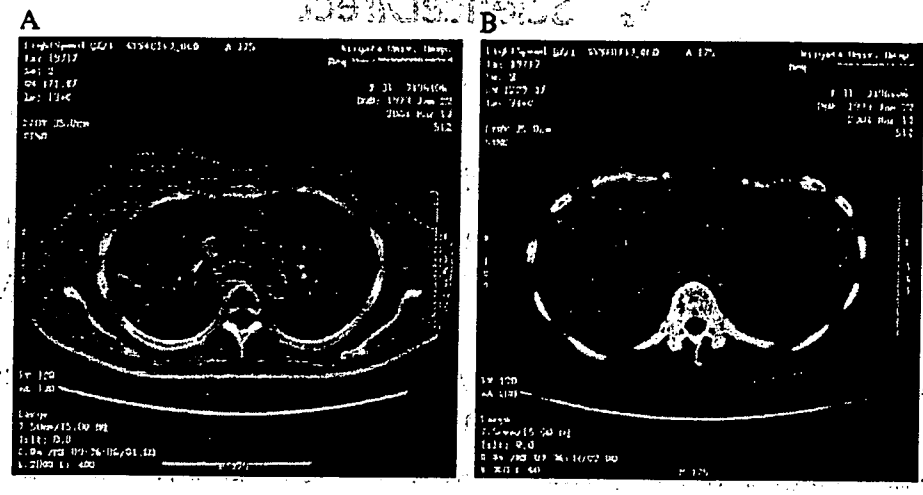

Fig. 1. (A) CT scan revealing 5 × 4 cm tumor in the right lung field. (B) CT scan demonstrating multiple metastatic tumors in the liver.

magnetic resonance imaging (MRI) revealed no abnormality. She was diagnosed as having metastatic choriocarcinoma. She was commenced on EMA-CO as an initial chemotherapy regimen (Day 1, Actinomycin D 0.5 mg, Etoposide 100 mg/m^2, Methotrexate 100 mg/m^2 then 200 mg/m^2 over 12 h; Day 2, Actinomycin D 0.5 mg, Etoposide 100 mg/m^2, Leucovorin 15 mg quarterly (4 doses, 24 h after the 1st Methotrexate); Day 8, Vincristine 1 mg, Cyclophosphamide 600 mg/m^2) for seven cycles. Her beta-hCG dropped to 2.2 ng/ml. At 11 days after 7th cycle of EMA-CO treatment, however, high fever, dyspnea, hypoxemia, and elevated serum levels of C reactive protein were observed. The arterial blood gases in room air were: pH 7.433; PO_2, 40.3 mm Hg; PCO_2, 40.3 mm Hg. It was difficult at that time to determine whether the patient's respiratory failure was caused by severe infectious pneumonia, hypersensitivity pneumonia, or pneumonitis carcinomatosis. Antibiotic therapy was not effective, and due to bilateral ground-glass opacity on CT scan and the examination of the bronchoalveolar lavage fluid, drug-associated interstitial pneumonitis was strongly suspected. After high-dose steroid therapy consisting of predonisolone 500 mg/day for 3 days, symptoms and ground-glass opacity on CT scan were remarkably improved (Figs. 2A, B). We had to change the chemotherapy regimen not including Actinomycin D, Etoposide, Methotrexate, Vincristine, and Cyclophosphamide. She then commenced a regimen of Carboplatin (AUC 5) and Paclitaxel (180 mg/m^2). After completing 8 cycles, her beta-hCG dropped to <0.2 ng/ml. Three additional cycles were administered and the patient remained clinically free of disease, with normal beta-hCG levels for 11 months.

Discussion

Most chemotherapeutic agents can cause 'chemotherapy lung', acute interstitial lung disease. Incidence is estimated at 10%, although it is difficult to obtain accurate estimates due to the complexities of diagnosis and the small patient numbers involved [5]. Identification of drug-associated interstitial lung disease is further hampered, as clinical imaging and pathological patterns are not diagnostically reliable [6]. High-resolution

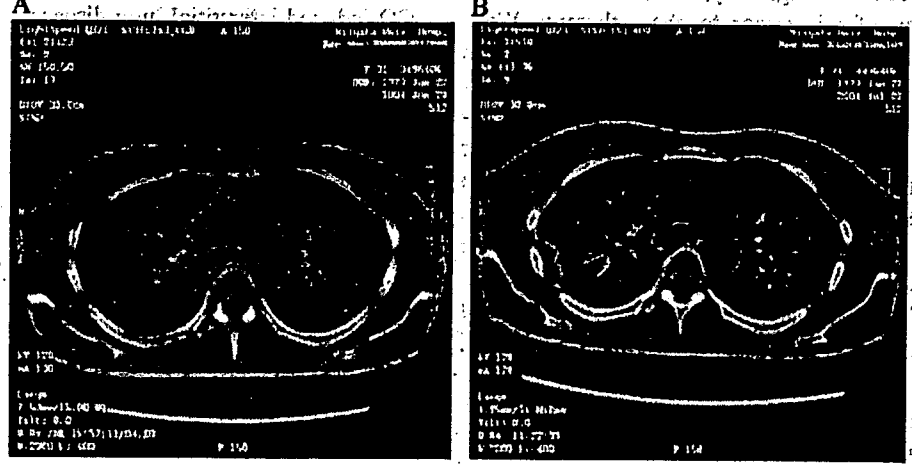

Fig. 2. (A) Lung CT scan showed the extensive bilateral ground-glass opacity, and airspace consolidation. (B) After high-dose steroid therapy, ground-glass opacity on CT scan was remarkably improved.

computed tomography scans demonstrate extensive bilateral ground-glass attenuation and areas of airspace consolidation [7]. Bronchoalveolar lavage is helpful in diagnosis, but it does not always provide a specific diagnosis. A detailed recent drug history is essential in making the diagnosis and steroid therapy useful. A standard of drug-associated disease is the use of re-exposure or rechallenge to confirm diagnosis. However, there is a natural reluctance to put the patient at risk of further illness, particularly if the drug-associated disease is severe.

In our patient, acute interstitial lung disease induced by EMA-CO had been developed after 7 cycles of the chemotherapy. Since any drug of EMA-CO regimen could induce interstitial lung disease, we changed EMA-CO regimen to the combination of paclitaxel and carboplatin. A cisplatin-based regimen such as EMA-EP is generally agreed to be the most appropriate second line regimen. BEP, VIP, and ICE are accepted as the third line and all produce cures in these settings [2–4]. The use of these second and third line regimes is hesitated after EMA-CO-induced interstitial lung disease. It is in the setting of highly resistant tumors necessitating the use of toxic combinations that taxane-based regimens are finding a role. Paclitaxel was investigated for the efficacy and biologic properties in choriocarcinoma cell lines. Proliferation of choriocarcinoma cells was inhibited in a dose-related manner [8]. In vitro chemotherapeutic response by paclitaxel was also demonstrated in treatment of choriocarcinoma [9]. Activity of paclitaxel in chemorefractory choriocarcinoma in clinical setting has been described in several case reports [10–15]. We chose paclitaxel and carboplatin combination as a salvage regimen with the hope of completely eradicating the remnant tumors. This rationale was based upon experimental evidence suggesting antineoplastic synergism between these agents. Carboplatin use in gestational choriocarcinoma has been described previously, and was well tolerated in the patient who would not otherwise have been able to continue platinum-based therapy [16]. In that case, the response to paclitaxel and carboplatin was clearly demonstrated and appeared to have eradicated all foci of tumor except for brain metastasis. Then, after completing 8 cycles of paclitaxel and carboplatin combination, serum beta-hCG level of our patient dropped to normal range, and metastatic tumors in the lung and the liver were resolved. She achieved remission state without serious adverse effects with paclitaxel and carboplatin for 11 months. Paclitaxel and carboplatin combination is active and appears to be a viable alternative to EMA-CO combination chemotherapy in metastatic choriocarcinoma. The role of paclitaxel as replacements or established regimens or in combination with other active agents merits further investigation in high-risk choriocarcinoma.

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