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# Proposed characterization of the syndrome of epidural pneumatosis (pneumorrhachis) in patients with forceful vomiting from diabetic ketoacidosis as a clinico-radiologic pentad based on systematic literature review & an illustrative case report

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**Abstract**

**Background:** Previous literature on epidural pneumatosis (pneumorrhachis, or air in epidural cavity) associated with forceful vomiting in a patient with diabetic ketoacidosis (DKA) has consisted of individual case reports without comprehensive syndrome characterization due to syndromic rarity, with the largest previous literature review comprising 6 cases. Presumed pathophysiology is air escaping from alveolar rupture from forceful vomiting via tissue planes to cause epidural pneumatosis.

**Aim:** Systematically review literature to facilitate syndromic diagnosis, evaluation, and treatment. A new illustrative case is reported.

**Methods:** Systematic review of literature using 2 independent readers, 2 computerized databases, and the following medical terms/keywords: ["epidural pneumatosis" OR "pneumorrhachis"] AND ["diabetes" OR "diabetic ketoacidosis" or "DKA"]. Discrepancies between 2 readers were resolved by consensus using prospectively developed study inclusion criteria. Two readers independently abstracted case report. Prospective review protocol and patients, problems, intervene, comparison group, outcomes discussed in Methods section of paper.

**Results-systematic-literature-review:** Revealed 10 previously reported cases plus 1 new case (see below) that shows this syndrome presents rather stereotypically with the tentatively proposed following pentad (% of patients fulfilling individual criterion): 1-forceful vomiting (100%), 2-during DKA (100%), 3-pneumomediastinum from forceful alveolar rupture (100%), 4-epidural pneumatosis from air escape from pneumomediastinum (100%), and 5-no complications of Boerhaave syndrome or of focal neurological deficits (100%). Pentad is pathophysiologically reasonable because forceful vomiting can cause alveolar rupture, pneumomediastinum, and air entry into epidural space.

**Results-illustrative-case-report:** Epidural pneumatosis occurred in a 33-year-old-male with poorly controlled diabetes mellitus type 1 who presented with forceful vomiting while in DKA. Radiologic findings also included subcutaneous emphysema,

*Editor: Narothama Reddy Aeddula.*

*Obtained exemption/approval from Beaumont Health System Institutional Review Board on December 16, 2019 (see separately submitted form).*

*Manuscript was thoroughly revised and major additions made by Dr. Cappell who converted the paper from a case report to a systematic review), and who served as mentor to Drs. Gill and Edhi. Dr. Gill and Dr. Cappell are equal and primary authors.*

*Guarantor of review: Dr. M. Cappell.*

*The authors have no conflicts of interest to disclose.*

*None of the authors received any financial support for writing this article. In particular, Dr. Cappell, as a consultant of the United States Food and Drug Administration (FDA) Advisory Committee for Gastrointestinal Drugs, affirms that this paper does not discuss any proprietary, confidential, pharmaceutical data submitted to the FDA. Dr. Cappell was also a member of the speaker's bureau for AstraZeneca and Daiichi Sankyo, co-marketers of Movantik until more than 2 years ago. Dr. Cappell received a 1-time honoraria from Shire and Mallinckrodt more than 2 years ago. This work does not discuss any drug manufactured or marketed by AstraZeneca, Daiichi Sankyo, Shire, or Mallinckrodt.*

*All data generated or analyzed during this study are included in this published article [and its supplementary information files].*

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*How to cite this article: Gill I, Edhi AI, Cappell MS. Proposed characterization of the syndrome of epidural pneumatosis (pneumorrhachis) in patients with forceful vomiting from diabetic ketoacidosis as a clinico-radiologic pentad based on systematic literature review & an illustrative case report. Medicine 2020;99:35(e21001).*

*Received: 29 January 2020 / Received in final form: 28 April 2020 / Accepted: 29 May 2020*

*http://dx.doi.org/10.1097/MD.0000000000021001*

pneumomediastinum, and small pneumothorax. The patient rapidly improved while receiving acute therapy for DKA, and was discharged after 2 hospital days.

**Study limitations:** Limited number of analyzed, retrospectively reported cases. Case reports subject to reporting bias. Specificity, positive predictive value, and negative predictive value not meaningfully analyzed in this homogeneous population.

**Conclusions:** Based on systematic review, syndrome is tentatively proposed as a pentad with: 1-forceful vomiting, 2-during DKA, 3- pneumomediastinum, 4-epidural pneumatosis, and 5-no complications of Boerhaave syndrome or focal neurological deficits. Proposed pentad should be prospectively tested in a larger population including patients with this versus closely related syndromes.

**Abbreviations:** BUN = blood urea nitrogen, CT = computerized tomography, IV = intravenous.

**Keywords:** Boerhaave syndrome, diabetic ketoacidosis, epidural pneumatosis, forceful, pneumomediastinum, pneumorrhachis, vomiting

## 1. Introduction

Epidural pneumatosis (pneumorrhachis or air in epidural cavity) is a rare radiologic entity often secondary to epidural trauma from spinal fracture, epidural injection usually for epidural anesthesia, and epidural instrumentation for lumbar puncture,[1–2] or apparently "spontaneous" pneumomediastinum.[3] Another rare cause is forceful vomiting in patients with diabetic ketoacidosis (DKA) which presumably causes pulmonary alveoli to rupture and alveolar air to escape and dissect through tissue planes to produce pneumomediastinum and epidural pneumatosis. This systematic literature review identifies 10 reported cases of this syndrome,[3–12] expanding the largest previous review of 6 cases[3]; reports a new, eleventh (illustrative) case; and tentatively characterizes this syndrome as a novel pentad that facilitates syndrome evaluation, diagnosis, and therapy.

## 2. Methods

Systematic literature review used 2 computerized databases of PubMed & Medline with last search performed on January 20, 2020, 2 independent reviewers/authors, and the following medical terms/keywords: ["epidural pneumatosis" OR "pneumorrhachis"] AND ["diabetes" OR "diabetic ketoacidosis" OR "DKA"]. Cases were included in this systematic review by consensus to resolve discrepancies, according to the following prospective criteria: confirmed diabetes mellitus (DM); antecedent vomiting; DKA conclusively diagnosed by standard laboratory criteria; and radiologic diagnosis of epidural pneumatosis. Review included all types of publications beginning in 2001 (earlier publications omitted due to inferior computerized tomography [CT] quality). The systematic review followed the PRISMA guidelines,[13] and used the PRISMA Flow Diagram to show filtering of articles for this systematic review (Fig. 1). All clinical parameters (eg, symptoms, signs, laboratory values) for every reported patient were independently abstracted by 2 readers to minimize errors. Statistical analyses were performed independently by 2 analysts to minimize errors. "Patients, problems, intervene, comparison group, outcomes" parameters[14,15] included: Patients–all patients, male or female, and of any age or race except for patients with abnormal esophageal anatomy from major esophageal surgery or congenital anomalies which could anatomically interfere with the vomiting causing epidural pneumomediastinum; Problem–forceful vomiting during DKA causing epidural pneumatosis from escape of air from pulmonary alveoli via pneumomediastinum; Intervene–diagnose syndrome and aggressively treat DKA; treatment of epidural pneumatosis unnecessary in absence of neurologic symptoms of cord compression; Comparison group–failure to implement prompt specific therapy for DKA (no failures occurred); and Outcomes-morbidity or mortality from DKA, missed esophageal rupture, or undiagnosed spinal cord compression.

Prospective review protocol per patient per analyzed publication included: (history & symptoms) presence, type, and duration of DM; presence of vomiting; type of vomiting, whether forceful, severe, or recurrent; other symptoms including neck pain, dyspnea, pyrexia, epigastric pain, pyrosis, confusion & headache, and other; (signs) including tachycardia, signs of dehydration (dry mucous membranes, absent axillary sweat, poor skin turgor, or orthostasis), tachypnea, hypertension, Kussmaul breathing, subcutaneous crepitations, Hamman sign (defined as a crunching and rasping sound, synchronous with the pulse, heard by auscultation over the precordium in mediastinal emphysema, attributed to the heart beating against air-filled mediastinal tissue), epigastric tenderness, focal neurologic deficits, and other; (metabolic abnormalities characteristic of DKA on admission) including highly elevated serum glucose, acidic pH on arterial blood gas, decreased serum bicarbonate level due to metabolic acidosis, ketone bodies in blood and urine, and high anion gap acidosis; (other laboratory abnormalities) including elevated blood urea nitrogen (BUN), elevated serum creatinine, leukocytosis, and polycythemia from hemoconcentration; (radiolologic findings of abnormal air collections on chest radiographs and chest CT) including epidural pneumatosis, pneumomediastinum, subcutaneous emphysema, pneumothorax, pneumopericardium, and pneumoretroperitoneum; (barium or gastrograffin esophageal swallow findings) of no esophageal leak/rupture; (patient treatment) including intravenous (IV) insulin, IV fluid, IV sodium bicarbonate, IV potassium, and supplemental oxygen; and (patient outcome) including intensive care unit admission, length of hospital stay, resolution of DKA, resolution of radiologic abnormalities before discharge, patient morbidity, and mortality,

The case report received exemption/approval from the Institutional Review Board of Beaumont Hospital at Royal Oak on December 16, 2019. The case report followed the CARE guidelines. All authors took full responsibility for anonymization of patient data. The patient agreed to publication of the anonymized case report as submitted. To prevent errors, 2 authors independently abstracted the case report from the electronic medical record, and resolved discrepancies by consensus. Radiologic films were professionally re-reviewed.

## 3. Systematic review

Systematic literature review revealed 10 previously reported patients (Table 1), to which is added a newly reported patient (see

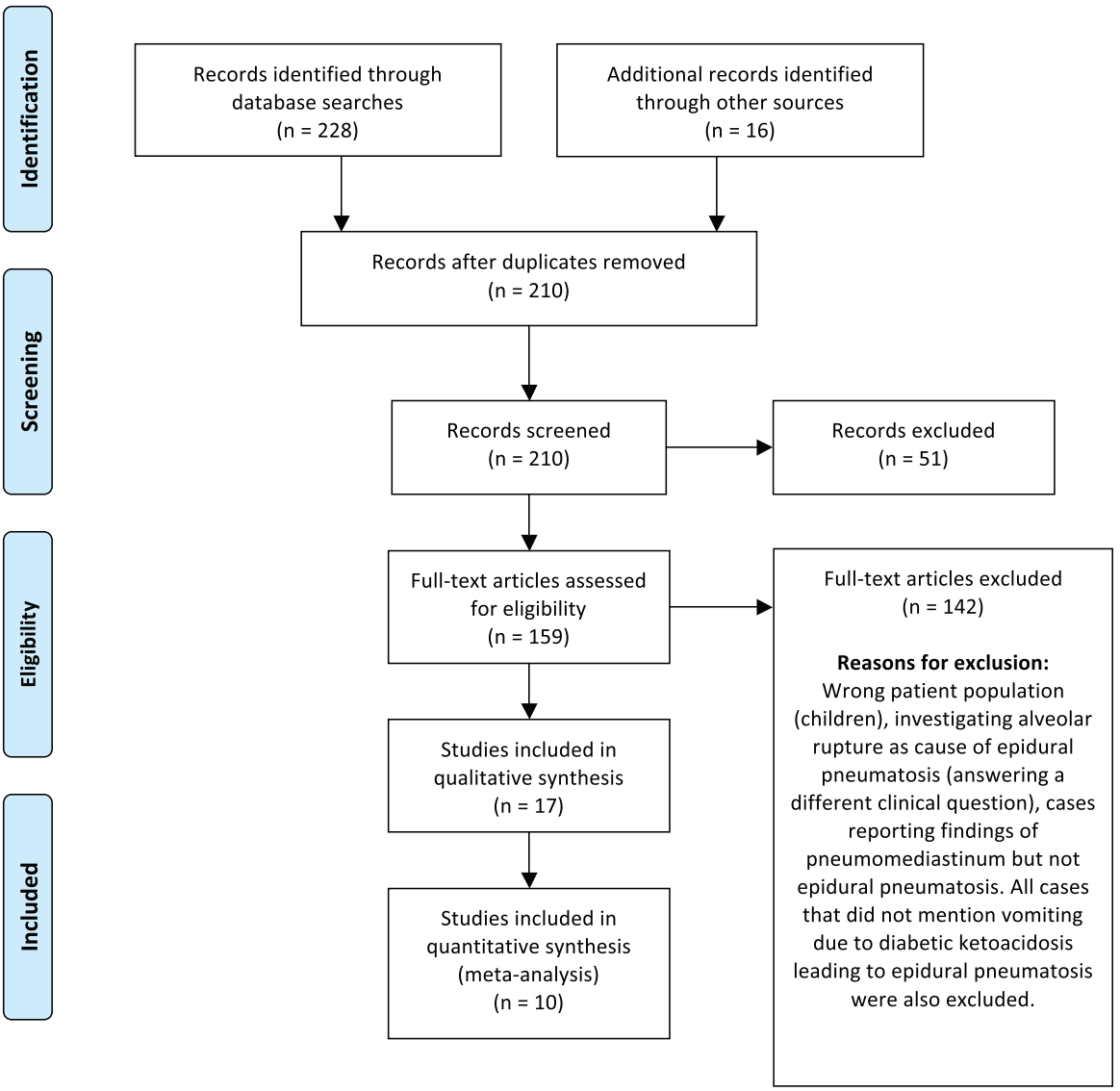


**Figure 1.** Flow diagram showing filtering of relevant articles using the computerized search strategy described in Methods for a systematic review.

below). All 11 patients had (severe, forceful, or recurrent) vomiting. All patients had DM: history of DM type 1 in 6 patients (3.4, 6, 10, 12, current report), DM of unspecified type-3,[7,8,11] and DM newly diagnosed on admission-2.[5,9] All patients had metabolic abnormalities "characteristic of DKA," including 4 case reports not listing their initial laboratory values,[4,8,10,11] and 7 patients with listing of the following metabolic abnormalities that were highly characteristic of DKA (3, 5, 6, 7, 9, 12, current report): mean glucose level = 633 ± 152 (SD) mg/dL (range: 426–823 mg/dL, median = 667 mg/dL, N = 7); severely acidotic pH on arterial blood gas-5[3,5,7,9,12]; decreased serum sodium bicarbonate level due to metabolic acidosis-5[3,5,6,7,12] or borderline low serum bicarbonate-1 (current report); excessive ketone bodies in blood-4,[3,5,7,9] or in urine-4[5,6,9,12]; high anion gap acidosis-2[7,9] or severe base deficit-2[6,12]; and elevated beta hydroxybutyrate-1 (current report).

All patients (100%), had epidural pneumatosis, as uniformly diagnosed by chest CT. Pneumomediastinum was diagnosed by chest radiographs, performed in 10 patients (not performed in 1–11) (100%; 3, 4, 5, 6, 7, 8, 9, 10, 12, current report), and was diagnosed by chest CT, performed in all 11 patients (100%; 3–12, current report). The 10 chest radiographs also revealed subcutaneous emphysema-8 (80%; 4, 6–10, 12, current report); pneumothorax-1 (10%; 5), and pneumopericardium-1 (10%; 6). Subcutaneous emphysema was localized to the lower neck and/or upper chest wall. The 11 chest CTs also revealed subcutaneous emphysema-7 (4, 5, 7, 10, 11, 12, current report); pneumothorax-3 (6, 8, current report); pneumopericardium-1[6]; and pneumoretroperitoneum-1.[11] Signs of air in subcutaneous planes or in other cavities included subcutaneous crepitations-6 (3, 4, 8, 11, 12, current report), or Hamman sign-5.[4,5,6,7,12]

Symptoms included chest pain-5 (4, 7, 8, 10, current report); neck pain-3[3,10,12]; dyspnea-3 (4, 9, current report); pyrexia-3[7,8,11]; and 1 each with epigastric pain,[12] pyrosis,[6] and confusion & headache.[9] Other signs included tachycardia-7 (3, 6, 7, 8, 9, 12, current report); signs of dehydration of dry

**Table 1**

**Clinical presentation in 11 reported cases of epidural pneumatosis associated with vomiting in diabetic ketoacidosis.**

| Clinical presentation | Laboratory values | Radiologic and endoscopic findings | Clinical course | Reference (type of publication) |
|---|---|---|---|---|
| Case reports | | | | |
| 33 y. o. M with poorly controlled DM type 1 presented with forceful vomiting followed suddenly by chest pain and dyspnea. PE: HR = 118 beats/min, BP = 131/85 mm Hg, RR = 18 breaths/min. Dry mucous membranes, absent axillary sweat, poor skin turgor. Subcutaneous crepitance over upper chest wall and lower neck. | WBC = 14,000/$mm^3$, Hgb = 17.3 gm/dl, BUN = 17 mg/d/, creatinine = 1.76 mg/dL, glucose = 426 mg/dL, sodium bicarbonate = 20 mmol/L, beta hydroxy-butyrate = 2.4 mmol/L. | Chest radiograph: pneumomediastinum and subcutaneous emphysema in anterior neck and chest wall. Chest CT: epidural pneumatosis, trace right pneumothorax, pneumo-mediastinum, and subcutaneous emphysema of anterior neck and chest wall. Barium esophagram: no esophageal leak/perforation. | Treated for DKA with IV fluids, IV insulin, and IV potassium. Repeat chest radiograph showed improved subcutaneous emphysema. Discharged on day 2. | CURRENT REPORT |
| 19 y. o. F with DM type 1 presented with vomiting for 3 d and neck pain. Receiving intramuscular insulin. (History of HgA1c = 8.9%). PE: Kussmaul breathing at 34 breaths/min. HR = 120 beats/min, O2 sat = 91% on RA. Palpable crepitus of neck. | Initial blood glucose = 24 mmol/L, ketones = 5.9 mmol/L, ABG pH = 7.24, bicarbonate = 12.3 mmol/L, WBC = 38,800/$mm^3$, Hgb = 16.5 g/dL, creatinine = 14.3 mmol/L, BUN = 29.7 mg/dL | Chest radiograph: pneumomediastinum Chest CT: pneumomediastinum, epidural pneumatosis Barium swallow: No esophageal leak/perforation | DKA treated with insulin and IV fluids (according to protocol). Discharged after 4 d without specific treatment for pneumomediastinum or epidural pneumatosis | Ahmed M, et al, 2016[3] |
| 18 y. o. M with DM type 1 had sudden onset of retrosternal pain and dyspnea after 3 d of severe vomiting, New onset of headache. PE: Normal vital signs. Signs of dehydration, cervical crepitus. Hamman crunch sign. | Severe hyperglycemia. Other laboratory abnormalities "consistent with DKA." | Chest radiograph and CT: massive pneumomediastinum, cervical subcutaneous emphysema, epidural pneumatosis. No pneumothorax or pleural effusions. Barium swallow: no esophageal leak/perforation. | Treated for DKA with IV fluid hydration and IV insulin. Discharged after 48 h when symptoms resolved and pneumomediastinum decreased | Drolet S, et al, 2007[4] |
| 27 y. o. F with forceful vomiting. PE: Hamman crunch sign. | Glucose = 823 mg/dL, pH = 7.13, bicarbonate = 2.6 mmol/L, pCO2 = 8 mm Hg, positive serum and urine ketones | Chest radiograph: Air streaks in neck and chest suggesting pneumomediastinum and pneumothorax. Chest CT: Pneumomediastinum with air in prevertebral soft tissue, in bilateral neck and in chest wall. Epidural pneumatosis of cervical and thoracic spine. EGD: lower esophageal ulcers and candidiasis | DKA treated with IV insulin, IV fluids, and potassium supplementation. Received supplemental oxygen at 3 L/min via nasal cannula. Esophageal candidiasis treated with diflucan and proton pump inhibitor therapy. Discharged at day 4 after complete radio-graphic resolution of pneumomediastinum. | Lan HH, et al, 2012 (case report)[5] |
| 31 y. o. F with DM type 1, recurrent vomiting, and pyrosis. PE: respiratory rate = 20/min, large tidal volumes, HR = 130 bpm, BP = 166/99 mm Hg, skin crepitations in supraclavicular fossae, Hamman sign, and modest abdominal tenderness. No signs of dehydration. | Blood glucose = 6.8 mmol/L (650 mg/dL), pH of ABG = 7.42, bicarbonate = 14 mmol/L, pO2 = 14.6 Kpa, base excess –8.4 mmol/L, BUN = 45.1 mg/dL, creatinine = 88 mmol/L (normal), urine ketone bodies, WBC = 8.8 $\times 10^9$ /L. | Chest x-ray: subcutaneous emphysema and pneumopericardium. Chest CT: minor pneumothorax, epidural pneumatosis, and pneumopericardium, Esophageal swallow: normal, EGD: grade D distal reflux esophagitis. | DKA treated with IV insulin, IV fluids, and potassium supplementation. Discharged after 5 d when subcutaneous emphysema resolved. | Pauw RG, et al, 2007[6] |
| 20 y. o. F with DM presented with recurrent vomiting, pleuritic left-sided chest pain, and fever. PE: HR = 106 bpm, BP = 150/78 mm Hg, orthostasis present, RR = 20/min, subcutaneous crepitations on left neck and Hamman crunch sign. | Initial glucose = 671 mg/dL, Hgb = 16.7 gm/dl, pH = 7.17, bicarbonate = 16 meq/L, anion gap = 24, elevated serum ketones, BUN = 31 mg/dL, creatinine = 2 mg/dL | Chest radiograph: Mediastinal air along left heart border and along left neck. No pneumothorax. Chest CT: Air in soft tissues of neck, pneumomediastinum, epidural pneumatosis along prevertebral area of thoracic spine. | Treated for DKA. All the pneumatosis resolved radiologically. Discharged home in good condition. | Pooyan P., et al2004[7] |

(*continued*)

**Table 1**

**(continued).**

| Clinical presentation | Laboratory values | Radiologic and endoscopic findings | Clinical course | Reference (type of publication) |
|---|---|---|---|---|
| | | Gastrografin swallow: no esophageal leak/ perforation. | | |
| Single case described briefly in a table or in a clinical series | | | | |
| 30 y. o. M presenting with chest pain and neck swelling after 3 d of vomiting. History of poorly controlled DM. PE: pyrexia, tachycardia, subcutaneous crepitus. | "Severe DKA" | Chest radiograph: pneumomediastinum, subcutaneous emphysema. Chest CT: pneumomediastinum, bilateral pneumothorax, epidural pneumatosis. Contrast swallow: no esophageal perforation/leak. | Treatment for DKA including insulin, and fluid and electrolyte resuscitation. Discharged after 5 d in hospital. | Forshaw MJ et al, 2007 (case #4 in a clinical series)[8] |
| Abstracts, letters to editor, or clinical images | | | | |
| 18 y. o. M presented with vomiting, confusion, and dyspnea after administration of high dose oral prednisone for rash of neck and chest. PE: altered mental status, tachycardia, and Kussmaul respirations. Patient not previously known to be diabetic. | WBC = 24.8/mm$^3$, bicarbonate = 5 mmol/L, BUN = 47 mg/dL, glucose = 667 mg/dL, anion gap = 32, serum and urine ketones >150 mg/dL, pH of venous blood = 6.90, pCO2 = 21 mm Hg. | Chest radiograph: subcutaneous emphysema, pneumomediastinum. Chest CT: epidural pneumatosis, pneumomediastinum. Barium swallow not performed because no suspicion of esophageal injury. | Treated for DKA with IV fluids and insulin. Initially required endotracheal intubation and mechanical ventilation. Prompt DKA therapy resulted in rapid extubation and resolution of radiographic abnormalities. | Desa PP, et al, (Abstract)[9] |
| 23 y. o. M with DM type 1 presenting with vomiting and sharp pain of neck and chest wall | "Consistent with DKA" | Chest radiograph: subcutaneous emphysema, pneumomediastinum. Chest CT: soft tissue emphysema in chest wall paraspinal musculature, and soft tissues; extensive pneumomediastinum, epidural pneumatosis. Barium swallow: no esophageal leak/perforation | Patient fully recovered from treatment with DKA with regression of radiologic findings of pneumatosis. | Hall WB, et al, 2012 (clinical image)[10] |
| 19 y. o. M with history of DM and bronchial asthma presented with cough, fever, nausea, and vomiting for 4 d. PE: cervical crepitus. | Hyperglycemia and other laboratory tests "demonstrating DKA." | Chest CT: pneumomediastinum, pneumoretroperitoneum, cervical and thoracic emphysema, and epidural pneumatosis | Underwent otolaryngologic exploration which revealed no abscess. Received standard therapy for DKA, IV antibiotic therapy, and anti-nausea medications. Epidural pneumatosis resolved completely and discharged after 12 d feeling well. | Oertel MP, et al, 2004 (neurology picture)[11] |
| 23 y. o. M with DM type 1 presented with persistent vomiting and anorexia for 1 d, and epigastric and neck pain. PE: HR = 127 bpm, BP = 134/76 mm Hg, RR = 24 breaths/min, venous $O_2$ saturation = 100% on RA. Dry mucous membranes. Subcutaneous crepitations over lung apices and lateral neck, Hamman crunch sign, mild epigastric tenderness. | Initial blood glucose = 42.2 mmol/L, positive urine ketones, Hgb = 17.3 g/dL, WBC = 44.5 $\times 10^9$/L, BUN = 31.1 mg/dL, creatinine = 158 micromol/L, bicarbonate = 9 mmol/L, ABG pH = 7.17, pCO2 = 27 kPa, base excess = −18.5. | Chest radiograph: subcutaneous emphysema, pneumomediastinum. Chest CT: air in soft tissues, pneumomediastinum, epidural pneumatosis. Gastrografin swallow: no esophageal perforation/leak. | "Standard treatment for DKA" and administration of supplemental oxygen. Did well and discharged. | Ripley DP, et al, 2009 (letter)[12] |

ABG = arterial blood gas, BP = blood pressure, BUN = blood urea nitrogen, CT = computerized tomography, DKA = diabetic ketoacidosis, EGD = esophagogastroduodenoscopy, F = female, Hgb = hemoglobin, HR = heart rate, IV = intravenous, M = male, PE = physical exam, RA = room air, RR = respiratory rate, WBC = white blood cell (count), y. o. = years old.

**Table 2**

**Laboratory values on admission showing reported patient presented with diabetic ketoacidosis.**

| Laboratory parameter | Patient laboratory values on admission | Laboratory normal values |
|---|---|---|
| Leukocyte count | 14,000 leukocytes/mm$^3$ | 3500–10,100 leukocytes/mm$^3$ |
| Hemoglobin level | 17.3 g/dL | 13.5–17 g/dL |
| Blood urea nitrogen | 17 mg/dL | 7–25 mg/dL |
| Creatinine level | 1.76 mg/dL | 0.6–1.3 mg/dL |
| Glucose | 426 mg/dL | 66–99 mg/dl |
| Sodium bicarbonate level | 20 mmol/L | 20–29 mmol/L |
| beta hydroxybutyrate | 2.4 mmol/L | 0.02–0.27 mmol/L |
| Potassium level | 4.6 mmol/L | 3.5–5.2 mmol/L |

mucous membranes, absent axillary sweat, poor skin turgor, and/or orthostasis-4 (4, 7, 12, current report); tachypnea-4 (≥20 breaths/min; 3, 6, 7, 12); hypertension-3 (6, 7, current report); Kussmaul breathing-2[3,9]; and epigastric tenderness-2.[6,12]

Other laboratory abnormalities included elevated BUN-5,[3,6,7,9,12] and creatinine-4 (3, 7, 12, current report), which most likely arose from hypovolemia due to polyuria or acute kidney injury from DKA. Four patients had leukocytosis (3, 9, 12, current report), most likely from physiologic stress or infection associated with DKA. Two patients had polycythemia (Hgb >17.0 mg/dL; 12, current report), and 2 others had borderline polycythemia (Hgb >16.5 mg/dL; 3, 7), most likely from hemoconcentration from hypovolemia with DKA.

Exclusion of Boerhaave syndrome is important because vomiting sufficiently forceful to produce pneumomediastinum and epidural pneumatosis might cause esophageal rupture, which is life-threatening if not diagnosed and treated quickly.[14,15] Eight patients had no esophageal leak/perforation as confirmed by barium swallow-4 (3,4,10, current report), gastrograffin swallow-2,[7,12] or swallow using an unspecified contrast agent-2.[6,8] Oral contrast swallow was not performed in 3,[5,9,11] but their benign subsequent clinical course was inconsistent with Boerhaave syndrome. Excluding focal neurologic deficits is important because patients with such deficits may require laminectomy or other neurosurgery, as reported for patients with epidural pneumatosis without DKA.[2,16] No patient had focal neurologic deficits.

Patients typically presented as acutely ill, required initial management in an intensive care unit due to DKA, and recovered rapidly, with rapid resolution of symptoms and reversal of metabolic abnormalities after treatment of DKA with IV insulin, IV fluids, and frequent administration of IV sodium bicarbonate, IV potassium, and supplemental oxygen. While the radiologic phenomenon of pneumatosis in body cavities including epidural pneumatosis is typically a relatively benign radiologic phenomenon, the DKA is initially a life-threatening emergency requiring prompt emergency therapy. Radiologic regression of pneumatosis in body cavities usually took more time than symptomatic relief.

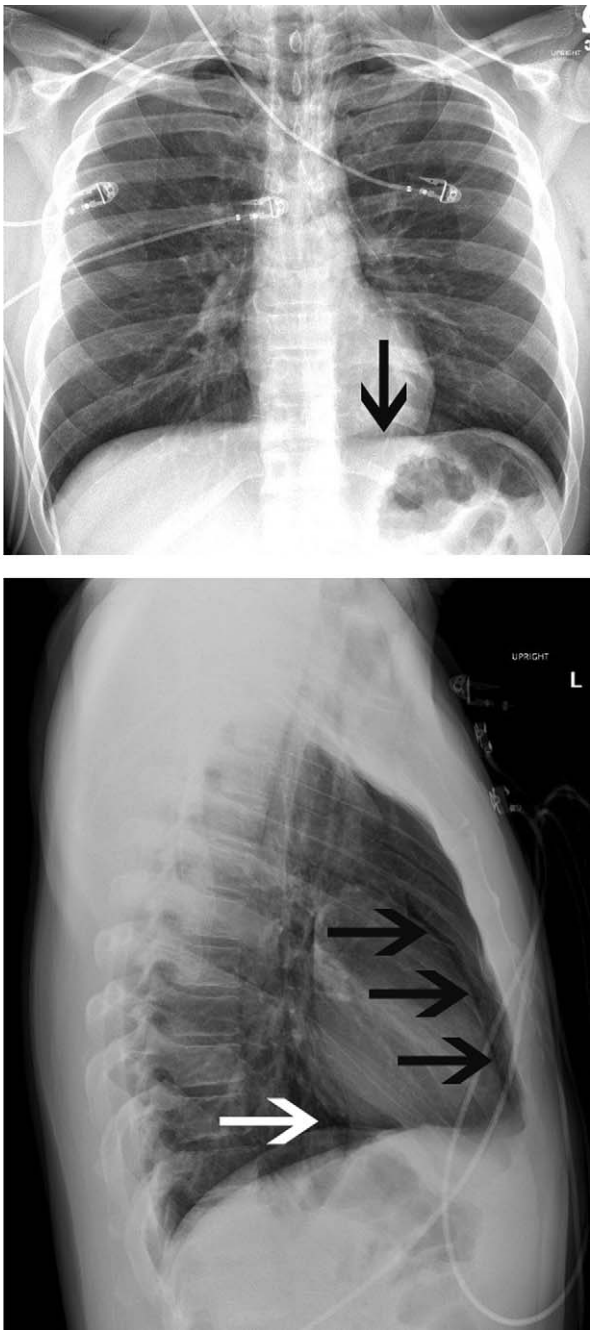


**Figure 2.** Chest radiographs show pneumomediastinum as an air-density beneath the left side of the heart on the PA view (Figure 2A, arrow); and as air-densities posterior to the heart (white arrow), and coursing along the anterior mediastinum (black arrows) on lateral view (Figure 2B).

## 4. Case report

A 33-year-old-male with a past medical history of poorly controlled DM type 1, and 1 prior episode of DKA, presented with nausea and multiple episodes of forceful vomiting, suddenly followed by pleuritic chest pain and dyspnea. On admission, vital signs revealed a pulse of 118 beats/min, blood pressure of 131/85 mm Hg, respiratory rate of 18 breaths/min, and $O_2$ saturation of 97% on room air. Physical examination revealed dry mucous membranes, absent axillary sweat, and poor skin turgor; subcutaneous crepitance over the upper chest and neck; and soft, non-tender, and non-distended abdomen, with normal bowel sounds, and no hepatosplenomegaly. Routine laboratory tests on admission revealed DKA with leukocytosis, hemoconcentration (from dehydration), normal BUN level, elevated creatinine level (from mild acute kidney injury), hyperglycemia,

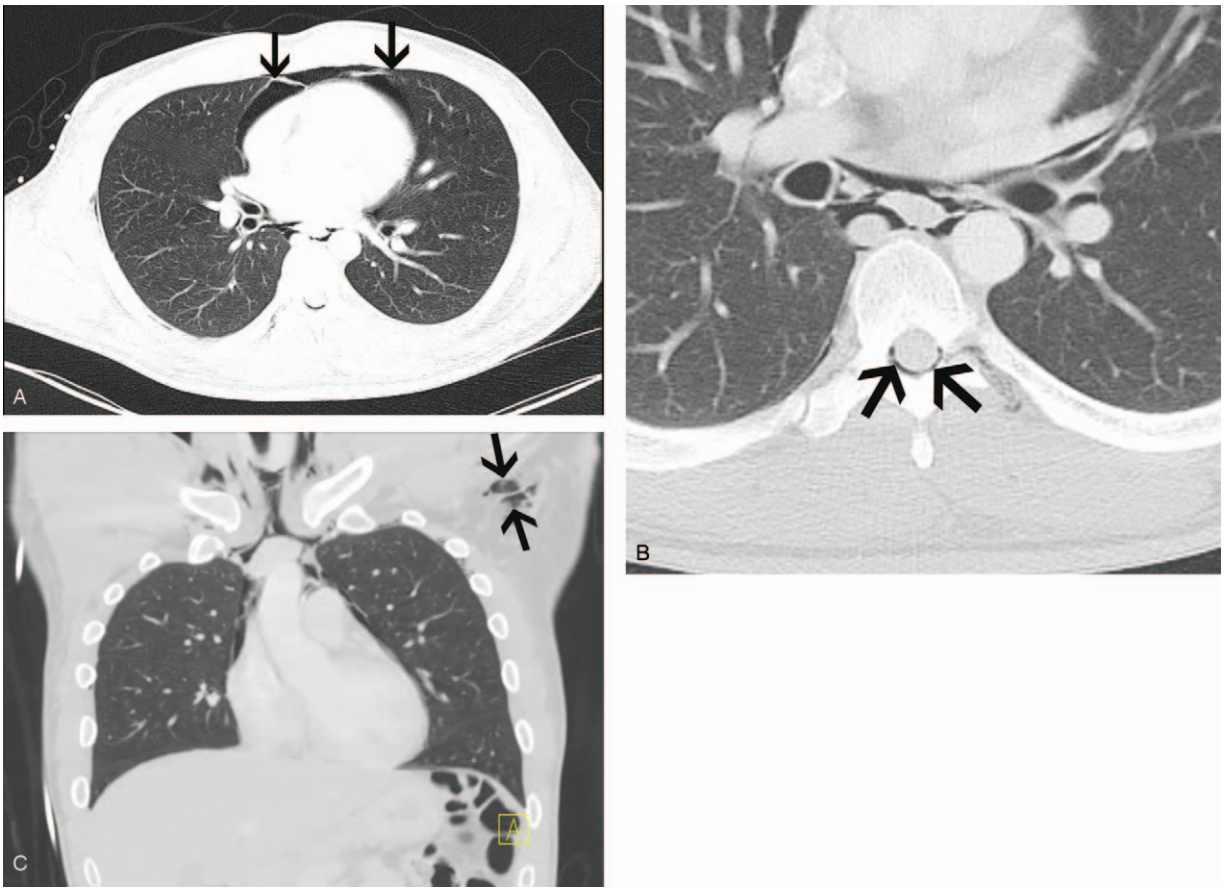


**Figure 3.** (A) Transverse section of chest computerized tomography (CT) at the level of T7-T8 using lung windows shows pneumomediastinum identified as prominent bilateral, antero-medial, air-densities outlined by the curvilinear mediastinal wall (arrows). (B) Zoomed in view of transverse section of chest CT at a nearby level (T6-T7) using lung windows shows epidural pneumatosis identified as prominent, semi-circular, air-densities enclosing the spinal cord within the epidural space (arrows). (C) Coronal section of CT using lung windows shows multiple prominent air densities located at the right infraclavicular level (arrows).

borderline low sodium bicarbonate level, elevated beta hydroxybutyrate, and normal potassium level (Table 2).

Chest radiographs showed pneumomediastinum, and subcutaneous emphysema in neck and chest wall (Fig. 2A and B). Chest CT with IV contrast revealed epidural pneumatosis, pneumomediastinum, subcutaneous emphysema, and trace right pneumothorax (Fig. 3A–C). Patient received supplemental oxygen at 2 L/min via nasal cannula. DKA, diagnosed by the aforementioned laboratory abnormalities, was treated with profuse IV fluid hydration, IV insulin therapy, and potassium at 20 meq/L. Barium esophagram revealed no contrast extravasation from the esophagus. Neurosurgical and thoracic surgery consultations recommended conservative management due to absence of neurological deficits and of esophageal leak/rupture, respectively. Repeat chest radiograph on hospital day 2 demonstrated improvement in subcutaneous emphysema, with no change in pneumomediastinum. Patient was discharged home 2 days after admission, with supportive management, and has been asymptomatic during 3 months of follow-up.

## 5. Discussion

Review of 10 prior cases identified by systematic literature review, plus the currently reported case, showed that this syndrome presents stereotypically. This syndrome is tentatively proposed as a novel clinico-radiologic pentad of:

(1) (severe, forceful or recurrent) vomiting (reported in 100%);
(2) in a diabetic patient with a constellation of metabolic abnormalities characteristic of DKA (reported in 100%);
(3) pneumomediastinum from forceful vomiting (shown by chest radiograph or chest CT in 100% of cases);
(4) epidural pneumatosis (in 100% of cases), as demonstrated by chest CT; and
(5) no complications of esophageal rupture (Boerhaave syndrome) as demonstrated by barium/gastrografin swallow, and no focal neurologic deficits, as determined by formal neurological/neurosurgical examination (in 100%).

Epidural pneumatosis rarely presents with neurological deficits and resolves on its own with conservative therapy in 98% of cases due to air resorption via the bloodstream.[1] Life-threatening infection should be excluded as precipitating the DKA.

This proposed pentad is pathophysiologically reasonable. Diabetic patients frequently experience forceful vomiting (#1) during DKA (#2). This force can cause alveolar rupture and pneumomediastinum (#3), with air penetrating into epidural space via the posterior mediastinum because it lacks fascia separating it from epidural space (#4; 1). Boerhaave syndrome

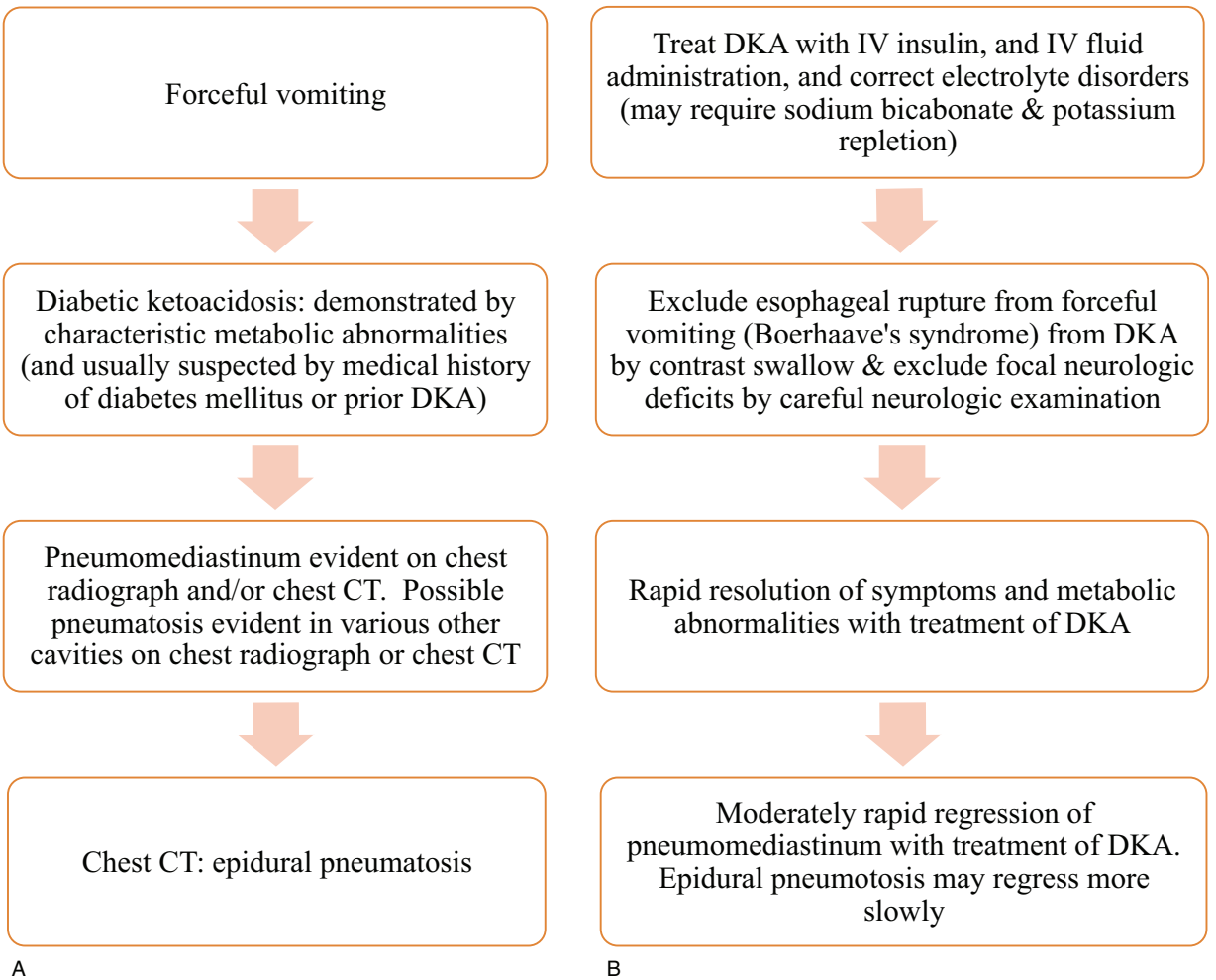


**Figure 4.** (A) Algorithm showing initial presentation of syndrome, including 4 of the 5 proposed clinical pentad. (B) Algorithm showing therapy for diabetic ketoacidosis, further work-up of patient to excluded Boerhaave syndrome and focal neurologic deficits (pentad criterion #5), and typical clinical course.

and focal neurologic deficits, such as radiculopathy, must be excluded because these complications of forceful vomiting may necessitate esophageal surgery or neurosurgery (eg, laminectomy), respectively.[16–18] The clinical presentation, work-up, and proposed pentad are illustrated in Figures 4A and B.

Thoracoscopic interventions or posterior peroral endoscopic myotomy for achalasia can cause severe benign pneumomediastinum with submucosal emphysema, but unlike forceful vomiting during DKA, do not produce epidural pneumatosis. These iatrogenic perforations, unlike forceful vomiting, produce a focal traumatic rent of serosal or enveloping tissue due to extreme direct pressure mediated by an instrument with secondary air leak without propagating a pressure wave, whereas forceful vomiting during DKA produces a forceful pressure wave of air flow that can reach the epidural space.

Clues of Boerhaave syndrome include chemical mediastinitis from leakage of acidic gastric contents,[8] pleural effusion, or hydropneumothorax.[8,19] Chest CT scan with oral contrast can identify areas of esophageal inflammation and rupture with moderate sensitivity and specificity,[8,17,19] but esophageal contrast swallow is much more definitive.[8,17,20] For contrast swallows, gastrografin (water soluble) contrast may be superior to barium (oil soluble) contrast because barium can cause chemical mediastinitis in case of esophageal rupture.[10]

## 6. Study limitations

This systematic review is limited by the relatively small number of reported cases, by all cases consisting of individual, retrospectively reported, case reports, and potential reporting (selection) bias in that dramatic cases are more likely to be reported. Each of the 5 criteria in the pentad has a diagnostic sensitivity of 100%, but specificity, positive predictive value, and negative predictive value of each criterion could not be meaningfully assessed without studying a larger population containing patients with this and closely related, but different, syndromes. This pentad should be tested in a larger prospective trial including patients with this syndrome versus closely related disorders.

## 7. Conclusions

Systematic literature review revealed 10 reported cases, plus 1 currently reported illustrative case, of epidural pneumatosis

associated with forceful vomiting in a patient in DKA. This syndrome is tentatively proposed as a novel pentad including: 1-forceful vomiting, 2-during DKA, 3-causing pneumomediastinum, 4-causing epidural pneumatosis from air leak, and 5-without esophageal rupture or focal neurologic deficits. This pentad has 100% reported sensitivity in the 11 reported cases. This novel pentad may be clinically useful for diagnosis and treatment.

## Author contributions

**Conceptualization:** Inayat Gill, Ahmed Edhi, Mitchell Cappell.
**Data curation:** Inayat Gill, Mitchell Cappell.
**Investigation:** Inayat Gill, Ahmed Edhi, Mitchell Cappell.
**Systematic review:** Mitchell Cappell.
**Writing – original draft:** Inayat Gill, Ahmed Edhi, Mitchell Cappell.

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