Titanium mesh reconstruction of a dog’s cranium after multilobular osteochondrosarcoma resection

Reconstructie van de schedel van een hond met een titanium mesh na het verwijderen van een multilobulair osteochondrosarcoom

A. Dierckx de Casterlé, 1B. Van Goethem, 1A. Kitshoff, 1S.F.M. Bhatti, 1I. Gielen, 1T. Bosmans, 2H. De Cock, 1H. de Rooster

1Small Animal Medicine, Faculty of Veterinary Medicine, Ghent University, Salisburylaan 133, 9820 Merelbeke, Belgium
2Medical Imaging and Small Animal Orthopedics, Faculty of Veterinary Medicine, Ghent University, Salisburylaan 133, 9820 Merelbeke, Belgium

bart.vangoethem@Ugent.be

INTRODUCTION

Multilobular osteochondrosarcoma (MLO) is an uncommon malignant tumor occurring most often in the flat bones of the canine skull (McGavin and Zachary, 2007). Similar names used for this tumor type include chondroma rodens, multilobular tumor of bone, multilobular osteosarcoma, multilobular osteoma, calcifying aponeurotic fibroma, multilobular chondroma, cartilage analogue of fibromatosis, and juvenile aponeurotic fibroma (Dernell et al., 1998). The majority of dogs with MLO are middle-aged to older dogs (median age at presentation eight years), usually belonging to medium or large breeds (median weight 29 kg) (Straw et al., 1989; Groff et al., 1992; Popvitch et al., 1994; Dernell et al., 1998; Loukopoulos et al., 2003; Jubb et al., 2007).

Clinically, these tumors are slow-growing, locally invasive, firm immobile masses on the surface of the skull (Hathcock and Newton, 2000; Pakhrin...
et al., 2006). Although the bone may be invaded by the tumor, the brain is often compressed rather than infiltrated by the mass, resulting in late-onset neurological signs (Pool, 1990; Dernell et al., 1998). MLO has a characteristic ‘popcorn ball’ appearance on radiographic imaging, CT and MRI with sharply demarcated, limited lysis of adjacent bone and a course granular mineral density throughout the tumor (Seler, 1981; Dernell et al., 1998; Webb et al., 2009; Boston, 2010; Forrest, 2013).

The biological behavior makes complete excision the treatment of choice (Straw et al., 1989; Gallegos et al., 2008). Following surgical resection, local tumor recurrence has been reported in 47-58% of dogs with a median time to local recurrence of 420-542 days (Straw et al., 1989; Dernell et al., 1998). The key surgical challenge is therefore to obtain adequate surgical margins. This is complicated by the direct presence of vital structures, of which damage may lead to severe or fatal outcomes, and by the necessity to reconstruct the created skull defect to protect these structures.

A metastatic rate of 56-58% in treated dogs has been reported with a median time to metastasis between 420-797 days (Straw et al., 1989; Dernell et al., 1998). The metastatic sites include mostly the lungs, but also the cerebral cortex, kidneys, pancreas, rib and long bones (Mc Lain et al., 1983; Straw et al., 1989; Dernell et al., 1998).

A histologic grading system has been described in an attempt to predict the biological behavior of this tumor (Banks and Straw, 2004) (Table 1). Local tumor recurrence, metastasis and survival time appear to be correlated to histologic grade (Dernell et al., 1998) (Table 2).

In this case report, the occurrence of MLO in a previously unreported breed, the surgical removal and the use of a designated contourable titanium mesh for the reconstruction of the bone defect in the skull com-

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<td>13 or greater</td>
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*HPFs = high-powered fields

Table 1. Histological grading criteria for MLO (Dernell et al., 1998).

<table>
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<tr>
<th>Grade</th>
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<th>II</th>
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<tr>
<td>Number of cases</td>
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<tr>
<td>Time to local recurrence (days)</td>
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<tr>
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<td>288</td>
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<tr>
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<td>30-782</td>
<td>82-534</td>
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<td>Time to metastasis (days)</td>
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<td>Median</td>
<td>&gt;820</td>
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<tr>
<td>Range</td>
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<td>28-1.225</td>
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</tr>
<tr>
<td>Survival time (days)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>&gt;897</td>
<td>520</td>
<td>405</td>
</tr>
<tr>
<td>Range</td>
<td>66-797</td>
<td>28-1.487</td>
<td>82-1.670</td>
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Table 2. Survival outcome for MLO based on tumor grade (Dernell et al., 1998).
CASE DESCRIPTION

An eleven-year-old female castrated cavalier King Charles spaniel with a body weight of 8.6 kg was examined for a large mass on the skull of an eleven-months duration. The mass was approximately 5 cm in diameter and centered on the top of the skull. The dog was alert, responsive and able to ambulate well on all limbs. Although no neurologic dysfunction was noted, the owners mentioned the recent appearance of behavioral changes, i.e. anxiety and hiding in the corner of the room. Physical examination was unremarkable other than bilateral breed-related exophthalmia and a systolic heart murmur (3/6). The results of complete blood count were within the reference limits; so were the results of serum biochemical analyses except for the elevated activity of alkaline phosphatase (571 U/L; reference range, 23-212 U/L).

A CT scan of the head was performed to evaluate the extent of bone involvement and to determine the intracranial extension of the mass. The CT scan revealed a 5.5 x 5.0 x 3.7 cm lobulated, mineralized mass arising from the caudal portions of the frontal bones, both parietal bones, the external sagittal crest and the cranial part of the supraoccipital bone (Figure 1). The mass had a heterogeneous aspect with multiple granular, sharply demarcated hyperdense regions. Transcranial extension exerted a mass effect on the brain parenchyma. A CT scan of the thoracic cavity was performed and no pulmonary metastases could be detected. However, partial, positional atelectasis prevented the complete evaluation of all lung lobes.

Due to the increasing severity of tumor-related behavioral changes and the potential long survival time after surgical resection, the owners opted for surgery. The dog was premedicated intravenously with 0.5 mg/kg midazolam (Dormicum, Roche B.V., the Netherlands) combined with 0.5 mg/kg methadone (Comfutan, Eurovet Animal Health B.V., the Netherlands). Induction occurred with 4 mg/kg propofol (PropoFlo Plus, Abbott Logistics B.V., the Netherlands) IV, after which a 6-mm endotracheal tube was placed. Maintenance of anesthesia was done with isoflurane (IsoFlo, Abbott Logistics B.V., the Netherlands) in 100% oxygen through a circle rebreathing system (Cicero, Dräger, Germany). Intraoperative analgesia consisted of a continuous rate infusion of fentanyl (Fentadon, Dechra, Belgium) at 5 μg/kg/h. At the time of the induction of anesthesia, 20 mg/kg cefazolin (Cefazoline, Sandoz N.V., the Netherlands) was administered and repeated every two hours until the end of surgery.

The dog was positioned in sternal recumbency with the head elevated and fixed in a 45-degree angle between head and neck, to avoid intracranial venous congestion that might occur from both jugular compression or positional hypostatic congestion (Otto, 2015) (Figure 3). In order to decrease the risk for tumor recurrence, the overlying skin and a 1-cm margin of surrounding soft tissues and bone, ensuring to include the previous biopsy tract, was resected (Figure 4). Hemostasis was achieved with bipolar electrocoagulation. The temporalis muscles were elevated from the parietal bones and the skull around the mass was cut with a 3-mm high-speed pneumatic burr. The endostium was removed with 2-mm Kerrison rongeurs, after which the entire mass was carefully elevated and dissected from the underlying dura by use of blunt probes (Figure 5). Hemorrhage from the right transverse sinus resulted in a subdural hematoma. To avoid an increase of the intracranial pressure, the dura was incised, the hematoma was evacuated, and the dura was closed with a continuous suture pattern using 5-0 polyglycaprone (Monocryl, Ethicon, Belgium).

Figure 1. A. Transverse and B. sagittal CT images of the skull. A well-circumscribed, space-occupying mass is present on the skull with a granular, hyperdense aspect (black arrows). Intracranial expansion with dorsal compression of the brain is present (red arrows).

Figure 2. Microscopy of the MLO demonstrating multilobular patterns, consisting of a core of bone matrix (asterisk) surrounded by multiple connective tissue cells (Hematoxylin and eosin stain, 40x).
Figure 3. Surgical positioning of the dog in sternal recumbency with the head elevated, and the head and neck in a 45-degree angle not to obstruct venous head flow.

Figure 4. A circular incision was made around the base of the tumor, the underlying muscles were incised and the bone was prepared for cranioplasty.

Gross inspection of the removed mass revealed margins varying from 5 to 10 mm (Figure 6). The excised mass was submitted for histologic evaluation. The results confirmed the diagnosis of a grade-1 MLO and considered the surgical margins free of tumor tissue.

The bone defect was reconstructed by means of a 0.4 mm titanium mesh (MatrixNEURO, Contourable Mesh, DePuy Synthes, Belgium). Briefly, the mesh was molded as a dome overlapping the burred bone edges for 1 cm to allow fixation with 1.5 mm diameter low-profile, self-tapping cortical screws (Figure 7). Since the overlying temporalis muscle was removed, no muscle layer was available to cover the mesh. From the abundant dorsal cervical skin, a single-pedicle advancement flap was elevated and used to cover the mesh and close the skin defect (Figure 8). The underlying cutaneous muscle and deep subcutaneous tissues were closed with 3-0 polyglecaprone in a simple continuous pattern, and the skin was apposed with a subcuticular pattern of 3-0 polyglecaprone.

Postoperative radiographs showed the mesh to be contoured anatomically correct, without any apparent compression of the brain parenchyma (Figure 9). The dog recovered from anesthesia without complications. Postoperative IV analgesics consisted of a continuous rate infusion of lidocaine (Xylocaine, Eurovet Animal Health B.V., the Netherlands) for 2 days at a rate of 30 µg/kg/minute preceded by a single IV loading dose of 2 mg/kg, 10 µg/kg buprenorphine (Vetergesic Multidosis, Patheon UK Limited, United Kingdom) q8h for 11 days, 4 mg/kg carprofen (Rimadyl, Pfizer, Belgium) q24h for 7 days. In addition, 20 mg/kg cefazolin (Cefazolin, Sandoz N.V., the Netherlands) was continued q12h for 11 days. Twenty-four hours after surgery, the dog was quiet and alert but unable to walk due to left-sided hemiparesis. During blinking, the upper eyelids incompletely covered the cornea, for which vitamin A eye ointment (Opticorn A, Ecuphar, Belgium) was instilled q4h. Wound healing occurred without complication, and from the fifth day on, the general condition improved and a progressive improvement of ambulation was noted. On the seventh day, only slight delayed proprioceptive reflexes remained.

Despite the preventive eye ointment, the right eye developed an acute ‘melting’ corneal ulcer with hypopyon and conus cornea. Initially, atropine sulphate 5 mg/ml eye drops (Atropine, Alfasan B.V., the Netherlands) were instilled q12h and 5 mg/g oxytetracycline + 10,000 I.E./g polymyxin B eye ointment (Terramycin, McNeil Manufacturing, France) q8h. Due to disease progression, there was a risk of corneal perforation on the eight postoperative day, a 360-degrees conjunctival flap was used as a salvage procedure (Pumphrey et al., 2011). Both anesthesia and surgical procedure were without complications. Postoperatively, ophthalmic medication consisted of 3 mg/g ofloxacin (Trafloxal collyre, Baush & Lomb Pharma nv, Belgium) q8h, acetyl cysteine (Lysomucil 10%, Zambon n.v., Belgium) q12h, ketorolac trometamol (Aculare 0.5%, Allergan Pharmaceuticals, Ireland) q6h, and 0.02 mg/kg atropine sulphate (Atropine, Alfasan B.V., the Netherlands) q12h.

On the ninth postoperative day, the dog was bright, alert and ambulating with only mild ataxia. The dog was discharged two days later with continued antibiotics (clavulanic potentiated amoxicillin for 7 days), analgesics (carprofen for 14 days), and local eye medication (ofloxacin, acetyl cysteine, and ketorolac trometamol for 3 weeks).

Eight weeks after surgery, the conjunctival flap dehisced spontaneously, with some remaining mucosa reinforcing the weakened cornea at the ulcer site. The eye medication was discontinued. Six months after surgery, the dog was neurologically normal (ambulation and behavior), the eyelids closed during blinking, and all that remained from the corneal ulcer was some pigmented scar tissue (Figure 10). Lung auscultation was unremarkable, but unfortunately skull and thoracic radiographs were declined by the owner because of financial reasons.

Seven and nine months after surgery, the dog developed a single seizure, which started during rest and was characterized by tonic-clonic convulsions, loss of
Figure 5. After tumor removal, a large partial craniectomy defect remained that needed reconstruction. A subdural hematoma is seen in the right hemisphere (purple discoloration).

Figure 6. View at the ventral (intracranial) aspect of the tumor. The rim of normal bone present at the craniectomy location determines the macroscopic tumor margins.

Figure 7. The 0.4-mm titanium mesh (MatrixNEURO, Contourable Mesh, DePuy Synthes, Belgium) was shaped conforming the removed skull piece and fixed with 1.5-mm screws.

Figure 8. From the dorsal neck, a single-pedicle advancement flap consisting of skin and sphincter colli muscle, was mobilized and directed cranially to cover the implant.

Figure 9. Postoperative lateral radiograph showing the titanium mesh fixed on the calvarium after partial craniectomy.

Figure 10. Six months after tumor resection, the dog is fully functional. There is some remaining scar tissue visible on the right cornea, but no evidence of local tumor recurrence or metastasis.
consciousness and abnormal autonomous activity. Intercurrently, the dog behaved normal. On general clinical and neurological examination, no abnormalities were detected. Eleven and thirteen months after surgery, new seizures developed. Complete blood count and serum biochemistry were normal and cardiac ultrasound revealed stable stage B1 mitral endocardiosis. Further diagnostics (magnetic resonance imaging) to search for underlying structural cerebral disorders were offered but unfortunately declined by the owner. The dog was started on 2.5 mg/kg phenobarbital (Phe-noletil, Le Vet B.V., the Netherlands) q12h. At the time of writing, seventeen months after surgery, no further seizures had occurred.

DISCUSSION

Because of its location, complete surgical removal of MLO is often difficult resulting in local recurrence in about 57% of the cases (McLain et al., 1983; McCalla et al., 1989; Straw et al., 1989; Dernell et al., 1998; Jubb et al., 2007). In a retrospective study on 39 dogs with MLO, complete excision resulted in a disease free interval of 1.332 days versus only 320 days for incomplete removal (Dernell et al., 1998). In addition, the development of metastases is also correlated to the completeness of surgical resection, with the metastatic rate for complete excision being 25% versus 75% for incomplete removal (Dernell et al., 1998). Therefore, aggressive surgical excision with wide margins is the treatment of choice.

In earlier studies on canine cranioplasty, the use of cranial bone allograft (Moissonnier et al., 1997), polymer prostheses (including polytetrafluoroethylene, high-density polyethylene, polyester, polyamide mesh), and polymethylmethacrylate (Moissonnier et al., 1997; Mouatt, 2002; Bryant et al., 2003), and metal plates including platinum, tantalum, cobalt-chromium alloys, aluminum, titanium and stainless steel (Bordelon and Rochat, 2007) have been described.

Polymethylmethacrylate is the most widely used implant material because it is radiolucent, can be easily molded, has acceptable tensile and flexural strength, is widely available, and relatively inexpensive in relation to other implant materials (Moissonnier et al., 1997; Park et al., 2001; Mouatt, 2002; Bryant et al., 2003). Preforming the PMMA using a mold avoids potential for tissue necrosis and creates a custom, lightweight and durable implant (Rosselli et al., 2017). However, potential disadvantages include exothermic reaction associated with polymerization, the brittle nature of the material once it has polymerized, variations in porosity depending on mixing technique, the potential to provide for bacterial colonization (Arens et al., 1996), and the extended duration of surgery caused by the multiple steps for molding (Rosselli et al., 2017). To provide sufficient protection, a thickness of 5-10 mm is recommended (Moissonnier et al., 1997). Thus, in smaller patients and in patients with defects of the dorsal aspect of the skull, where excessive tension of the overlying soft tissues may lead to necrosis or dehiscence, PMMA may not be the best choice (van Gool, 1985; Moissonnier et al., 1997; Mouatt, 2002; Bryant et al., 2003).

Titanium has been reported to be the most promising of metallic implants (Bordelon and Rochat, 2007). Potential disadvantages include poor malleability, lack of availability and high cost (Moissonnier et al., 1997). Advertised advantages include radiolucency, lower density, corrosion resistance and potentially lower susceptibility to infection (Arens et al., 1996; Rosselli et al., 2017). Bordelon and Rochat (2007) used a 1.5-mm-thick sheet of rigid titanium mesh for a cranioplasty and concluded the benefits in terms of fit, strength, low profile and secure fixation to the remaining calvarium outweighed the costs. The controllable 0.4-mm titanium mesh used in this case is a technologically improved version of the previously described titanium implant, which is even more malleable, yet maintains substantial rigidity due to its dome shape. In a case series of five dogs, Rosselli et al. (2017) demonstrated the titanium mesh did not interfere with postoperative CT or MR images, thereby allowing postoperative imaging for ongoing assessment.

Postoperative radiographs confirmed the correct placement and anatomical contouring of the titanium mesh over the skull defect. The titanium mesh in this case report was secured to the skull with screws. No complications were recorded during or after the procedure attributable to the titanium implant. In previous case series, the use of sutures to secure the mesh to the skull has been documented, claiming that the use of screws could prolong and increase the cost of surgery, create iatrogenic damage to underlying brain parenchyma, and might be associated with postoperative loosening or migration (Rosselli et al., 2017). The screws used in this case report were low-profile, self-tapping screws that were placed monocortically, thereby eliminating the aforementioned potential disadvantages. Follow-up radiographs at seventeen months after surgery showed no signs of implant loosening or migration. Screw fixation to the skull offers a more rigid fixation of the implant than fixing it to overlying soft tissues. Furthermore, suturing the mesh to the overlying temporalis fascia might work for smaller reconstructions, but may not be applicable when there is insufficient overlying muscle or fascia.

Because MLO’s are considered to be locally invasive tumors, the overlying skin, biopsy tract and surrounding muscles were removed together with the tumor. A wide deep resection was not necessary since this tumor does not usually invade across the meninges. Other authors have removed MLO’s with a linear skin incision and the conservation of superficial muscle layers (Bordelon and Rochat, 2007; Gallegos et al., 2008). Unfortunately, due to the size of the tumor, the location on the sagittal crest and the presence of a biopsy tract, conservation of either skin or muscles would endanger complete surgical resection.
A single pedicle skin flap that advances skin from the dorsal cervical region was used to close the skin defect. The incorporated sphincter colli and cutaneous muscle allowed to cover the mesh with a muscular layer. However, positional differences between the head in the surgical field and in the awake dog may result in undue traction when using this type of skin flap. A ninety-degree rotation flap would have increased surgical morbidity, but could have provided skin for closure without any traction on the upper eyelids (Smith et al., 1991).

Both CT and MR imaging were offered postoperatively for ongoing assessment. Rosselli et al. (2017) have shown there is no interference of image quality using a titanium mesh. Since elemental titanium has a low molecular number, it is minimally attenuating and since it is non-ferrous, it does not create magnetic field inhomogeneities.

The description of the dog of the present study was different from that of previous reviews and case reports (Straw et al., 1989; Groff et al., 1992; Dernell et al., 1998; Loukopoulos et al., 2003; Banks and Straw, 2004; Jubb et al., 2007; Webb et al., 2009; Leonardi et al., 2014). Although multilobular osteochondrosarcoma appears to be a disease of middle-aged to older, medium- to large-breed dogs, scarce reports of young and small dogs do exist (Jacobson, 1971; Diamond et al., 1980; Fukui and Takamori, 1986; Pakhrin et al., 2006; Bordelon and Rochat, 2007).

The dog’s exophthalmos was originally attributed to breed-related conformation. But the combination of neurologic changes (behavioral) and ocular changes (exophthalmia) with intracranial tumor growth has been described before (Pletcher et al., 1979; Straw et al., 1989; Pakhrin et al., 2006; Psychas et al., 2009; Leonardi et al., 2014). In a review study on 39 dogs, 5% had neurologic symptoms and 15% exophthalmia (Dernell et al., 1998). It is therefore possible that the presurgical exophthalmia was, at least partially, tumor-induced.

According to some studies, elevated levels of alkaline phosphatase are a negative prognostic factor for osteosarcoma (Ehrhart et al., 1998; Garzotto et al., 2000). For MLO, such a correlation has not been established. Earlier reports have also found elevated levels of alkaline phosphatase and have linked this to tumor-induced increased bone metabolism (Gallegos et al., 2008).

Skull radiographs can easily differentiate between osteoma and MLO (Ling et al., 1974). However, some MLO’s don’t display typical radiographic characteristics and in these patients, a preoperative histological biopsy is necessary for accurate diagnosis (Stoll et al., 2000). In the current case, the diagnosis was made based on the radiographs, but the biopsy was performed to establish a tumor grade. Dernell et al. (1998) found that the tumor grade is not only correlated to local recurrence (30% for grade I MLO, 47% for grade II MLO, and 78% for grade III MLO), but also to the presence of metastasis (30% for grade I MLO, 60% for grade II MLO, and 78% for grade II MLO). The identification of a low-grade MLO in the present case offered the owner a more informed decision on the expected course after surgical therapy.

Risk factors for postoperative wound infection are the presence of a metallic implant and a surgical duration longer than two hours (Brown et al., 1997). Prolonged antibiotic therapy is, however, essential when there is a communication between the frontal sinus and mesh implant (Moissonnier et al., 1997). In the present case, where no communication with the frontal sinus existed and where a metallic implant was used that is less susceptible to harboring bacteria, antibiotic therapy was pursued for the postoperative corneal ulcer development and the pending risk for eye perforation.

The role of chemotherapy and radiation therapy in the management of MLO is not well defined. No increase in survival time, time to local recurrence and metastasis have been found between the surgical excision alone and the surgical excision followed by adjuvant therapy (Straw et al., 1989; Dernell et al., 1998; Koch et al., 2000). However, adjuvant therapy may provide some benefit for local tumor control or palliation of unresectable or recurrent lesions (Boston, 2010).

Idiopathic epilepsy was considered very unlikely in this case as the dog developed seizures at the age of eleven years, whereas in most of the dogs with idiopathic epilepsy, the seizure onset is between the age of six months and six years (De Risio et al., 2015). Metabolic and toxic causes of the seizures were also considered unlikely as the blood examination was normal, and no history of toxin exposure was mentioned in the anamnesis. In this case, the possibility of a structural cause for the seizures seemed most likely (De Risio et al., 2015). Taking into account the previous medical issues in this dog, regrowth of the skull tumor or the development of scar tissue at the surgery site seem the two most likely possibilities (De Risio et al., 2015). However, other structural causes, such as neoplasm, inflammation and vascular disorders, should be taken into account as well (De Risio et al., 2015).

**CONCLUSION**

Despite the extensiveness of the process in the skull and the compression of intracranial structures, a dog with MLO may reach a prolonged survival time if the tumor has been removed with complete margins. The titanium mesh used in this case offers a smooth, fast and uncomplicated method to reconstruct the cranium of a dog.
REFERENCES


Popvitch C.A., Weinstein M.J., Goldschmidt M.H., Shofer


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