

# Hyaluronic acid pulmonary embolism: a critical consequence of an illegal cosmetic vaginal procedure

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## ABSTRACT

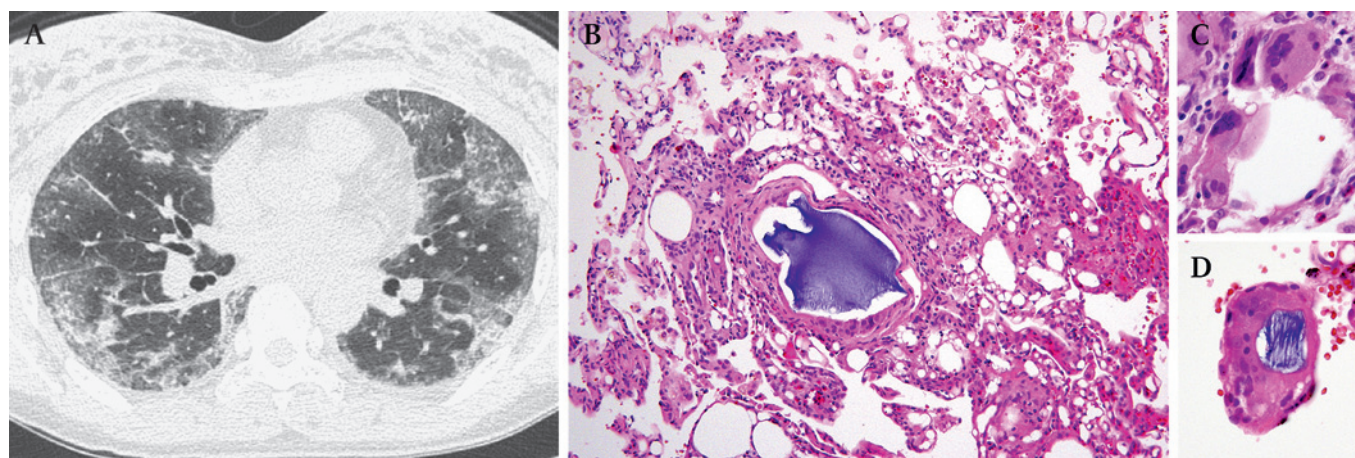
The materials used for cosmetic procedures by physicians as well as illegally by non-medical personnel can cause non-thrombotic pulmonary embolism (NTPE). The case history is presented of a woman with acute respiratory failure after an illegal cosmetic vaginal procedure using hyaluronic acid (HA) dermal filler by an unlicensed medical practitioner on the day of symptom onset. Histopathological examination of a video-assisted thoracoscopic lung biopsy specimen showed a granulomatous foreign body reaction with multinucleated giant cells around amorphous basophilic materials in the pulmonary vessels and lung parenchyma, suggesting NTPE by HA. HA is approved for dermal implantation for the correction of facial wrinkles and folds. All other uses are considered off label. Although HA is supposedly devoid of immunological reactions, localised complications with granulomatous foreign body reactions by HA injection have been reported after cosmetic facial procedures. However, the case of a typical NTPE syndrome has not yet been reported. This is the first reported biopsy-proven case of a patient developing NTPE caused by HA.

In August 2009 a 49-year-old woman visited the emergency room with a 3-day history of progressive shortness of breath and cough. She did not smoke and was not on any medications, and denied a history of drug abuse. She was afebrile but tachypnoeic. Physical examination was significant only for diffuse inspiratory crackles in both lower lungs. She was mentally alert and skin and extremities were normal. Laboratory test results showed mild leukocytosis ( $11.9 \times 10^9/l$  with 76.7% neutrophils) and increased C-reactive protein concentration (5.664 mg/dl; normal 0.02–0.3 mg/dl). Arterial blood gas analysis at room air revealed an arterial oxygen tension ( $P_{aO_2}$ ) of 53.4 mm Hg, arterial carbon dioxide tension ( $P_{aCO_2}$ ) of 32.1 mm Hg and bicarbonate of 20.3 mmol/l, with a pH 7.42. A plain chest x-ray and high-resolution CT scan (figure 1A) showed bilateral diffuse ground glass opacities from lower to apical zones. These opacities were dominant in the periphery with central sparing. Tests for cardiac function were normal. An HIV test was negative and no specific organisms were revealed by sputum studies. During precise history taking the patient stated that she had undergone an illegal G-spot amplification, a cosmetic vaginal procedure, by an unlicensed medical practitioner on the day of symptom onset. According to her medical record, 1 year earlier she had visited our hospital

for mild dyspnoea with cough and a plain chest x-ray had shown patchy infiltrations in both lower lung fields. Although she had received the same procedure at that time, she had not informed the doctors and her symptoms and radiographic abnormalities improved spontaneously. We were able to get the information about the injection material. The material was hyaluronic acid (HA) dermal filler and the injection volume was about 5 ml in total. Vaginal examination revealed no specific evidence of a local reaction. One day after admission the patient worsened progressively and was placed on mechanical ventilation. High-dose corticosteroid therapy was started because rapidly progressing interstitial lung diseases such as acute interstitial pneumonia could not be ruled out. A video-assisted thoracoscopic (VATS) lung biopsy was performed to confirm the diagnosis of a non-thrombotic pulmonary embolism (NTPE) by HA and to differentiate the condition from other lung diseases. Histopathological examination (figure 1B–D) showed a granulomatous foreign body reaction with multinucleated giant cells around amorphous basophilic materials in the pulmonary vessels and lung parenchyma, suggesting NTPE by HA. After confirmatory diagnosis, the corticosteroid was rapidly tapered and supportive treatment was maintained. The patient gradually improved and was weaned from mechanical ventilation 7 days after intubation.

## DISCUSSION

NTPE is defined as embolisation to the pulmonary circulation of different cell types, bacteria, fungi, foreign material or gas. The particulate material used for cosmetic procedures by physicians as well as illegally by non-medical personnel can cause NTPE.<sup>1</sup> G-spot amplification is medically non-indicated and deficient of safety and efficacy data. The procedure is usually performed by the injection of collagen into the anterior wall of the vagina.<sup>2</sup> Because an extensive venous plexus immediately surrounds the vagina,<sup>3</sup> procedures using injectable materials can cause potential complications including NTPE. HA dermal filler has been developed in the search for fillers that do not require allergy testing and is approved for dermal implantation for the correction of facial wrinkles and folds. All other uses are considered off label.<sup>4</sup> Although HA, which is produced by a microbiological engineering technique, is of non-animal origin and supposedly devoid of immunological reactions,<sup>5</sup> there have been some reports of



**Figure 1** (A) High-resolution CT scan of the chest showing bilateral and peripheral diffuse ground glass opacities (GGO) from the lower to apical zones. Histopathological examination of the lung biopsy specimen showed amorphous basophilic materials (B, H&E stain,  $\times 200$ ) and granulomatous reaction (C,  $\times 400$ ), with multinucleated giant cells engulfing foreign materials (D,  $\times 400$ ).

complications such as inflammatory nodule, blue bump, allergic reactions, vascular occlusion and granulomas.<sup>4</sup> The predominant histological finding in this case was a granulomatous foreign body reaction with multinucleated giant cells around amorphous basophilic materials, which is consistent with those of granulomatous reactions to HA reported in complicated facial cosmetic procedures.<sup>6–8</sup> This pathological change is similar to talcum-induced pulmonary granulomatosis, which is characterised by arteriolar wall penetration of talcum with a giant cell granulomatous reaction, but different from those of fat embolisms which include endothelial and pneumocyte damage, capillary leak and clot formation.<sup>1</sup> Alveolar haemorrhage, a feature of fat and silicone embolisms,<sup>9</sup> was not observed in the present case. Although there is a presumptive mild case of pulmonary embolism after intra-articular injection of HA,<sup>10</sup> there are no reports of typical NTPE syndrome associated with HA. The patient described in this report repeatedly experienced dyspnoea with radiological chest abnormalities after the illegal G-spot amplification with HA, and the second episode was serious enough to cause acute respiratory failure and the need for mechanical ventilation. This is the first reported biopsy-proven case of a patient developing NTPE caused by HA. Despite an initial clinical presentation that was critical, she recovered with supportive care with mechanical ventilation. Although high-dose corticosteroid therapy was tried due to possibility of acute interstitial pneumonia, the corticosteroid was rapidly tapered after diagnosis of NTPE by HA because the granulomatous lesions secondary to HA cosmetic injection had disappeared with time,<sup>7,8</sup> and the clinical evidence of corticosteroid efficacy is limited in NTPE with granulomatous reactions such as talcum-induced pulmonary granulomatosis.<sup>1</sup> It was therefore difficult conclusively to determine the therapeutic effect of

corticosteroids in NTPE by HA. However, VATS lung biopsy played an important role in the diagnosis and differentiation from other lung diseases such as acute interstitial pneumonia, hypersensitivity pneumonitis, chronic eosinophilic pneumonia and *Pneumocystis jiroveci* pneumonia.

**Competing interests** None.

**Patient consent** Obtained.

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