Treatment of progressive metastatic glomus jugulare tumor (paraganglioma) with gemcitabine

J. Marc Pipas¹ and Robert F. Krywicki

Dartmouth-Hitchcock Medical Center/Norris Cotton Cancer Center, Lebanon, NH 03756 (J.M.P.); and Phoebe Putney Memorial Hospital/Phoebe Cancer Center, Albany, GA 31701 (R.F.K.)

Paragangliomas are rare tumors of the paraganglia composed of specialized neural crest cells arising in association with sympathetic ganglia. Here we report a case of progressive, metastatic paraganglioma (glomus jugulare tumor) responsive to single agent gemcitabine. In addition, a brief review of chemotherapy for paraganglioma follows the case presentation. *Neuro-Oncology* 2, 190-191, 2000 (Posted to *Neuro-Oncology* [serial online], Doc. 00-012, May 16, 2000. URL <neuro-oncology.mc.duke.edu>)

Case Study

A 17-year-old African-American female presented in January, 1995, with history of headaches, nausea, vomiting and left sixth nerve palsy. Evaluation revealed a large left-sided glomus jugulare tumor with extensive posterior fossa and cavernous sinus involvement. The patient underwent extensive surgical debulking, with gross tumor left at the time of surgery. Histology revealed paraganglioma.

Ten months later, the patient was treated for extensive recurrence in the tumor bed. External-beam radiotherapy to 4500 cGy was directed to the entire posterior fossa, with considerable reduction in the bulk of the tumor mass on scan. She did well until November of 1998, when she developed vague decreased sensation in the right arm and right hand. MRI scan revealed increase in tumor size with pontine involvement and mass effect on

the fourth ventricle, the aqueduct of Sylvius, and the posterior aspect of the floor of the third ventricle. The patient was referred to medical oncology.

At the time of her evaluation, the patient had a left sixth nerve palsy, left facial droop, and 3/5 weakness in her body on the right. She was treated with CyVADIC (cyclophosphamide 500 mg/m² by i.v. day 1, vincristine 1.4 mg/m² by i.v. days 1 and 5, doxorubicin 50 mg/m² by i.v. day 1, and dacarbazine 250 mg/m² by i.v. days 1 through 5. Treatment was delivered on a planned q-28-day schedule but was complicated by recurrent episodes of febrile neutropenia requiring hospitalization on 2 separate occasions despite the use of growth factor support. After 2 cycles of chemotherapy, brain MRI revealed stable disease. After a third cycle of chemotherapy, a chest X-ray done at the time of a febrile neutropenic episode revealed small nodular densities bilaterally. Marked bilateral pulmonary nodules were confirmed on chest CT scan, and the patient was taken to open lung biopsy, which confirmed the presence of metastatic paraganglioma. The patient and her family insisted upon further treatment, and single-agent gemcitabine was instituted at a standard dose of 1000 mg/m² on days 1, 8, and 15 on a q-28-day cycle. The patient tolerated her treatment well with no further episodes of neutropenia.

After 2 cycles of gemcitabine, the patient was restaged with a CT scan of the chest, which revealed improved appearance of the pulmonary metastatic lesions, with a decrease in both size and number of the lesions (Figs. 1 and 2). Repeat MRI scan of the brain confirmed a greater than 50% reduction in the size of the intra-axial component of the left skull-based mass, with improvement in the degree of mass effect involving the brain stem (Figs. 3 and 4). Clinically, the patient had resolution of her right-sided weakness. Her cranial nerve palsies remained unchanged. She continues on therapy with gemcitabine.

Received 16 February 2000, accepted 13 March 2000.

¹Address correspondence and reprint requests to Marc Pipas, Norris Cotton Cancer Center, Dartmouth-Hitchcock Medical Center, Lebanon, NH 03756.

Fig. 1. Pretreatment chest CT.

Fig. 2. Posttreatment chest CT.

Fig. 3. Pretreatment brain MRI.

Fig. 4. Posttreatment brain MRI.

Discussion

Paragangliomas (chemodectomas) are tumors of the paraganglia and are composed of specialized neural crest cells arising in association with sympathetic ganglia (Patel et al., 1995). Glomus jugulare tumors are nonchromaffin paragangliomas that arise from the temporal paraganglia (Gabriel et al., 1995). These tumors frequently display an indolent course, often spanning a decade or more. They tend to be invasive and are associated with a high rate of local recurrence, especially after inadequate resection (Patel et al., 1995). Approximately 1000 cases of glomus jugulare tumors have been reported in the literature, making these the most common tumors of the nonchromaffin paraganglia (Zak and Lawson, 1982). Metastatic disease occurs in less than 3% of cases, with metastatic sites including lungs, liver, and, rarely, bone (Zak and Lawson, 1982).

There is a paucity of data regarding chemotherapy for paragangliomas in general, and glomus jugulare tumors in particular. Patel et al. (1995) reviewed the 15-year experi-

ence with paragangliomas at M.D. Anderson Cancer Center and reported a 46% response rate with doxorubicin, dacarbazine, and cyclophosphamide-containing regimens. Solitary case reports have demonstrated activity for several agents, including carboplatin, cisplatin, and etoposide (Cairnduff and Smith, 1986; Mertens et al., 1993). In contrast, Massey and Wallner (1992) reported the Memorial Sloan-Kettering experience for metastatic paraganglioma and reported no responses to a variety of chemotherapeutic regimens including cyclophosphamide, cisplatin, doxorubicin, and dacarbazine (Massey and Wallner, 1992).

We believe that this is the first reported experience using gemcitabine in the treatment of paraganglioma, and the patient's response is especially encouraging given the prior development of metastatic disease during multi-agent chemotherapy. It is also encouraging that the patient had a response of both her metastatic disease and her intracranial mass. Further investigation of gemcitabine for glomus jugulare tumors and other paragangliomas is warranted.

References

- Cairnduff, F., and Smith, I.E. (1986) Carboplatin chemotherapy for malignant paraganglioma. *Lancet* **2**, 982. (letter)
- Gabriel, E.M., Sampson, J.H., Dodd, L.G., and Turner, D.A. (1995) Glomus jugulare tumor metastatic to the sacrum after high-dose radiation therapy: Case report. *Neurosurgery*, **37**, 1001-1005.
- Massey, V., and Wallner, K. (1992) Treatment of metastatic chemodectoma. *Cancer* **69**, 790-792.
- Mertens, W.C., Grignon, D.J., and Romano, W. (1993) Malignant paraganglioma with skeletal metastases and spinal cord compression: Response and palliation with chemotherapy. *Clin. Oncol.* **5**, 126-128.
- Patel, S.R., Winchester, D.J., and Benjamin, R.S. (1995) A fifteen year experience with chemotherapy of patients with paraganglioma. *Cancer* **76**, 1476-1480.
- Zak, F.G., and Lawson, W. (1982) *The Paraganglionic Chemoreceptor System: Physiology, Pathology, and Clinical Medicine*. New York: Springer-Verlag.