Jugular paraganglioma treatment at the UMC Maribor

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Key words:
tumor; glomus jugulare; surgery; embolization

Received: 8. 2. 2017
Accepted: 4. 6. 2017

Abstract

Background: Jugular paragangliomas are rare, almost exclusively benign and slowly growing tumors. Arising from the cells of paraganglia in jugular bulb, they infiltrate the temporal bone and later grow intracranially. Because of insidious onset, their diagnosis is relatively late. Patients at presentation usually complain of pulsatile tinnitus and hearing loss, lasting for years. Also common are palsies of the cranial nerves in the area of tumor growth – i.e., facial, glossopharyngeal, vagal, accessory and hypoglossal nerves. Surgical resection is the standard treatment, though technically demanding because of difficult approach to the lateral cranial base and vital structures in the area. The team for treating such patients comprises an ENT specialist, interventional radiologist and a neurosurgeon. The purpose of this article is to review clinical experiences with the treatment of jugular paragangliomas at our Department of ENT and Maxillofacial Surgery of the University Medical Centre Maribor.

Methods: We reviewed the documentation of ten patients treated for jugular paraganglioma in the last 15 years, and presented the clinical data in a table.

Results: Nine patients were treated by preoperative embolization and surgical resection. Surgery was contraindicated in one patient with highly dominant venous drainage on the side of the tumor and aplastic transverse sinus on the opposite side. She was treated by primary radiotherapy. One patient with intracranial tumor growth was treated by subtotal resection and adjuvant radiotherapy. At presentation, lower cranial nerve palsies were present in 60 % of our patients. With the other 40 % we managed to preserve the nerve function postoperatively. Facial nerve function practically normalized in all patients with anterior transposition of the nerve. Our patients were provided with postoperative rehabilitation and corrective procedures such as vocal cord medialization and BAHA hearing aid implantation.

Conclusion: Despite the risks, the surgical treatment is effective in halting the disease and preserving cranial nerve function. The results of our work demonstrate that our patients are provided with a thorough and comprehensive care.

Cite as: Rebol J, Lanišnik B, Ravnik J, Jevšek M, Ložar M. [Jugular paraganglioma treatment at the UMC Maribor]. Zdrav Vestn. 2017;86(9–10):381–9.

DOI: 10.6016/ZdravVestn.2491

1. Introduction

Jugular paragangliomas are rare, slowly growing tumours arising from paraganglion cells in adventitia of the jugular bulb. Because of their low prevalence, slow growth and hidden location on physical examination, the disease is usually quite advanced at diagnosis, with symptoms present for years (1,2). The standard treatment is microsurgical resection, which is technically challenging because of difficult accessibility of the lateral skull base and the vital structures located there. The multidisciplinary team for treating such patients usually consists of an ENT surgeon, a neurosurgeon and an interventional radiologist. At the Department of ENT and Maxillofacial Surgery of the University Medical Centre Maribor, we started operating jugular paragangliomas 15 years ago. The purpose of this article is to present our work and clinical experience.

2. Definition

Paragangliomas are neuroendocrine tumours arising from extra-adrenal paraganglia of the autonomic nervous system (3,4). Glenner and Grimley developed a classification of paraganglia, based on embryologic origin, anatomic location and histologic features, as adrenal and extra-adrenal paraganglia.

Tumours of this tissue – i.e. paragangliomas, are classified in the same fashion (5). 90 % of paraganglion system tumours arise in adrenal glands, they are called pheochromocytomas. Of the remaining 10 %, 85 % arise in the abdomen, 12 % in the thorax, and 3 % in the head and neck (3). Branchiomeric and intravagal paragangliomas are distributed in the head, neck and mediastinum and have the lowest catecholamine content (5). This article pertains to jugular paragangliomas.

In the literature, paragangliomas are traditionally named glomus tumours, due to the prevalent opinion that their chief (neurosecretory) cells originate from vessel wall pericytes, as is true with actual glomus tumours found in skin. However, paraganglion cells are of neuroectodermal origin and have no connection to these arterio-venous malformations (6,7).

Zak and Lawson (1982) described nonchromaffin paraganglia as mostly microscopic sized bodies, consisting of lobules of epithelioid cells lying in richly vascularised stroma. They are located along cranial nerves containing autonomous fibres, e.g. the glossopharyngeal nerve and the vagal nerve. They are able to produce and store biogenic monoamines (catecholamines and serotonin). The best studied is the function of carotid and aortic bodies, which are known to serve as chemoreceptors.

The rest of nonchromaffin paraganglia are structurally identical, but their chemoreceptor function has never been proven.

Guild (1953) made a study of 88 temporal bones and found 248 such bodies, on average 2.82 bodies in one ear. No connection was found between number of the paraganglia and gender, race or side of head. However, the number of these bodies was connected with age, rising until the 4th

decade of life and decreasing afterwards. The anatomic position of temporal bone paraganglia was inconsistent but always related to the course of Jacobson's (n. tympanicus) and Arnold's (auricular branch of n. vagus) nerves. A half were found in the jugular bulb, a quarter on the promontorium, and a fifth

inside the bony canals of the two nerves. Vascular supply was from the tympanic branch of the ascending pharyngeal artery. They probably received innervation from the glossopharyngeal nerve (8,9).

The incidence of jugulotympanic (temporal) paragangliomas is approximately 1:1.3 million (10). They are the second commonest tumours of the temporal bone, being 4 to 6 times more frequent in women than in men (3,11). In women they most often appear sporadically between 40 and 60 years of age. In men, hereditary forms are relatively commoner, appearing at younger age. Some syndromes with a high incidence of paraganglioma are multiple endocrine neoplasia type II (MEN II), Von Hippel-Lindau syndrome, and neurofibromatosis type I. Multicentric paragangliomas are sporadic in 10–20 % of cases and hereditary in up to 80 %. They are mostly benign; 2–4 % are malignant (5,13). Approximately 3 % of these tumours cause clinically detectable signs of paraneoplastic syndrome due to catecholamine secretion (3).

2.1. Presentation

Hearing loss and tinnitus are the most frequent symptoms at presentation. Pain and vertigo are somewhat less common. When the tympanic membrane is injured by the tumour, ear discharge or haemorrhage can be seen. Compression of cranial nerves VII, IX, X, XI and XII is often manifested as facial palsy, dysphagia, hoarseness, shoulder elevation palsy, and tongue hemiparesis, respectively (10). At otoscopy, the tympanic membrane can be intact with a red tumour behind it or red polypoid tissue in the ear canal (12) (Figure 1). When the tumour is growing intracranially, signs of high intracranial pressure can join the clinical picture.

2.2. Diagnosis

Besides a thorough clinical examination, contrast enhanced computed tomography or magnetic resonance imaging is essential. A diffusely infiltrative growth pattern with bone erosion and high contrast uptake can be seen, which differentiates a paraganglioma from a meningioma or schwannoma. The latter two also rarely invade the middle ear. A four-vessel angiography is needed at preoperative planning, to show the vascular anatomy of the tumour, the possibility of preoperative embolization, and the intracranial circulation (Figure 2). For diagnosing metastatic disease or multicentric tumours, PET is a useful imaging modality (5). Most often used for grading the tumour size is the Fisch classification of temporal paraganglioma (Table 1) (13).

2.3. Treatment

Surgical treatment with total resection is the standard treatment for these tumours (14-16). Preoperatively, a CT angiography is done to demonstrate the intracranial arterial and venous circulation and tumour embolization options. Embolization is usually done via arterial approach, by superselective catheterisation and embolization of the supplying arteries. The most frequently used embolization materials for glomus tumours are particles (polyvinyl alcohol or trisacryl gelatin microspheres) and liquid embolization materials (n-butyl cyanoacrylate and ethylene vinyl alcohol copolymer). The goal is to reduce the tumour vascularisation. The effect of embolization can be transient or permanent, depending on the material used. Therefore, coordinated scheduling of procedures is important.

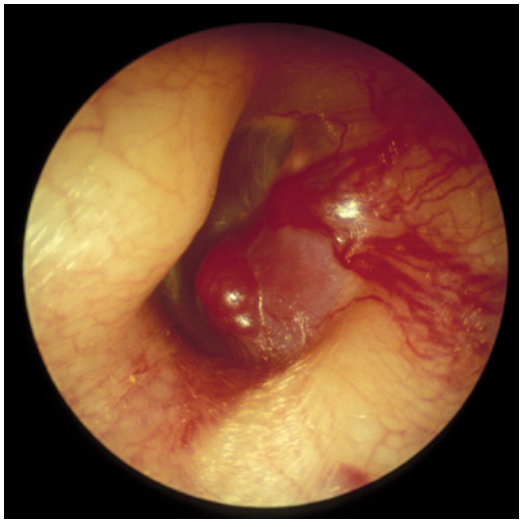

Figure 1: Otoscopic appearance of jugular paraganglioma. The tumour is growing into the middle ear and bulging the ear drum in the posterior quadrant area. Under the microscope, pulsations of the tumour can be observed.

To access the tumour via the infratemporal fossa, the Fisch type-A approach is most frequently used. This is done by retroauricular incision and radical mastoidectomy. The facial nerve is mobilised from its bony canal distally to the geniculate ganglion and transposed anteriorly (Figure 3). Next, the sigmoid sinus is ligated, and the remaining part of the mastoid and the styloid process removed to fully expose the jugular fossa (Figure 4). Then the tumour can be extirpated along with the lateral wall of the sigmoid sinus. The internal jugular vein is ligated. The tissue gap is then filled with abdominal fat, and additional support can be provided by inferior rotation of the temporal muscle (14).

An alternative treatment option is (stereotactic) radiation, which is usually considered in inoperable, recurrent or residual tumours (14).

Table 1: Fisch classification of temporal paragangliomas.

Class	Description
A	Tumours confined to the tympanum and arising from the promontory
B	Tumours involving the tympanum, with or without mastoid involvement but always arising from the hypotympanic region; the cortical bone over the jugular bulb must be intact
C	Tumours eroding the bone over the jugular bulb; the tumour may extend into and destroy the bone of the infralabyrinthine and apical compartments of the temporal bone
C1	Tumours involving the foramen caroticum
C2	Tumours involving the vertical segment of the carotid canal
C2	Tumours involving the horizontal segment of the carotid canal
C4	Tumours extending to the ipsilateral foramen lacerum and cavernous sinus
D	Tumours with intracranial extension
De1	Tumours with intracranial extradural extension of up to 2 cm
De2	Tumours with intracranial extradural extension of up to 2 cm
Di1	Tumours with intracranial intradural extension of up to 2 cm
Di2	Tumours with intracranial intradural extension of up to 2 cm
D3	Tumours with inoperable intracranial extension

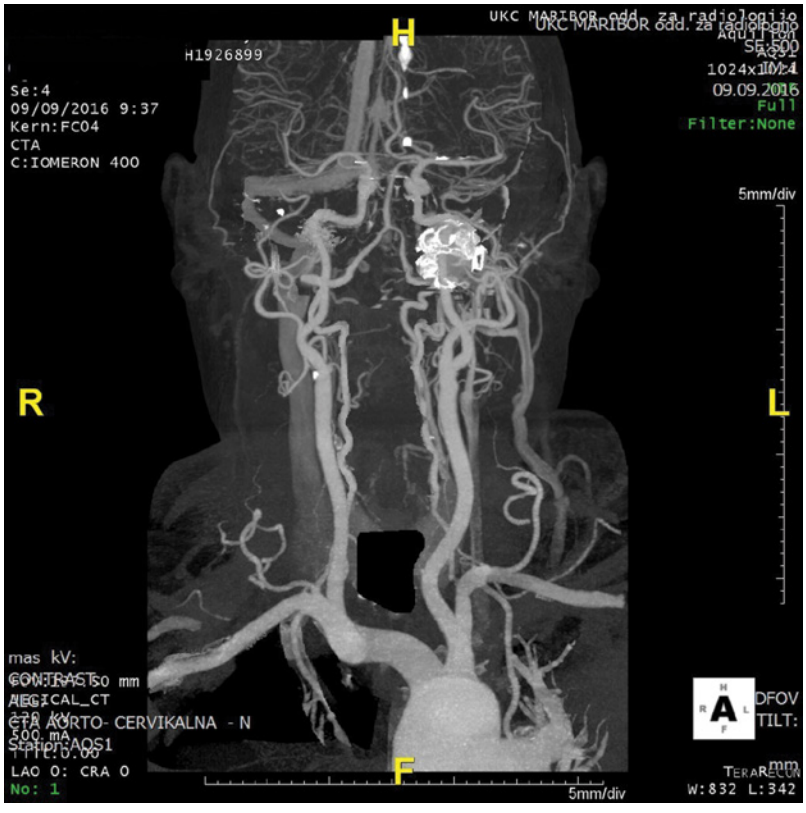

Figure 2: CT angiography shows an intensely opacifying tumour in the area of the left jugular bulb, surrounding one third to one half of internal carotid artery. Its blood supply comes from branches of the retroauricular, maxillary, and ascending pharyngeal arteries.

3. Methods

We reviewed the documentation of ten patients treated for jugular paraganglioma. Their clinical course is presented in Table 2. Each patient's initials and year of birth are presented. Age refers to the patient's age at the time of surgery. As seen in the table, the most frequent symptoms were pulsatile tinnitus and hearing loss present for years, in one case even decades, with the hearing loss slowly progressing. Four patients had vestibular symptoms such as vertigo and a feeling of instability while walking. Tumour size was estimated from CT images and graded according to the Fisch classification. All patients but one were treated with preoperative embolization and surgical resection. In one patient, surgery was contraindicated because of markedly dominant venous drainage on the tumour side and an aplastic transverse sinus on the contralateral side. She was treated with radiation. In another patient, we combined embolization, partial resection and radiation because of the tumour size. In the follow-up column, we marked with an asterisk those patients whose status was known at the time of writing this article. The others had discontinued their follow-up visits for various reasons or were visiting clinics in other regions of the country. Thus we had no information on their current condition. All patients whose status was known were alive at the time of writing this article. Because of anterior facial nerve transposition, the patients initially had a high grade of facial palsy, which was expected to improve over the course of one year postoperatively. The final functional status of the facial nerve was assessed using the 6-stage House-Brackmann scale. Two patients had the facial nerve resected due to tumour infiltration. A total facial palsy resulted despite reanastomosis of the nerve. The histology report in all cases showed a paraganglioma with characteristic nests of chief cells with hyperchromatic nuclei.

4. Results

The results of treatment are presented in Table 2.

5. Discussion

The treatment of jugular paragangliomas is demanding and requires a team approach. Jugular paragangliomas are slowly growing tumours that remain clinically silent for a long time. Most of our patients

were around 60 years of age. Their tumours had grown over many years, causing irreversible damage to cranial

nerves. Surgery cannot restore function when nerve palsies are seen preoperatively. The most bothersome in everyday life is usually vagal nerve paralysis, causing dysphonia and, most notably, dysphagia and risk of aspiration. Other nerve deficits seen in our patients were glossopharyngeal, accessory and facial nerve palsies. Although surgical removal of jugular paragangliomas is a deman-

Table 2: Degree of facial nerve paresis assessed using the House-Brackmann score (HB). Age refers to the patient's age at the time of surgery.

Patient	Gender	Age	Symptoms	Stage	Therapy	Follow-up	Results
J. I. 1934	f	66	p. tinnitus; hearing loss; vertigo; dysphagia; hoarseness	C2	embolization and resection	15 years*	paresis of CN VII - HB 1; pre-existing paresis of CN IX, X, XII
K. S. 1937	f	67	p. tinnitus; hearing loss	C1	embolization and resection	12 years*	no new nerve deficits, CN VII - HB 1
A. M. 1944	f	60	p. tinnitus; hearing loss; otorrhoea; dysphagia; hoarseness; shoulder weakness	C2	embolization (blindness in ipsilateral eye) and resection	11 years*	no new nerve deficits, pre-existing paresis of CN IX, X, XI
R. A. 1937	f	68	hearing loss; vestibular disorder; dysphagia; hoarseness; shoulder weakness; tongue palsy	De1	embolization, subtotal resection and adjuvant radiation	7 years	paresis of CN VII – HB 3; pre-existing paresis of CN IX, X, XI and XII
P. M. 1944	f	61	p. tinnitus; hearing loss	C2	embolization and resection	1 year	paresis of CN VII
K. M. 1952	m	62	hearing loss; vestibular disorder; dysphagia; hoarseness; shoulder weakness	C2	embolization and resection	2 years *	no new nerve deficits; improvement of vestibular symptoms
H. A. 1983	f	31	p. tinnitus; dysphagia; hoarseness; shoulder weakness; tongue palsy	C2	embolization and resection	2 years *	no new nerve deficits; pre-existing paresis of CN IX, X, XI and XII; tumour residue; CN VII - HB 1
V. N. 1953	f	61	hearing loss; total paresis of facial nerve	C2	embolization and resection	1 year	paresis of CN VII – HB 6;
G. D. 1951	f	65	hearing loss; dysphagia; hoarseness; tongue palsy	C2	embolization and resection	4 months*	CN VII – improving, current HB 2; partial necrosis of auricle
V. S. 1955	f	59	p. tinnitus; hearing loss; vertigo	C1	primary radiation	2 years	significant tumour reduction; no new nerve deficits

(CN = cranial nerve.)

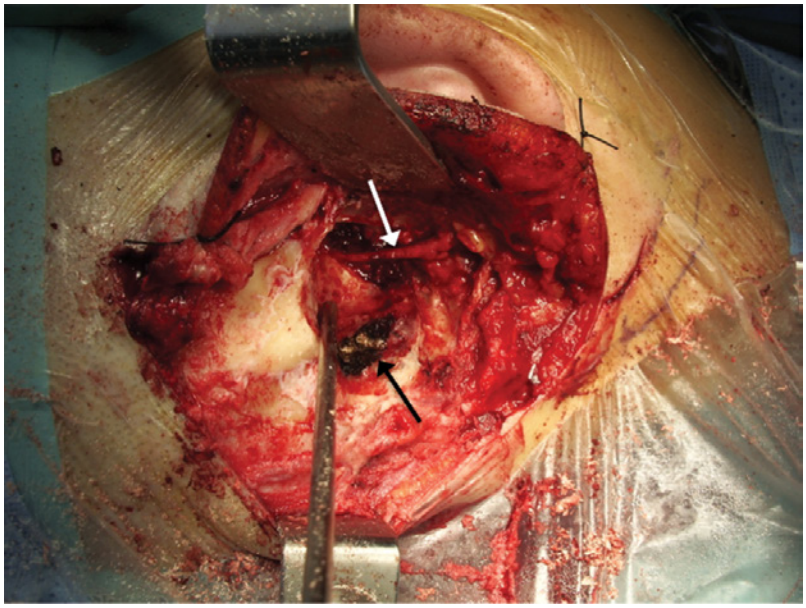

Figure 3: Mastoidectomy with obliteration of the sigmoid sinus (black arrow). The facial nerve (white arrow) is dissected from first genu down to the parotid level.

ding procedure, the operation is reasonable in order to prevent further damage to cranial nerves.

Total resection is achievable in the majority of cases, but it carries the possibility of cranial nerve or, less often, vessel injury.

Wanna et al. (2015) reported their 35-year experience with the treatment of jugular paragangliomas. Out of 202 patients intended for total resection, 90 % had a successful operation with a recurrence rate of 6 %. Preoperatively, 47 % of patients had cranial neuropathies. Additional postoperative neuropathies occurred in 60 %; most frequently the glossopharyngeal nerve was involved. Elective subtotal resection, performed in 12 patients, proved to be a good treatment choice. None of these patients showed signs of additional nerve damage postoperatively, and none had evidence of residual tumour enlargement within the average follow-up period of 45 months. The authors point out that the patient sample was small and the follow-up period relatively short, which must be taken into account in interpreting these results. Fifteen patients were treated with observation only, either because of advanced age or refusal to undergo surgery. In this group, 40 % of tumours showed an average growth of 0.9 mm per year. No changes in cranial nerve status were noted during the average follow-up of 7 years, and no deaths occurred as a result of tumour progression (13). Fayad et al. (2010) reported their experience with the surgical treatment of tumours in the jugular foramen area. Out of 83 patients treated for jugular paraganglioma, 81 % had a total resection, and 18.9 % had new cranial nerve deficits postoperatively (17).

Sixty per cent of our patients had lower cranial nerve paresis at presentation. In the rest, we managed to preserve the nerves when removing the tumour. Facial nerve function practically fully recovered after anterior transposition in all patients. In two patients in whom a reanastomosis of the nerve was made, we did not observe any recovery postoperatively. The most likely reason is that a long segment of the nerve had been lifted out of its canal, whereby its blood supply was compromised.

Tumour embolization technique has advanced over the last fifteen years. We usually perform embolization two to three days prior to surgery. In all our patients it was done transarterially, although embolization by direct (percutaneous) puncture is also possible (18). Selection of appropriate particle size is important: smaller particles penetrate deeper into the tumour, but pose a greater risk of occlusion of the vasa vasorum, which may result in nerve injury. Smaller particles can also enter the intracranial circulation via anastomoses. This occurred in one of our patients, who lost sight in one eye after embolization. From our literature review it is evident

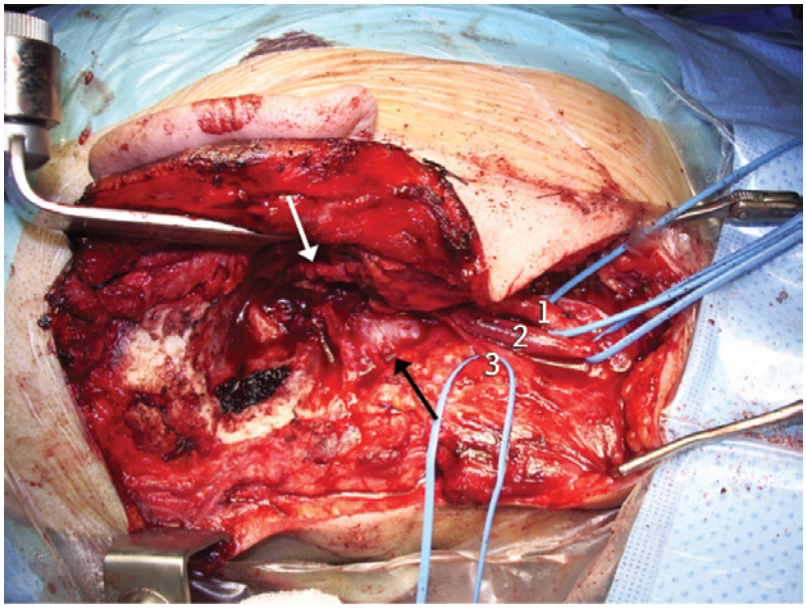

Figure 4: Status before final removal of the tumour (black arrow) from the jugular bulb region. Facial nerve is rerouted anteriorly (white arrow). In the neck, internal carotid artery (1), internal jugular vein (2) and accessory nerve (3) are dissected. Tumour from the mastoid region is already removed.

that preoperative embolization reduces blood loss (19), operating time (20) and chance of recurrence (21).

Embolization also facilitates tumour resection, which can be difficult when bleeding is profuse. In such circumstances, tumour removal from the vertical part of the carotid artery and identification of lower cranial nerves can pose considerable difficulty. Success of embolization is evaluated based on contrast uptake before and after the procedure. The aim of the procedure is to decrease contrast enhancement by at least 80 %. We can perform embolization either in general or in local anaesthesia. Local anaesthesia allows us to observe the neurologic status and perform provocative testing of potentially dangerous anastomoses. It also avoids the risks of general anaesthesia, which is chosen for uncooperative or anxious patients or for long lasting procedures. In our patients, most embolization procedures were done in local anaesthesia. In the last few operations, there was no need for transfusion because of successful embolization.

In recent years, stereotactic radiosurgery has gained a role in the treatment of jugular paraganglioma. In a multicenter study from 2012, the authors presented data on 132 patients treated with stereotactic radiosurgery. This treatment was preceded by subtotal resection in 39.6 %, and by extracorporeal radiotherapy in 4.5 %. In the average follow-up period of 50.5 months, the tumour decreased in size or remained unchanged in 93 % of cases. A new neurologic deficit or worsening of an existing one occurred in 15 %, whereas improvement of neurologic deficits was seen in 11 % (22). Two of our patients received radiotherapy: one as the primary treatment and one as an adjuvant treatment. In both patients, the tumour decreased in size and no new cranial nerve deficits appeared.

Postoperatively, our patients were offered corrective procedures for vagal and facial nerve palsies and for mixed hearing loss. One patient had a vocal cord medialization procedure, while all other patients with vocal cord paresis underwent only speech therapy for dysphagia. Both patients with total paralysis of the facial nerve treated by anastomosis had a tarsorrhaphy. One patient was fitted with a bone anchored hearing aid (BAHA) on the operated side.

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