Arsenic Trioxide Newly Joins Treatment Strategies for Acute Promyelocytic Leukemia

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Treatment of acute promyelocytic leukemia (APL) has made a marked advance since all-trans retinoic acid (ATRA), alone or in combination with chemotherapy, was included in an induction regimen (1-3). Many reports have revealed that about 90% of patients achieved complete remission (CR) and 60 to 70% of them survived over 3 to 5 years (4-8). These excellent results show that ATRA differentiation therapy is firstly succeeded in APL of all malignancies. But about 30% of APL patients in the initial CR eventually relapsed. It is difficult to re-induce the relapsed patients into the second CR with regimens including ATRA.

Recently, a Chinese group showed that arsenic trioxide could induce CR in 14 out of 15 relapsed patients with APL (9). Then a group in the United States also demonstrated the second CR of 11 out of the same 12 patients (10). The remarkable effect of arsenic trioxide is associated with incomplete cytodifferentiation and the induction of apoptosis in leukemic cells (11, 12). Now arsenic trioxide is taking an important position in the treatment strategy for APL (13).

In Japan arsenic trioxide has been considered to be a poison, not a drug for a long period, thus there are only a few reports on APL treated with arsenic trioxide (14). Hirayama et al reported that a case of relapsed APL was treated with arsenic trioxide and had a second CR with minimal adverse effects such as mild neuralgia and skin eruption (15).

The most common arsenic trioxide-related toxicities are as follows; skin rash, nausea, vomiting, diarrhea, headache, peripheral neuropathy, hyperglycemia, hypokalemia, hypomagnesemia, leukocytosis, tachycardia and QT prolongation (14, 16). Sudden death among patients treated with arsenic trioxide was also reported and was considered to due tocardiotoxicity (17, 18). Therefore, arsenic trioxide may be significantly or even fatally toxic at low doses and that caution is warranted in its use.

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References