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CASE STUDY

Response to metronomic chemotherapy in a metastatic adenoid cystic carcinoma of the Parotid Gland

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KEYWORDS
Adenoid cystic carcinoma;
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Metronomic chemotherapy;
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Abstract
Formerly, salivary gland cancer was considered to be chemoresistant. Chemotherapy is indicated when distant metastases or inoperable locorregional disease are observed, although the chemotherapy schedule is not well defined.
Data on chemotherapy treatment for adenoid cystic carcinoma consist of phasell trials. Most of these studies analyze therapies with a combination of agents at full dose, although there is no clear evidence that such treatment improves survival.
The administration of cytotoxic agents with low doses at frequent, regular intervals with no drug-free interruptions is known as metronomic chemotherapy. Most head-to-head studies show similar or even superior therapeutic results with metronomic scheduling than with a maximum tolerated dose regime.
Our case report shows for first time the clinical activity of low-dose paclitaxel and cisplatin chemotherapy given separately as a single agent in metastatic adenoid cystic carcinoma of the parotid.

PALABRAS CLAVE
Carcinoma adenoide quístico;
Quimioterapia metronómica;
Paclitaxel;
Parótida;
Cisplatino

Respuesta a quimioterapia metronómica en un carcinoma adenoide quístico metastásico de parótida

Resumen
Los tumores de glándulas salivares han sido considerados hasta hace pocos años quimiorresistentes. El tratamiento con quimioterapia está indicado en el contexto de enfermedad locorregional irresecable o enfermedad metastásica.
La experiencia de quimioterapia en el carcinoma adenoide quístico de parótida se basa en estudios fase II; la mayoría con esquemas de quimioterapia en combinación y a dosis plenas, y sin evidencia de que aumenten la supervivencia.

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Se conoce como quimioterapia metronómica a la administración de agentes citotóxicos a bajas dosis y a intervalos cortos y regulares, sin interrupciones en el tratamiento. La mayoría de estudios demuestran una eficacia similar o incluso superior y una menor toxicidad que cuando se administra con la máxima dosis tolerada.
Nuestro caso clínico muestra, por primera vez, la eficacia del paclitaxel y el cisplatino en monoterapia y a dosis metronómicas en el tratamiento del carcinoma adenoide quístico de parótida metastásico.

Case study

The patient was a 64-year-old woman who presented with tumour of the left parotid, 3 cm in diameter and of stony consistency, that was biopsied and diagnosed as a high-grade adenoid cystic carcinoma of the parotid gland. Cervical and thoracic tomography showed no adenopathies or pulmonary metastases, and it was classified as T2N0M0. As the initial treatment, a left superficial parotidectomy was performed with radical lymphadenectomy in cervical regions II and III and adjuvant radiation therapy (55 Gy). Surgical margins were disease-free, and no lymphatic metastases were observed.

After being disease-free for four years, patient was diagnosed with two pulmonary metastases in the left lower lobe requiring a segmentectomy.

Three months later, new lesions appeared in the lungs, and patient was started on palliative chemotherapy (capecitabine 1.25 mg/m^2 q12h for 14 days).

At three months, there was evidence of further lung progression, which was treated with imatinib (400 mg/24 h); this was not effective, either, and was replaced with paclitaxel (80 mg/m^2 weekly). There was a partial response to this treatment (according to RECIST criteria[1]: reduction of more than 30% in maximum tumour diameter, measured directly via radiological imaging) with clinical improvement, mild toxicity, and a grade 1 peripheral neuropathy for 9 months–after which a new pulmonary progression was diagnosed (Figure 1).

Because of her good general condition (performance status 1), patient was started on a new chemotherapy regimen with cisplatin 40 mg/m^2 weekly; at 2 months, this achieved a significant decrease in the size and number of pulmonary lesions (Figure 2). After 6 months of weekly cisplatin treatments, patient maintained an objective response.

Discussion

Because the treatment objective in metastatic disease is usually palliation, disease stabilization accompanied by improvement in the symptomatology is considered success.

In the only Phase II study of patients with adenoid cystic carcinoma treated with paclitaxel, there were no partial responses.[2] In our patient, disease stabilization was achieved for 7 months, the peculiarity being that paclitaxel doses were administered on a metronomic schedule. An objective response was subsequently obtained with a regimen of cisplatin 40 mg/m^2 weekly for another 4 months.

Current research on development of new chemotherapies is focused, in part, on inhibition of tumour angiogenesis. Drugs such as paclitaxel that are already in use have recently been shown to have this antiangiogenic effect when administered metronomically.[3,4] The hypothesis is that the brief period of rest from treatment does not allow regeneration of vascular endothelial cells in the tumour niche[5,6]; there is also a delay in the appearance of cellular mechanisms of treatment resistance via acquired mutations.[7]

Figure 1 Pulmonary metastasis, pleural and costal.

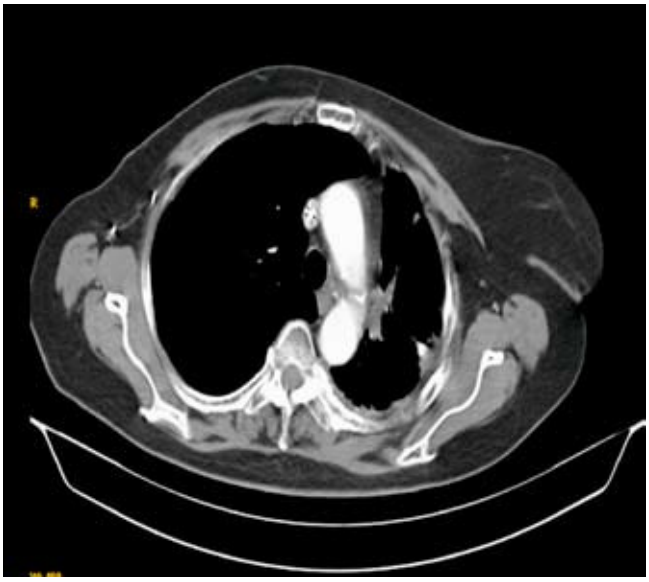

Figure 2 Partial response following cisplatin therapy.

The objective of this clinical case was to draw attention to the sensitivity, good tolerance, and low acute toxicity of paclitaxel and cisplatin in low metronomic doses for treatment of metastatic adenoid cystic carcinoma of the parotid gland. On the basis of these results, we suggest that clinical trials be conducted with metronomic chemotherapy (at repeated low doses) to confirm its efficacy in the parotid tumours that are normally considered chemoresistant to standard-dose chemotherapy. Pending these studies, we would advise using chemotherapy on a metronomic schedule for patients with pulmonary metastasis from an adenoid cystic carcinoma of the parotid gland.

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