Incidence of cranial nerve palsy after preoperative embolization of glomus jugulare tumors using Onyx

Clinical article

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Object. The resection of glomus jugulare tumors can be challenging because of their inherent vascularity. Preoperative embolization has been advocated as a means of reducing operative times, blood loss, and surgical complications. However, the incidence of cranial neuropathy associated with the embolization of these tumors has not been established. The authors of this study describe their experience with cranial neuropathy following transarterial embolization of glomus jugulare tumors using ethylene vinyl alcohol (Onyx, eV3 Inc.).

Methods. The authors retrospectively reviewed all cases of glomus jugulare tumors that had been treated with preoperative embolization using Onyx at their institution in the period from 2006 to 2012. Patient demographics, clinical presentation, grade and amount of Onyx used, degree of angiographic devascularization, and procedural complications were recorded.

Results. Over a 6-year period, 11 patients with glomus jugulare tumors underwent preoperative embolization with Onyx. All embolization procedures were completed in one session. The overall mean percent of tumor devascularization was 90.7%. No evidence of nontarget embolization was seen on postembolization angiograms. There were 2 cases (18%) of permanent cranial neuropathy attributed to the embolization procedures (facial nerve paralysis and lower cranial nerve dysfunction).

Conclusions. Embolizing glomus jugulare tumors with Onyx can produce a dramatic reduction in tumor vascularity. However, the intimate anatomical relationship and overlapping blood supply between these tumors and cranial nerves may contribute to a high incidence of cranial neuropathy following Onyx embolization.

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Key Words • Onyx • glomus jugulare tumor • embolization • ethylene vinyl alcohol • cranial nerve palsy • vascular disorders

Glomus tumors of the jugular foramen are surgically challenging lesions because of their inherently vascular nature and proximity to cranial nerves. Also referred to as paragangliomas, chemodectomas, and glomus jugulare tumors, these rare neoplasms arise from paraganglion cells in the adventitia of the jugular bulb. The primary treatment for these tumors is surgical removal.¹⁶

Preoperative embolization has been advocated as a means of reducing operative time, blood loss, and surgical complications. Various embolic agents have been used, including polyvinyl alcohol, polymerized glue, and more recently ethylene vinyl alcohol (Onyx, eV3 Inc.).¹²,¹⁹,²⁰

Outcomes following embolization of glomus jugulare tumors using Onyx and in particular the incidence of cranial neuropathy have not been established. The authors present a series of glomus jugulare tumors preoperatively embolized using Onyx.

Methods

All cases of glomus jugulare tumors preoperatively embolized in the period from 2006 to 2012 were reviewed retrospectively. Patient characteristics, clinical presenta-

Abbreviations used in this paper: ICA = internal carotid artery; NBCA = N-butyl cyanoacrylate; PVA = polyvinyl alcohol.

This article contains some figures that are displayed in color online but in black-and-white in the print edition.
tion, imaging studies, procedural notes, percentage of tumor devascularization, and endovascular complications were evaluated. The institutional review board at the University of Miami approved the study.

**Embolization Technique**

Our technique for tumor embolization with Onyx has been described elsewhere. All embolizations were performed with the patient under general anesthesia. Pre-embolization angiograms were obtained following percutaneous femoral arterial catheterization. Images were analyzed to determine the extent of tumor blush. Intravenous heparin was administered to maintain activated clotting times between 250 and 300 seconds. A 5-Fr catheter (Envoy, Cordis Corp.) was positioned in the external carotid branch that fed the tumor. Selective catheterization of the feeding vessels was subsequently performed using a Marathon microcatheter (eV3 Inc.). A microangiogram was then obtained to assess the tumor blush supplied by the feeding artery as well as the presence of dangerous extracranial to intracranial anastomoses. Dead space within the microcatheter was slowly flushed with 0.3–0.4 ml dimethyl sulfoxide. Onyx embolization was then performed under a subtracted roadmap. The grade of Onyx selected was based on the rapidity of flow demonstrated on the pre-embolization angiogram and the desired degree of Onyx penetration within the tumor parenchyma. The standard technique for Onyx embolization was used until the desired degree of tumor penetration or the maximal degree of reflux along the microcatheter was reached. Embolization of other feeding pedicles then proceeded in a similar manner as necessary. Once embolization was completed and the microcatheter was removed, a final postembolization arterial angiogram was obtained to assess the degree of tumor devascularization and to ensure that there was no inadvertent embolization into the cerebral vasculature.

**Evaluation of Angiographic Devascularization**

Determining if there was intraparenchymal penetration of Onyx was based on whether the embolic agent reached the tumor capillary bed or remained in the feeding arterial pedicle. The percentage of tumor devascularization was determined by tracing the pre- and postembolization tumor blush using ImageJ software (version 1.41, National Institutes of Health). The ratio of post- and pre-embolization tracing in pixels was then calculated.

**Results**

Over a 6-year period, 11 patients with glomus jugulare tumors underwent preoperative embolization with Onyx (Table 1). All embolization procedures were completed in a single session. The mean fluoroscopy time was 83 minutes (range 40–157 minutes). The mean volume of Onyx used was 4.9 ml (range 1.7–10 ml). Twenty-three vessels were selectively catheterized for embolization. Eight patients required selective embolization via multiple vessels, and 8 required embolization via the ascending pharyngeal artery. All but 2 patients underwent embolization with lower-viscosity Onyx 18. Migration of Onyx within the tumor parenchyma was achieved in all cases. There was no evidence of nontarget embolization. The mean percent of tumor devascularization was 90.7%. The mean time from embolization to surgery was 3.1 days (range 1–7 days). The mean follow-up was 30 months (range 4–72 months). Two cases (18%) of cranial neuropathy were attributed to the embolization procedures; one patient suffered permanent facial paralysis, and another developed permanent lower cranial nerve dysfunction.

**Illustrative Cases**

**Case 5**

A 35-year-old woman presented with a 1-year history of right-sided pulsatile tinnitus and hearing loss. The mass was biopsied at an outside clinic, resulting in copious bleeding. An angiogram showed a vascular tumor blush fed by multiple small vessels from the right ascending pharyngeal, middle meningeal, and posterior auricular arteries as well as a large aberrant feeding vessel arising from the cervical internal carotid artery (ICA; Fig. 1A). The patient underwent superselective catheterization of the large ICA feeder (Fig. 1B) followed by embolization using 4.5 ml of Onyx 18. Final postembolization angiography demonstrated 90% tumor devascularization with marked intraparenchymal Onyx penetration (Fig. 1C). No evidence of nontarget embolization was seen. The patient woke up from the procedure with complete facial paralysis on the right side. Seven days after embolization, the tumor was completely resected via a subtotal petrosectomy with facial nerve decompression. At surgery, Onyx material was observed tracking along the facial nerve and its vasa vasorum (Fig. 1D). Final pathological results were consistent with a glomus tumor. The patient had not recovered any facial nerve function at the 6-month follow-up.

**Case 10**

A 45-year-old woman presented with left-sided hearing loss and tinnitus. Further workup demonstrated a “salt and pepper” mass in the jugular foramen on MRI and positive uptake on an octreotide scan. Angiography showed a vascular tumor blush fed primarily by vessels from the occipital and ascending pharyngeal arteries (Fig. 2 left). Selective catheterization and embolization of ascending pharyngeal and occipital artery feeders were performed using 2.5 ml of Onyx 18. The final postembolization angiogram demonstrated complete tumor devascularization (Fig. 2 right). The patient experienced postprocedural ipsilateral shoulder weakness and hoarseness. Uneventful surgical removal was performed 5 days later. Pathology was consistent with a glomus tumor. The postembolization deficit did not resolve after 9 months of clinical follow-up.

**Discussion**

Onyx is a nonadhesive, liquid embolic agent approved by the FDA in 2005 for the treatment of cerebral arteriovenous malformations. The unique properties of Onyx, which have been discussed by Gore et al., facilitate its penetration into the deep vasculature.
Cranial nerve palsy after glomus jugulare embolization

TABLE 1: Clinical summary of 11 patients with glomus jugulare tumors embolized with Onyx

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Onyx Grade</th>
<th>Onyx Volume (ml)</th>
<th>Tumor Devascularization (%)</th>
<th>Complication</th>
<th>Vessels Catheterized</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>26, F</td>
<td>18</td>
<td>10</td>
<td>100</td>
<td>none</td>
<td>APA, PAA, IMAX</td>
</tr>
<tr>
<td>2</td>
<td>66, M</td>
<td>34</td>
<td>2</td>
<td>70</td>
<td>none</td>
<td>APA, OA</td>
</tr>
<tr>
<td>3</td>
<td>47, M</td>
<td>18</td>
<td>2</td>
<td>100</td>
<td>none</td>
<td>3 ECA feeders</td>
</tr>
<tr>
<td>4</td>
<td>46, F</td>
<td>18</td>
<td>4.5</td>
<td>70</td>
<td>none</td>
<td>APA</td>
</tr>
<tr>
<td>5</td>
<td>35, F</td>
<td>18</td>
<td>4.5</td>
<td>90</td>
<td>facial paralysis</td>
<td>cervical ICA feeder</td>
</tr>
<tr>
<td>6</td>
<td>57, M</td>
<td>18</td>
<td>8</td>
<td>95</td>
<td>none</td>
<td>OA</td>
</tr>
<tr>
<td>7</td>
<td>43, M</td>
<td>18</td>
<td>2.2</td>
<td>95</td>
<td>none</td>
<td>APA, caroticotympanic, IMAX</td>
</tr>
<tr>
<td>8</td>
<td>40, M</td>
<td>18</td>
<td>4.5</td>
<td>90</td>
<td>none</td>
<td>APA, accessory meningeal, MMA</td>
</tr>
<tr>
<td>9</td>
<td>34, F</td>
<td>18</td>
<td>10</td>
<td>98</td>
<td>none</td>
<td>OA, APA</td>
</tr>
<tr>
<td>10</td>
<td>45, F</td>
<td>18</td>
<td>2.5</td>
<td>100</td>
<td>vocal cord paralysis</td>
<td>APA, PAA</td>
</tr>
<tr>
<td>11</td>
<td>67, F</td>
<td>34</td>
<td>5</td>
<td>90</td>
<td>none</td>
<td>OA, APA</td>
</tr>
</tbody>
</table>

* APA = ascending pharyngeal artery; ECA = external carotid artery; IMAX = internal maxillary artery; MMA = middle meningeal artery; OA = occipital artery; PAA = posterior auricular artery.

Fig. 1. Case 5. A: Anteroposterior angiogram demonstrating right ascending pharyngeal, middle meningeal, and posterior auricular artery feeders as well as a large aberrant feeding vessel arising from the cervical ICA. B: Superselective angiogram of aberrant ICA feeder. C: Final angiogram showing 90% tumor devascularization. D: Intraoperative photograph demonstrating the facial nerve (yellow arrows) encased with Onyx. The stapes is seen within the mastoid antrum (blue arrowhead).

Fig. 2. Case 10. Left: Lateral angiogram demonstrating occipital and ascending pharyngeal tumor feeders. Right: Final angiogram showing complete tumor obliteration.

of Onyx in the treatment of cerebral vascular malformations has encouraged its off-label use for tumor embolization. We previously detailed our experience utilizing Onyx for the embolization of various head, neck, and spinal tumors.4 However, we recently noted 2 instances of permanent cranial nerve complications following Onyx embolization of glomus jugulare tumors even though the embolic material remained within the confines of the tumor blush and despite the absence of nontarget embolization or significant reflux in the feeding artery. Upon review of our series, we were surprised that 18% of the patients with glomus jugulare tumors had suffered permanent cranial nerve morbidity following embolization.

There is limited experience with the preoperative embolization of glomus jugulare tumors using Onyx. To our knowledge, this is the second report of permanent cranial neuropathy following superselective embolization of these lesions with Onyx. We provide a summary of previously documented cranial nerve complications due to preoperative embolization in Table 2. Gartrell et al. highlighted the potential risk of this procedure in their series of 3 patients with postembolization cranial neuropathy.5 They attributed the increased risk of embolization to anatomical variations in the cranial nerve blood supply. Another possible explanation is based on the frequently shared external carotid artery blood supply between glomus jugulare tumors and the vasa nervosa of the cranial nerves, which renders
them vulnerable to occlusion with Onyx during embolization.\textsuperscript{2,13}

Several potential strategies can enhance the safety of embolization for glomus jugulare tumors: defining the goal of embolization, using particulate embolics, or embolizing by direct puncture. It has been suggested that the goal of embolization should be occlusion of the capillary bed of the tumor parenchyma.\textsuperscript{7,8} Furthermore, there is some evidence that tumor embolization without intraparenchymal penetration of the embolic material may not optimally reduce intraoperative blood loss.\textsuperscript{4} Without arresting flow through the parenchymal capillary bed, occlusion of only the feeding artery pedicles may result in persistent tumor vascularity, especially if not all pedicles are embolized. However, given the absence of definitive evidence that parenchymal embolization is the only effective method of reducing blood loss and the high incidence of cranial neuropathy associated with Onyx embolization of glomus jugulare tumors, perhaps the goal of embolization should be pedicular occlusion with minimal reflux along the feeding artery.

There appears to be a lower risk of permanent cranial neuropathy following embolization of glomus jugulare tumors by using particulate embolics. LaRouere et al. found no significant complications in a series of 4 patients embolized with polyvinyl alcohol (PVA).\textsuperscript{10} These findings are corroborated by a larger study by White et al.\textsuperscript{19} in which 8 of 38 patients embolized with PVA had glomus jugulare tumors, and none experienced major complications. Particles ranging in size from 150 to 1000 μm were used in these studies. To our knowledge, only 4 cases of cranial nerve palsy from PVA have been reported since the 1980s, and all resolved.\textsuperscript{9,11,18,19} The low incidence of cranial nerve morbidity can be explained by the use of large particles that typically do not reach the vasa nervosa. Furthermore, because particulate embolics are known to dissipate over time, cranial neuropathies noted following PVA embolization have tended to recover, because of early recanalization of branches feeding the cranial nerves.\textsuperscript{9,11,15,19} Although recanalization of the tumor can also occur, it is generally not a concern, especially if the resection is performed in a timely manner after embolization. On the other hand, Onyx is believed to result in more permanent occlusion of the vasculature, which may explain the permanence of cranial nerve palsies. Although we cannot make definite conclusions regarding the influence of Onyx viscosity on the development of postembolization cranial nerve ischemia, both of the neuropathies encountered in our series occurred with the use of the lower-viscosity Onyx 18. One could hypothesize that just as the smaller particles of PVA have been associated with a higher incidence of nerve ischemia, the less viscous formulation of Onyx may also have a greater tendency to occlude the vasa nervosa.

An alternative to transarterial embolization is direct percutaneous intratumoral injection of embolic material. This approach was first reported by Casasco et al. using N-butyl cyanoacrylate (NBCA) in a series that included 2 glomus tumors.\textsuperscript{1} Özery et al. described 10 patients, 3 with glomus jugulare tumors, who underwent direct intratumoral embolization using Onyx, PVA, or NBCA without complication.\textsuperscript{14} Spelle et al. have also documented successful percutaneous embolization of glomus jugulare tumors with combined CT and fluoroscopic imaging guidance; however, complications were not explicitly mentioned.\textsuperscript{17} In our previously reported series of direct puncture embolizations for vascularized head and neck tumors, no permanent cranial nerve palsies were observed.\textsuperscript{3} Although no cases of cranial nerve palsies related to direct tumor embolization have been reported, glomus jugulare tumors constituted a minority of lesions in these series. Therefore, larger studies are needed to validate the safety and superiority of this technique as compared with standard transarterial embolization.

### Conclusions

Embolizing glomus jugulare tumors with Onyx can produce a dramatic reduction in tumor vascularity. However, the intimate anatomical relationship and overlapping blood supply between glomus jugulare tumors and cranial nerves may contribute to a high incidence of cranial neuropathy following Onyx embolization.

### Disclosure

Dr. Aziz-Sultan is a proctor for eV3 Inc.

Author contributions to the study and manuscript preparation include the following. Conception and design: Elhammady. Acquisition of data: Elhammady, Gaynor, Aziz-Sultan. Analysis and inter-

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**TABLE 2: Reports of cranial neuropathy after glomus jugulare tumor embolization**

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>No. of Patients Treated</th>
<th>Embolic Agent</th>
<th>No. of Patients w/ Postembolization Palsy (location)</th>
<th>Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>present series</td>
<td>11</td>
<td>Onyx</td>
<td>2 (CNVII, LCNs)</td>
<td>none</td>
</tr>
<tr>
<td>Gartrell et al., 2012</td>
<td>3</td>
<td>Onyx</td>
<td>3 (CNVII, LCNs × 2)</td>
<td>partial</td>
</tr>
<tr>
<td>Herdman et al., 1993</td>
<td>1</td>
<td>PVA</td>
<td>1 (facial)</td>
<td>complete</td>
</tr>
<tr>
<td>LaRouere et al., 1994</td>
<td>4</td>
<td>PVA</td>
<td>1 (facial)</td>
<td>complete</td>
</tr>
<tr>
<td>Marangos &amp; Schumacher, 1999</td>
<td>1</td>
<td>PVA</td>
<td>1 (facial)</td>
<td>complete</td>
</tr>
<tr>
<td>Özery et al., 2010</td>
<td>3†</td>
<td>NBCA, Onyx</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Valavanis, 1986</td>
<td>39</td>
<td>PVA</td>
<td>1</td>
<td>complete</td>
</tr>
<tr>
<td>White et al., 2008</td>
<td>8</td>
<td>PVA</td>
<td>0</td>
<td>NA</td>
</tr>
</tbody>
</table>

* CNVII = seventh cranial nerve; LCN = lower cranial nerve; NA = not applicable.
† Treated with direct puncture.
Cranial nerve palsy after glomus jugulare embolization

preparation of data: Elhammady, Gaynor. Drafting the article: Elhammady, Gaynor. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Elhammady. Statistical analysis: Gaynor. Administrative/technical/material support: Jethanamest, Angeli.

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