Radiographic regression of cranial meningioma in a NF2 patient treated by bevacizumab

Neurofibromatosis type 2 (NF2) is a rare genetic disorder characterized by the development of multiple tumors of the central nervous system including bilateral vestibular schwannomas (VSs) and multiple meningiomas. Treatment options in NF2 tumors include surgery and radiotherapy. Bevacizumab, a humanized mAb against vascular endothelial growth factor (VEGF), has recently been proposed to NF2 patients with inoperable VS, leading to hearing improvement and some decrease in VS size [1, 2]. Interestingly, regression under bevacizumab treatment has also been reported in a sporadic case of non-NF2 anaplastic meningiomas [3].

This case describes a 51-year-old female with NF2. A right 40-mm VS responsible for deafness was removed at the age of 34. The left VS that measured initially 30 mm in greatest diameter steadily grew and was 42 mm at the age of 50, with progressive hearing loss. Thus, bevacizumab was proposed as a treatment option. Serial magnetic resonance imaging monitored tumor response. Volume calculations of the contrast-enhancing portion of the targeted tumor were carried out using GE Advantage Windows workstation (GE Healthcare, Chalfont St. Giles, UK). The patient has been receiving i.v. bevacizumab at a dose of 5 mg/kg of body weight every 2 weeks for 15 months. No side-effect was noticed. The volume of the VS decreased from 13.9 to 11.8 cm$^3$ (15%). Unfortunately, hearing improvement (our primary objective) was not achieved.

Of note, the patient harbored seven intracranial meningiomas. The larger one was an asymptomatic parietal convexity meningioma measuring 30.4 mm (7.3 cm$^3$) at the beginning of bevacizumab treatment. This meningioma has been growing for 5 years, with a 38% increase in volume in the preceding 12 months. The other six meningiomas were small and have been stable for 5 years. We observed a decrease in the size of the parietal meningioma of 22% in 15 months of continuous bevacizumab treatment (Figure 1). Of note, this meningioma was not the primary target of bevacizumab and could also have been easily surgically removed. The patient is still under treatment, thus potential rebound after drug discontinuation cannot be assessed [4].

In summary, this report is the first evidence of activity of bevacizumab in a NF2 patient with growing meningioma and confirms reports showing activity of this drug in VS. While frequently considered as indolent tumors, meningiomas and schwannomas may evolve toward a more aggressive phenotype after several years of latency. This switch in clinical evolution has been frequently associated with the development of tumor angiogenesis. This significant tumor reduction might be explained by the high VEGF and VEGF receptor-1 expression in rapidly growing meningioma [5]. Interestingly, in our case, only the more rapidly growing and largest meningioma was sensitive to bevacizumab, while other smaller meningiomas did not present any change in tumor size. Although this case report suggests activity, more similar cases are needed to consider bevacizumab as a treatment option in NF2 patients with growing irremovable meningiomas outside of the frame of a clinical trial.

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references
Figure 1. Volumetric evolution of intracranial tumors in a neurofibromatosis type 2 patient treated by bevacizumab for 15 months. The largest growing parietal meningioma showed a 22% decrease in size during the treatment. No noticeable change in volume was noticed for six other meningiomas and a lower cranial nerve schwannoma, whose size has been stable for 52 months before onset of treatment.


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