CASE REPORT

Chemical injury caused by acute alendronic acid aspiration

Zoe Victoria Ottaway, Cara Hammond, Simon Merritt

East Sussex Healthcare NHS Trust, St Leonards-on-sea, East Sussex, UK

Correspondence to
Dr Zoe Victoria Ottaway,
Z.Ottaway1@uni.bsms.ac.uk

Accepted 25 March 2014

SUMMARY

A 79-year-old woman was prescribed bisphosphonates 3 years ago for osteoporosis. At the time of first prescription, she received counselling directions on how to take her medication, which she stringently adhered to. However, she accidentally aspirated an alendronic acid tablet and subsequently developed respiratory tract symptoms. An emergency bronchoscopy was performed. We describe the marked bronchoscopic changes following aspiration of alendronic acid.

BACKGROUND

This case describes a unique complication of bisphosphonate usage. Reflection on this case is clinically relevant for professionals in all disciplines; including general practitioners and endocrinologists who regularly prescribe these medications, emergency medicine consultants who may encounter bisphosphonate aspiration, respiratory consultants who may manage the long-term sequelae of respiratory tract damage and other healthcare professionals, such as physiotherapists, speech and language therapists and pharmacists.

CASE PRESENTATION

A 79-year-old woman presented to accident and emergency department after calling an ambulance with a 3-day history of cough and mucopurulent sputum, following accidental alendronic acid aspiration. Immediately after the event, she experienced an episode of choking which subsided after drinking water, but over the next 3 days her symptoms progressed into a productive cough, hoarseness of voice and decreased oral intake. The patient was taking her once weekly dose of bisphosphonate (alendronate sodium 70 mg weekly; Fosamax, Merck) for secondary prevention of osteoporosis; on the history of several fragility fractures. On the afternoon of admission, she had presented to the general practitioner who suggested the symptoms were probably due to a viral sore throat and advised supportive management. That evening her symptoms worsened and she began to feel breathless, reporting a 'gurgling' sound while breathing, and her neighbour called the ambulance services. To note, she had also consulted the general practitioner a week previously and mentioned that her alendronic acid tablets were difficult to swallow as they were 'too large', but no further action was taken. On examination in the emergency department the patient looked sweaty, her voice was dysphonic, oxygen saturations were 92% (on 2 L of oxygen) and she was febrile (temperature 38°C).

All other observations were within normal limits. On auscultation, there were soft crackles bibasally.

INVESTIGATIONS AND DIFFERENTIAL DIAGNOSIS

A chest radiograph was normal, but arterial blood gases showed hypoxia (partial pressure of oxygen 6.3 kPa, oxygen saturations 86% on 2 L of oxygen). Laboratory blood tests were all unremarkable apart from a raised C reactive protein (237 mg/L). An emergency fiberoptic flexible bronchoscopy was performed to assess the status of the patient's upper respiratory tract and showed sloughing of the mucosa over most of the tracheal surface down to the right main bronchus (figure 1A,B). Appearances were consistent with a diagnosis of severe chemical injury secondary to bisphosphonate aspiration. No tablet remnants were identified. Bronchial washings were negative for bacteria (including tuberculosis) and fungi (candida).

TREATMENT

A 7-day course of amoxicillin (1 g total dissolved solid three times daily (TDS)) and metronidazole (400 mg TDS) were prescribed as prophylaxis for aspiration pneumonia. She was prescribed salbutamol (2.5 mg PRN) and saline (5 mg PRN) nebulisers for 2 days to aid in secretion clearance. Blood and sputum cultures showed no growth. Histopathological examination of the bronchial biopsies revealed necroinflammatory slough and ulcerated, inflamed tissue with no surface epithelium and were consistent with the diagnosis of chemical injury secondary to alendronic acid aspiration. She received urgent physiotherapy and speech and language input. She was also reviewed by the ear, nose and throat team who indicated moderate inflammation of the vocal cords, prognostically they felt her voice should fully recover; she was discharged home a week later.

OUTCOME AND FOLLOW-UP

The patient's general practitioner followed her up and started the patient on strontium ranelate, as alternative secondary prevention of osteoporosis.

The respiratory team also reviewed her in the clinic 4 weeks postdischarge. In clinic she was entirely asymptomatic with normal swallow and voice projection. She had no shortness of breath or chest pain. Her examination was normal and her oxygen saturations were 96% on air.

DISCUSSION

Bisphosphonate aspiration is rare, with only two other published case reports of acute tracheobronchial

CrossMark

To cite: Ottaway ZV, Hammond C, Merritt S. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-200444

Figure 1 (A and B) Fiberoptic bronchoscopy at presentation. There are extensive white plaques over the tracheal surface and extending down the right immediate bronchus, which appear to be sloughed mucosa. The left bronchus was hyperaemic and all segmental and subsegmental bronchi were also hyperaemic but structurally normal.

damage found in the literature.^{1 2} The consequences of aspiration are severe and can result in long-term complications, such as localised bronchiectasis.³

This case highlights and confirms previous findings that alendronic acid aspiration leads to airway inflammation, tissue necrosis and copious mucopurulent secretions manifested by sloughing of the tracheobronchial mucosa. The early histological appearances on examination are consistent with the macroscopic changes seen on bronchoscopy. In this severe case, histology also identified a complete absence of respiratory surface epithelium. It would have been interesting, from an academic point of view, to repeat the bronchoscopy prior to her follow-up appointment to observe how these ulcerative changes have developed. One would expect granulation tissue formation and mucosal scarring, which in itself could cause further problems.

Although rare, physicians must recognise the need for prompt assessment in patients with a history of bisphosphonate aspiration. Perhaps more importantly though is the need for

physicians to be aware of the complications such medications can cause and consider this when prescribing them, thus reducing the risk of such adverse events.

More commonly bisphosphonates cause erosive oesophagitis, a well-recognised side effect of their usage.⁴ Research has shown the mechanism by which alendronic acid causes oesophageal erosions and tissue necrosis is through local irritation caused by the nitrogen it contains; however, the exact mechanism is not well understood.^{5 6} One pharmacodynamic study has shown that alendronic acid, a nitrogen-containing bisphosphonate, has caused apoptosis of a variety of cells in vitro; thus, again illustrating the probable mechanisms which occurred during the apoptosis of this patient's respiratory tract epithelial cells, thus demonstrating drug relatedness.^{7 8}

In this patient, with a significant medical history of fragility fractures, alternative osteoporosis treatment is needed. Both the medical team and the patient felt continued bisphosphonate treatment usage to be inappropriate. In this case, either strontium ranelate or denosumab would be an appropriate alternative treatment in terms of efficacy and appropriateness of their formulations, based on the National Institute for Health and Care Excellence (NICE) and the National Osteoporosis Guideline Group guidelines.^{9–11}

Learning points

- ▶ Alendronic acid aspiration is rare, but if it occurs can cause severe chemical injury to the tracheobronchial tree; with the potential for long-term sequelae as a result.
- ▶ The elderly population, in whom bisphosphonates are regularly prescribed, are at considerable risk of adverse events as a result of these medications.
- ▶ Such potentially harmful drugs should be prescribed only after careful risk versus benefit analysis and comprehensive patient counselling is also needed; as per British National Formulary guidelines.¹²

Contributors The main body of the case report was written by ZVO. CH and SM edited and reviewed the content prior to submission.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Kraft B, Al-Jishi W, Gilstrap D, *et al.* Severe airway damage due to aspiration of an alendronate pill. *Chest* 2011;140:85A.
- 2 Jungblut SA, Frickmann H, Achenbach HJ, *et al.* Damage to the respiratory tract due to aspirated alendronate. *Pneumologie* 2007;61:771–3.
- 3 MacDonald GI, Currie GP, Reid DM. Aspiration of alendronic acid leading to localized bronchiectasis. *Eur J Clin Pharmacol* 2012;68:451–2.
- 4 De Groen PC, Lubbe DF, Hirsch LJ, *et al.* Esophagitis associated with the use of alendronate. *N Engl J Med* 1996;335:1016–21.
- 5 Peter CP, Handt LK, Smith SM. Esophageal irritation due to alendronate sodium tablets: possible mechanisms. *Dig Dis Sci* 1998;43:1998–2002.
- 6 Lichtenberger LM, Romero JJ, Blank MA. Effect of bisphosphonates on the surface hydrophobicity and phosphatidylcholine concentration of gastric mucosa. *Gastroenterology* 1999;116:A237.
- 7 Gómez V, Xiao S-Y. Alendronate-induced esophagitis in an elderly woman. *Int J Clin Exp Pathol* 2009;2:200–3.
- 8 Sürü S, Mönkkönen J, Taskinen M, *et al.* Nitrogen-containing bisphosphonates induce apoptosis of Caco-2 cells in vitro by inhibiting the mevalonate pathway: a model of bisphosphonate-induced gastrointestinal toxicity. *Bone* 2001;29:336–43.
- 9 National Institute for Health and Clinical Excellence. *Alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the secondary*

- prevention of osteoporotic fragility fractures in postmenopausal women. Guidance No. 161. London: National Institute for Health and Clinical Excellence, 2011.
- 10 National Institute for Health and Clinical Excellence. *Denosumab for the prevention of osteoporotic fractures in postmenopausal women*. Guidance No. TA204. London: National Institute for Health and Clinical Excellence, 2010.
- 11 National Osteoporosis Guideline Group. *Osteoporosis: clinical guideline for prevention and treatment*. National Osteoporosis Guideline Group, 2010.
- 12 Joint Formulary Committee. *British National Formulary. Alendronic acid*. Edition No. 64. London: BMJ Group and Pharmaceutical Press; 2012.

Copyright 2014 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow