Long term remission of metastatic ovarian cancer after chronic treatment with the Na⁺-H⁺ antiport inhibitor amiloride

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The case of a patient who developed ovarian cancer in October, 1989 is here reported. At that time, a 7.5 cm. in diameter right ovarian mass with a broken capsule was removed (stage IC), which revealed malignant endometrioid carcinoma. No other staging procedures were done at that time. In December, 1989, chemotherapy with cyclophosphamide, 800 mg/m² and cis-platinum, 80 mg/m² q. 3 w. was started. This treatment was continued until May, 1990.

In light of persistent elevations of CA-125, both during and after chemotherapy (Figure 1, April, 1990), in May, 1990, the patient was started with amiloride, 5 to 10 mg tid. as the only antineoplastic medication. This therapeutic program was continued on a daily basis until December, 1992. Occasional elevations of K⁺ (up to 5.9 meq/l) and BUN (58 mg/dl) were found. Levels of CA-125 progressively diminished and became undetectable after a 11 months. However, since July, 1990 the patient had started to complain of increasing pain in the right inguinal area. In April, 1991, with Ca-125 already at undetectable levels, NMR revealed a 3x3 cm. mass in the minor adductor muscle of the right leg. In May, 1991 the mass was removed, revealing metastatic disease of poorly differentiated ovarian carcinoma. All the determinations of CA-125 during the next 10 years have been normal. The patient is in good health and free of disease more than 11 years after the diagnosis of ovarian metastatic disease and after failure to standard conventional chemotherapy. The presence of a continuous elevation of tumor marker CA-125 after failure to conventional chemotherapy and the presence of a single location of metastatic disease makes this case to fully conform the most strict criteria for progressive disease in ovarian cancer (1).

Na⁺-H⁺ inhibitors of the amiloride series have been repeatedly advocated in both the adjuvant and neo-adjuvant settings and in the control of the neovascularization process in cancer (2, 3). Different mechanisms have been proposed for their action, from inhibition of Na⁺/H⁺ antiporter activity and selective intracellular acidification to inhibition of urokinase-type plasminogen
Amiloride has been found to be most effective in achieving a complete suppression of the metastatic process in rats with R3230 breast carcinoma (5). Long term treatment with adjuvant and neo-adjuvant amiloride seems to be well tolerated, with occasional gastralgias and elevations of plasma K+ and BUN as the main side-effects. This case indicates that both the parental molecule and the more potent derivatives of the amiloride series deserve further attention in the adjuvant and neoadjuvant treatment of different malignant diseases in humans (4-8).

References:


FIGURE 1

Legend to Figure 1: Clinical and chemical evolution of the case of ovarian carcinoma here described.