Netherlands
The Journal of Medicine

REVIEW

Mediastinal emphysema complicating diabetic ketoacidosis: plea for conservative diagnostic approach

R.G. Pauw, T.S. van der Werf*, H.M. van Dullemen, R.P.F. Dullaart

Department of Internal Medicine, Divisions of Pulmonary Medicine & Tuberculosis, Infectious Diseases, Gastroenterology and Endocrinology, University Medical Centre Groningen, University of Groningen, PO Box 30001, 9700 RB Groningen, the Netherlands, *corresponding author: tel.: +31 (0)50-361 15 01, fax: +31 (0)50-361 93 20, e-mail: t.s.van.der.werf@int.umcg.nl

ABSTRACT

Background: Spontaneous pneumomediastinum has been infrequently reported as a complication of diabetic ketoacidosis. Evidence-based guidelines are currently not available to help in choosing the best diagnostic approach.
Methods: We conducted a systematic review of the literature and looked for diagnostic clues that might indicate the need for a work-up to rule out oesophageal perforation.
Results: In all 56 published cases of spontaneous pneumomediastinum associated with diabetic ketoacidosis, the condition was self-limiting. We report one additional case of a 31-year-old female who presented with a spontaneous pneumomediastinum and also epidural pneumatosis, complicating diabetic ketoacidosis.
Conclusion: Important pathology, such as oesophageal rupture, was not detected in any of the reported cases, and we suggest a restrictive diagnostic work-up.

KEYWORDS

Diabetic ketoacidosis, epidural pneumatosis, pneumomediastinum

INTRODUCTION

Pneumomediastinum or mediastinal emphysema, which was first described by Hamman in 1937,[1] is defined as the presence of gas within the mediastinum. It may result from direct trauma or rupture of the oesophagus,[2] or mechanical ventilation ('barotrauma').[3] Primary or spontaneous pneumomediastinum[4] is believed to result from rupture of alveoli, following an activity that produces high intrathoracic pressure swings,[4-9] such as labour, vomiting, coughing, sneezing or Valsalva manoeuvres. Diabetic ketoacidosis with acidotic ('Kussmaul') respiration and/or vomiting is one such condition.[5] In a recent report,[5] 51 cases were reviewed, including one case that was previously reported from the Netherlands.[10] No guidelines are available to help in choosing the best diagnostic approach for patients presenting with diabetic ketoacidosis accompanied by pneumomediastinum.

METHODS

We searched MEDLINE and PubMed in English, Dutch, and German language publications, with the search strategy: '{pneumomediastinum OR (mediastin* AND emphysema}' in association with 'diabetic ketoacidosis'. We also used the references of all reviews and relevant papers that we retrieved, cross-checking for double publications. Two investigators (RP and TW) independently studied all relevant abstracts. Demographic data, blood gas analysis results, and all other laboratory data were entered in a data sheet for analysis. In addition, we report one additional case not previously published.

RESULTS

Until 2004, 51 cases of pneumomediastinum in association with diabetic ketoacidosis[5] and since then five more cases have been reported, including our patient who we describe in detail below.[11-14] Of these, we could summarise the clinical and laboratory data of the 40 cases that were

reported in the English, Dutch, and German literature (*table 1*). The mean age of these 40 evaluable patients was 41 years, and there were twice as many males as females. Not all features studied were available for all of the 40 patients. Vomiting was present in most but not all of these patients. Oesophageal rupture was not detected in any of these 40 patients during clinical follow-up. Computed tomography (CT) studies were negative in all of the five patients who had this test, and oesophageal integrity was not impaired in any of the 13 patients who underwent contrast swallow studies.

CASE REPORT

A 31-year-old woman with type 1 diabetes mellitus had complaints compatible with gastroenteritis that initially subsided with antiemetics. When the vomiting recurred, diabetic ketoacidosis was suspected; she received additional short-acting insulin and was referred. She had pyrosis but no chest pain. She was on short-acting insulin three times daily before meals and long-acting insulin nocte, and an oral contraceptive. On admission, large tidal ventilations 20/min were noted; there was no smell of acetone. Her pulse was regular at 130 beats/min; blood pressure was 166/99 mmHg. No clinical signs indicating dehydration (i.e., dry arm pits, or reduced skin elasticity) were noted. Body temperature was 37.8°C. She had palpable skin crepitations in the supraclavicular fossae, left hemi-thorax and neck. Hamman's sign, i.e. a crunching, popping noise over the cardiac apex and left sternal border, synchronous with each cardiac systole was present.[1,4,6] Apart from modest abdominal tenderness, no other abnormalities were found. Laboratory investigations showed blood glucose 16.8 mmol/l. Arterial blood gas analysis demonstrated a pH 7.42, bicarbonate 14 mmol/l, pCO_2 2.9 kPa, pO_2 14.6 kPa and base excess -8.4 mmol/l without elevated lactate. Blood urea was elevated (16.1 mmol/l) and creatinine was normal (88 µmol/l), sodium 132 mmol/l, chloride was not measured so the anion gap could not be calculated, potassium 3.9 mmol/l, C-reactive protein slightly elevated (13 mg/l) and white blood cell count (WBC) normal (8.8 x 10^9/l). A urine pregnancy test was negative; ketone bodies were present in the urine, as evidenced by a qualitative dip-stick analysis. Chest X-ray showed subcutaneous as well as pericardial emphysema, confirmed by chest CT scanning, showing a minor pneumothorax, a normal oesophageal wall and interestingly, epidural pneumatosis. Oesophageal swallow examination the next day (water-soluble contrast solution) was normal. With

Table 1. *Clinical and laboratory data of 40 patients reported in 30 papers retrieved from English, Dutch, and German publications with pneumomediastinum in association with diabetic ketoacidosis*[1,5,10-15,18-39]

Patients analysed (n=40)	**Recorded in (n)**		
Age (years)	21	Mean 41 (± SD 12) Range 7-78	
Female/male	40	13/27	
Vomiting	31	Present in 27	Absent in 4
Chest discomfort	23	Present in 18	Absent in 5
Temperature (°C)	19	Mean 36.9 (± SD 0.94) Range 34.2-37.8	>37.7 (n=3) Afebrile (n=7)
Pulse rate (beats/min)	30	Mean 131 (± SD 19) Range 92-160	
Systolic blood pressure (mmHg)	27	Mean 120 (± SD 19) Range 80-169	
Diastolic blood pressure (mmHg)		Mean 73 (± SD 14) Range 40-99	
Respiratory rate (breaths/min)	24	Mean 35 (± SD 8) Range 18-52	Tachypnoea, acidotic breathing ('Kussmaul') (n=10)
Hamman's sign	27	Present in 22	Negative in 5
pH	25	Mean 7.0 (± SD 0.14) Range <6.8-7.42	Acidosis (n=1)
$PaCO_2$ (kPa)	15	Mean 2.1 (± SD 0.9) Range 0.8-3.6	
Blood glucose concentration (mmol/l)	34	Mean 36.0 (± SD 15.2) Range 13.8-87.4	
WBC (x 10^9/l)	20	Mean 25.2 (± SD 8.9) Range 8.8-42.2	
CT scan	5	Epidural pneumatosis n=2	Oesophageal rupture: none
Oesophagus swallow study	13	Contrast leakage: none	
Pneumothorax (chest X-ray)	2		

intravenous insulin and fluid and potassium substitution, hyperglycaemia and metabolic derangements were readily corrected. Persistent pyrosis prompted an oesophago-gastroscopy that revealed grade D distal reflux oesophagitis, successfully treated with omeprazole. Five days later the chest X-ray had normalised, and she was discharged. A chest film was compatible with subcutaneous as well as pericardial emphysema (*figure 1*). CT scanning confirmed the presence of subcutaneous emphysema and demonstarted the presence of a pneumopericardium, pneumothorax and epidural pneumatosis (*figure 2*).

Figure 1. *Postero-anterior chest radiograph showing pericardial and mediastinal emphysema*

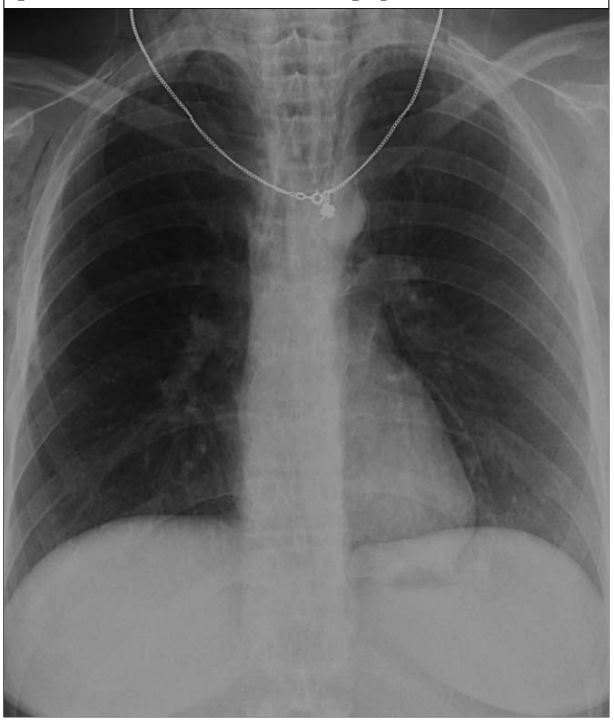
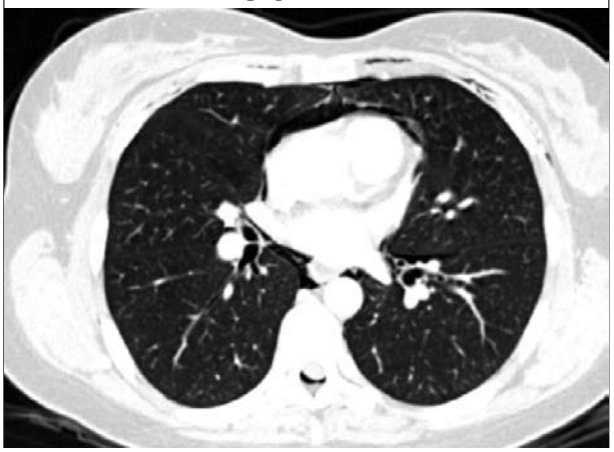


Figure 2. *CT scan showing gas collections in the mediastinum, pericardium, pleural en epidural space; and subcutaneous emphysema*



DISCUSSION

Pneumomediastinum is a benign, self-limiting complication of diabetic ketoacidosis. Epidural pneumatosis has only been reported once in association with diabetic ketoacidosis.[5] However, it might be more common and perhaps went unnoticed before CT scanning became readily available. Apparently, vomiting may not explain all cases of pneumomediastinum.[2,4-7] Acidotic ('Kusmaul') breathing alone may apparently induce transalveolar pressure swings that are sufficient to cause alveolar rupture. Chest discomfort (in 45%) may result from air collections in the mediastinum or pleural space. Three patients including ours had pneumothorax but none required pleural drainage.[15,16] If air collections accumulate in the pharynx and larynx, the voice may change ('hot potato voice'). Hamman's sign may be present.[1] Air collections may appear at different anatomical sites depending on the site of alveolar rupture. Subpleural alveolar rupture may result in pneumothorax, and subcutaneous emphysema which is often observed in association with pneumothorax. Rupture adjacent to bronchovascular bundles may cause pneumomediastinum and pneumopericardium, entities frequently associated with pneumothorax. Epidural gas collections may result from gas passing from the posterior mediastinum through the intervertebral foramina into the epidural space.

Severe persistent vomiting and chest pain suggests oesophageal rupture (Boerhaave syndrome).[5,11,12,16] However, oesophageal rupture was not detected in any of the 40 cases of ketoacidosis-associated pneumomediastinum that we reviewed. Oesophageal rupture in this setting is unlikely.[2,4,17] Spontaneous pneumomediastinum associated with conditions other than diabetic ketoacidosis also has a benign course.[2,4,6-9,17] Most of the clinical signs are likely to have subsided by the time metabolic control has been achieved, and when patients are able to drink, we suggest that they are started on clear fluids first.

Gastro-oesophageal endoscopy is only indicated when other pathologies are being considered. In our patient severe gastro-oesophageal reflux disease was diagnosed. Until perforation has been ruled out, endoscopy should not be performed. Oesophageal swallow imaging with water-soluble contrast solution is a safe procedure to rule out Boerhaave syndrome, provided that the patient is conscious.[5]

CONCLUSION

Pneumomediastinum associated with diabetic ketoacidosis has a benign course and a restricted diagnostic approach is justified.

NOTE

This report reviews the literature, and reports one additional case that cannot be recognised from the case description; ethics clearance by IRB was waived. The patient however declared to us that she would be pleased if her case was reported in the literature

REFERENCES

1. Hamman L. Spontaneous mediastinal emphysema. Bull Johns Hopkins Hosp 1939;64:1-21.
2. Chapdelaine J, Beaunoyer M, Daigneault P, et al. Spontaneous pneumomediastinum: are we overinvestigating? J Pediatr Surg 2004;39:681-4.
3. Weg JG, Anzueto A, Balk RA, et al. The relation of pneumothorax and other air leaks to mortality in the acute respiratory distress syndrome. N Engl J Med 1998;338:341-6.
4. Panacek EA, Singer AJ, Sherman BW, et al. Spontaneous pneumomediastinum: clinical and natural history. Ann Emerg Med 1992;21:1222-7.
5. Pooyan P, Puruckherr M, Summers JA, et al. Pneumomediastinum, pneumopericardium, and epidural pneumatosis in DKA. J Diabetes Complications 2004;18:242-7.
6. Jougon JB, Ballester M, Delcambre F, et al. Assessment of spontaneous pneumomediastinum: experience with 12 patients. Ann Thorac Surg 2003;75:1711-4.
7. Koullias GJ, Korkolis DP, Wang XJ, et al. Current assessment and management of spontaneous pneumomediastinum: experience in 24 adult patients. Eur J Cardiothorac Surg 2004;25:852-5.
8. Weissberg D, Weissberg D. Spontaneous mediastinal emphysema. Eur J Cardiothorac Surg 2004;26:885-8.
9. Kobashi Y, Okimoto N, Matsushima T, et al. Comparative study of mediastinal emphysema as determined by etiology. Intern Med 2002;41:277-82.
10. Wagenaar-Wilm MM, Nube MJ, de Pont CW. Pneumomediastinum als complicatie bij diabetische keto-acidose. Ned Tijdschr Geneeskd 1982;126:901-3.
11. Monjardino J, Smith D, Tisdall M, et al. Hyperpnoea and emesis in a diabetic man. J R Soc Med 2002;95:502-3.
12. Levsky JM, Feuer BH, Di Vito J Jr. Pneumomediastinum in a patient with diabetic ketoacidosis. J Emerg Med 2004;26:233-5.
13. Meron G, Kettenbach J, Kurkciyan I. Spontaneous pneumomediastinum in a patient with diabetic ketoacidosis. Wien Klin Wochenschr 2005;117:82.
14. Brodrib HS. Pneumomediastinum and diabetic hyperpnoea. BMJ 1968;4:773-4.
15. Weathers LS, Brooks WG, DeClue TJ. Spontaneous pneumomediastinum in a patient with diabetic ketoacidosis: a potentially hidden complication. South Med J 1995;88:483-4.
16. Gabor SE, Renner H, Maier A, et al. Tension pneumomediastinum after severe vomiting in a 21-year-old female. Eur J Cardiothorac Surg 2005;28:502-3.
17. Freixinet J, Garcia F, Rodriguez PM, et al. Spontaneous pneumomediastinum long-term follow-up. Respir Med 2005;99:1160-3.
18. Ruttley M, Mills RA. Subcutaneous emphysema and pneumomediastinum in diabetic keto-acidosis. Br J Radiol 1971;44:672-4.
19. Younis N, Austin MJ, Casson IF. A respiratory complication of diabetic ketoacidosis. Postgraduate Med J 1999;75:529-30.
20. Watson P, Barnett AH. Pneumomediastinum in diabetic ketoacidosis. Diab Med 1989;6:173-4.
21. Caramori MLA, Gross JL, Friedman R, et al. Pneumomediastinum and subcutaneous emphysema in diabetic ketoacidosis. Diab Care 1995;9:1311.
22. Meeking R, Krentz AJ. Pneumomediastinum complicating diabetic ketoacidosis. Diab Med 1996;13:587-8.
23. O'Sullivan AJ, Casey JH. Spontaneous pneumomediastinum and diabetic ketoacidosis. Med J Australia 1997;166:245-6.
24. Ba-Ssalamah A, Schima W, Umek W, et al. Spontaneous pneumomediastinum. Eur Rad 1999;9:724-7.
25. Mc Nicholl B, Murray JP, Egan B, et al. Pneumomediastinum and diabetic hyperpnoea. Br Med J 1968;4:493-4.
26. Clarke BF, Campbell IW. Multiple complications in severe diabetic ketoacidosis. Acta Diabetol 1975;12:327-37.
27. Grieve NWT, Bird DRH, Collyer AJ, et al. Pneumomediastinum and diabetic hyperpnoea. Br Med J 1969;1:186.
28. Mathias K. Magen- und alveoalarrupturen bei schwerer ketoazidose. Munch Med Wschr 1976;46:1503-4.
29. Myerson PJ, Myerson DA, Lawson JP. Diabetic acidosis and abnormal chest roentgenogram. Chest 1974;4:434-5.
30. McSweeney WJ, Stempel DA. Non-iatrogenic pneumomediastinum in infancy and childhood. Pediat Radiol 1973;1:139-44.
31. Toomey FB, Chinnock RF. Subcutaneous emphysema, pneumomediastinum, and pneumothorax in diabetic ketoacidosis. Radiology 1975;116:543-4.
32. Shavelle HS. Mediastinal emphysema during diabetic ketoacidosis. California Medicine 1971;4:63-5.
33. Girard DE, Carlson V, Natelson EA, et al. Pneumomediastinum in diabetic ketoacidosis: comment on mechanism, incidence, and management. Chest 1971;5:455-9.
34. Nessan VJ. Recurrent pneumomediastinum in diabetic ketoacidosis. Postgrad Med 1974;6:139-40.
35. Tashima CK, Reyes CV, Kerlow A. Mediastinal emphysema in diabetic coma. JAMA 1969;11:1720.
36. Beigelman PM, Miller LV, Martin HE. Mediastinal and subcutaneous emphysema in diabetic coma and vomiting. JAMA 1969;12:2315-8.
37. Zahller MC, Skoglund RR, Larson JM. Pneumomediastinum associated with diabetic ketoacidosis. J Ped 1978;3:529-34.
38. Schulman A, Fataar S, van der Spuy JW, Morton PC, Crosier JH. Air in unusual places: some causes and ramifications of pneumomediastinum. Clin Rad 1982;33:301e-6.
39. Bullaboy CA, Jenning RB, Johnson DH, et al. Radiological case of the month: Pneumomediastinum and subcutaneous emphysema caused by diabetic hyperpnea. Am J Dis Child 1989;143:93-4.