Treatment of Bronchorrhea by Corticosteroids in a Case of Bronchioloalveolar Carcinoma Producing CA19-9

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Abstract

A case of gastrointestinal cancer-associated antigen (CA19-9)-positive bronchioloalveolar carcinoma accompanied by bronchorrhea and respiratory failure successfully treated with corticosteroids is reported. The patient was treated with pulse methylprednisolone at a dose of 1,000 mg/day for three days, followed by oral prednisolone (60 mg/day). Within 2 days, the sputum volume decreased from >100 ml/day to 20 ml/day and it was finally controlled to 0–10 ml/day. The reduction in the sputum volume was associated with alleviation of dyspnea and hypoxemia. The levels of CA19-9 in the serum and the sputum were extremely high and an immunocytochemical study showed that the tumor cells were stained by CA19-9 antibody. This case demonstrates the therapeutic value of corticosteroids in the treatment of bronchorrhea in subjects with bronchioloalveolar carcinoma.

Case Report

A 64-year-old man was hospitalized with the chief complaint of severe dyspnea and production of large volumes of sputum. He had smoked a pack of cigarettes per day for 15 years until 30 years before the current admission and not thereafter. He had a productive cough and dyspnea on effort for 4 months. On admission, the volume of sputum was >100 ml/day. Chest examination revealed coarse crackles in the bilateral lung fields. Macroscopically the sputum was watery, clear, and frothy. A chest X-ray showed diffuse bilateral infiltrates. A chest CT showed extensive, multifocal, bilateral consolidation with multiple air bronchograms and discrete irregular nodules measuring, 0.5 to 3.0 cm (Fig. 1). Arterial blood gas values, with the patient breathing 3 liters of oxygen per minute by nasal prongs, were pH 7.38; PaCO₂, 47 Torr; PaO₂, 33 Torr; and oxygen saturation; 63%. Sputum cytology showed malignant cells consistent with BAC (Fig. 2A).

At the time of admission, the level of CA19-9 was 610 U/ml in the serum, and >10,000 U/ml in the sputum. Serum levels of other tumor markers were also elevated: carcinoembryonic antigen (CEA), 3.1 ng/ml; CA125, 311 U/ml; CA15-3, 26 U/ml; cytokeratin 19 fragment (CYFRA 21-1), 3.1 ng/ml; sialyl Lewis(x) antigen (SLX), 95.1 U/ml. Immunocytochemical staining showed that the tumor cells were positive for CA19-9 antigen (Fig. 2B).

The clinical course of the patient is presented in Fig. 3. The patient was treated with pulse methylprednisolone at a dose of 1,000 mg/day for three days, followed by oral prednisolone at 60 mg/day. Within 2 days, the sputum volume had decreased from >100 ml/day to 20 ml/day. The reduction in the sputum volume was associated with alleviation of dyspnea and hypoxemia with corticosteroids.
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Figure 1. CT on hospital admission shows bilateral consolidation with air bronchograms and discrete irregular nodules.

Figure 2. Sputum cytology (A) shows cuboidal cells with abundant, clear cytoplasm and small, centrally located hyperchromatic nuclei (Papanicolaou stain, ×200). Immunocytochemical staining (B) reveals that the secretory surface of tumor cells are positive for CA19-9 (×120).

Discussion

The production of large amounts of sputum is one of the unique characteristics of BAC. Although the precise mechanisms of bronchorrhea in BAC are unknown, hypersecretion of mucus glycoprotein and/or increased transepithelial Cl secretion may play important roles in excess sputum production. Prostaglandins stimulate transepithelial Cl secretion associated with the secretion of water (2), and an increase in the amount of water in the sputum may contribute to bronchorrhea. Inhaled indomethacin has been reported to reduce refractory bronchorrhea in BAC (3). The effectiveness of indomethacin in patients with BAC was associated with the expression of cyclooxygenase-2 messenger RNA in carcinoma cells, suggesting a decrease in Cl secretion via inhibition of the cyclooxygenase pathway by indomethacin (4). Macrolides, which reduce respiratory glycoprotein secretion (5) and inhibit Cl secretion (6), have also been reported to reduce the sputum volume in BAC (7). Although we did not try treatments with inhaled indomethacin or macrolides in the present case, it is assumed that the corticosteroids used reduced the sputum volume by inhibiting secretions of glycoprotein and Cl. Corticosteroids inhibit the gene encoding inducible cyclooxygenase (8), and decrease mucus secretion in the airways by direct inhibition of glycoconjugate secretion (9). Homma et al reported that inhaled indomethacin reduces bronchorrhea in BAC, when macrolide and corticosteroids are not effective (3). Although the reason the corticosteroids were not effective is not clear, their report suggests that the route of drug administration could be a critical factor in some cases. Inhaled corticosteroids have been reported to be effective in a case of BAC with bronchorrhea (10). Inhaled corticosteroids, which have fewer side effects than oral ones, could be another therapeutic choice. However, here, because intravenous and oral corticosteroids resulted in a dramatic improvement of bronchorrhea without severe side effects, we did not try inhaled corticosteroids. In patients with BAC, airway obstruction by copious amounts of bronchial secretion may induce respiratory failure. Thus, corticosteroids may be an effective therapeutic agent to reduce bronchorrhea and have the potential to prevent bronchorrhea-induced respiratory failure.

High levels of CA19-9 in the serum (610 U/ml) and sputum (>10,000 U/ml) were likely produced from the BAC cells. The presence of CA19-9 antigen has been reported on BAC cells (11). Immunocytochemical staining of tumor cells with anti-CA19-9 antibody revealed that the secretory surface stained stronger than the cytoplasm, suggesting that tumor cells themselves produced and secreted CA19-9. Despite the reduction in sputum volume, a 13-fold increase in serum CA19-9 and a progression of diffuse dissemination of cancer cells during the treatment with corticosteroids, suggest that corticosteroids were effective in bronchorrhea but not in the attenuation of tumor cell growth. It is possible that both the bronchorrhea and high levels of CA19-9 were due to hyperplastic bronchiolar cells producing mucus glycoprotein and CA19-9. Corticosteroids
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<tr>
<td>60 mg</td>
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<td>63 80 97 94 90 86 92 94 90 92 94 93 97 93</td>
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<td>CA19-9 (U/ml)</td>
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<td>Chest X-ray</td>
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Figure 3. The clinical course of the patient. MP: methylprednisolone, SpO2: oxygen saturation measured by a pulse oxymeter.

could be effective in reducing the secretion of glycoprotein from tumor cells. In conclusion, this case demonstrates that severe BAC-associated bronchorrhea with respiratory failure can be treated successfully with high-dose corticosteroids.

References


