematous infections of the abdomen and pelvis: A pictorial review. Radiographics 2002;22:543-61.
3. Kerr TA, Jonnalagadda S, Prakash C, Azar R. Pancreatitis following olanzapine therapy: A report of three cases. Case Rep Gastroenterol 2007;1:15-20.
4. Stockinger ZT, Corsetti RL. Pneumoperitoneum from gas gangrene of the pancreas: Three unusual findings in a single case. J Gastrointest Surg 2004;8:489-92.
5. Lee VT, Chung AY, Chow PK, Thng CH, Low AS, Ooi LL, *et al*. Infected pancreatic necrosis – An evaluation of the timing and technique of necrosectomy in a Southeast Asian population. Ann Acad Med Singapore 2006;35:523-30.
6. Engl J, Rettenbacher M, Fleischhacker WW, Ebenbichler CF. Atypical antipsychotic drugs directly impair insulin action in adipocytes: Effects on glucose transport, lipogenesis, and antilipolysis. Neuropsychopharmacology 2007;32:2431-2.
7. Weston-Green K, Huang XF, Deng C. Olanzapine treatment and metabolic dysfunction: A dose response study in female Sprague Dawley rats. Behav Brain Res 2011;217:337-46.
8. Wirshing DA, Wirshing WC, Kysar L, Berisford MA, Goldstein D, Pashdag J, *et al*. Novel antipsychotics: Comparison of weight gain liabilities. J Clin Psychiatry 1999;60:358-63.
9. Albaugh VL, Vary TC, Ilkayeva O, Wenner BR, Maresca KP, Joyal JL, *et al*. Atypical antipsychotics rapidly and inappropriately switch peripheral fuel utilization to lipids, impairing metabolic flexibility in rodents. Schizophr Bull 2012;38:153-66.
10. Weston-Green K, Huang XF, Lian J, Deng C. Effects of olanzapine on muscarinic M3 receptor binding density in the brain relates to weight gain, plasma insulin and metabolic hormone levels. Eur Neuropsychopharmacol 2012;22:364-73.
11. Solanki NS, Barreto SG, Saccone GT. Acute pancreatitis due to

diabetes: The role of hyperglycaemia and insulin resistance. Pancreatology 2012;12:234-9.
12. Berglund L, Brunzell JD, Goldberg AC, Goldberg IJ, Sacks F, Murad MH, *et al*. Evaluation and treatment of hypertriglyceridemia: An endocrine society clinical practice guideline. J Clin Endocrinol Metab 2012;97:2969-89.
13. Nitsche CJ, Jamieson N, Lerch MM, Mayerle JV. Drug induced pancreatitis. Best Pract Res Clin Gastroenterol 2010;24:143-55.
14. Linden GJ, Newman HN. The effects of subgingival irrigation with low dosage metronidazole on periodontal inflammation. J Clin Periodontol 1991;18:177-81.
15. Bassi C, Pederzoli P, Vesentini S, Falconi M, Bonora A, Abbas H, *et al*. Behavior of antibiotics during human necrotizing pancreatitis. Antimicrob Agents Chemother 1994;38:830-6.
16. O'Halloran E, Hogan A, Mealy K. Metronidazole-induced pancreatitis. HPB Surg 2010;2010:523468.
17. Bracamonte JD, Underhill M, Sarmiento P. Acute pancreatitis associated with lisinopril and olanzapine. Am J Health Syst Pharm 2010;67:214-6.

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Announcement

Conference Calendar Details

Name of the conference: 62nd Annual National Conference of the Indian Society of Anaesthesiologists, ISACON 2014
Date: 25th to 29th December 2014
Venue: Velammal Medical College "Velammal Village", Madurai – Tuticorin, Ring Road, Annupanadi, Madurai – 625009, Tamil Nadu, India
Organising Secretary: Prof. Dr. S C Ganesh Prabhu, ISACON 2014, Institute of Anaesthesiology, Government Rajaji Hospital, Panagal Road, Madurai – 625 020, Tamil Nadu, India
Contact: +91 93448 17143, 94434 96835
E-mail: isaconmadurai2014@gmail.com
Website: www.isacon2014.com

Name of the conference: ISA VISZAC 2014 - SOUTH ZONE
Date: 22nd to 24th August 2014
Venue: Amcosa Hall, Visakhapatnam
Organising Secretary: Dr. A Satyanarayana
Contact: +91 98491 26512
E-mail: isaconmadurai2014@gmail.com
Website: www.viszac2014.com

Name of the conference: 17TH RAJASTHAN STATE CONFERENCE 2014
Date: 04th to 5th October 2014
Venue: Tantia General Hospital, Sukhadiya Marg, Sri Ganganagar, Rajasthan
Organising Secretary: Dr. Seema Maheshwari
Contact: +91 94621 78561
E-mail: info@rajisacon2014.in
Website: www.rajisacon2014.com

Name of the conference: KISACON 2014, 30th Annual Karnataka State Conference
Date: 10th to 12th October 2014
Venue: Department of Anaesthesiology, SDM College of Medical Sciences and Hospital, Manjushree Nagar, Sattur, Dharwad - 580009, Karnataka
Organising Secretary: Dr. Shyam Sunder Kamath
Contact: +91 99004 13473
E-mail: kisacon2014@gmail.com
Website: http://kisacon2014.com

Name of the conference: NEZACON 2014 - NORTH EAST ZONE
Date: 11th to 12th October 2014
Venue: Department of Anaesthesiology, AGMC & GBP Hospital, Agartala, Tripura
Organising Secretary: Dr. Biswajit Chakraborthi
Contact: +91 94364 68156
E-mail: chakrabortibiswajit2@gmail.com

Name of the conference: 7th NATIONAL CONFERENCE, ASSOCIATION OF OBSTETRIC ANAESTHESIOLOGISTS (AOA)
Date: 17th to 19th October 2014
Venue: K N UDUPA Auditorium, Banaras Hindu University, Varanasi
Organising Secretary: Dr. P Ranjan
Contact: +91 94159 86684
E-mail: aoacon2014@gmail.com
Website: www.aoacon2014.com

Name of the conference: 17th MISACON and 11th WISACON 2014
Date: 31st October to 2nd November 2014
Venue: Hotel Grand International, Barshi Road, Latur, Maharashtra
Organising Secretary: Dr. Santosh Gitte
Contact: +91 98223 35235
E-mail: misaco2014@rediffmail.com
Website: www.misaco2014.com

Name of the conference: 15th Annual Conference of Indian Society of Anaesthesiologists-North Zone (NZISACON 2014)
Date: 31st October to 2nd November 2014
Venue: Acharya Srichander College of Medical Sciences and Hospital, Jammu
Organising Secretary: Dr. Nandita Mehta
Contact: +91 94191 95424
E-mail: drnanditamehta@gmail.com
Website: http://nzisacon2014.org

Name of the conference: RSAPCON 2014 - 24th Annual Conference of Research Society of Anaesthesiology Clinical Pharmacology
Date: 14th to 16th November 2014
Venue: Department of Anaesthesiology & Pain Management HIMS, HIHT University, Swami Ram Nagar, Jolly Grant, Dehradun, Uttarakhand - 248140
Organising Secretary: Dr. J P Sharma
Contact: +91 94117 18466
E-mail: info@rsacpcon2014.com

Name of the conference: ICA CON - 2014
Date: 21st to 23rd November 2014
Venue: Narayana Hrudayala Hospitals #258/A, Bommasandra Industrial Area Anekal Tk, Bangalore, Karantaka
Organising Secretary: Dr. Muralidhar Kanchi
Contact: +91 99801 63108
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