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CASE REPORT

Reconstruction of the Upper Cervical Spine Using a Personalized 3D-Printed Vertebral Body in an Adolescent With Ewing Sarcoma

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Study Design. Case report.
Objective: To describe a three-dimensional (3D) printed axial vertebral body used in upper cervical spine reconstruction after a C2 Ewing sarcoma resection in an adolescent boy.
Summary of Background Data. Ewing sarcoma is a malignant musculoskeletal neoplasm with a peak incidence in adolescents. Cervical spine as the primary site of the tumor has been related to a worse prognosis. Tumor resection is particularly challenging in the atlantoaxial region due to complexity of the anatomy, necessity for extensive resection according to oncological principles, and a lack of specialized implants for reconstruction. 3D printing refers to a process where 3D objects are created through successive layering of material under computer control. Although this technology potentially enables accurate fabrication of patient-specific orthopedic implants, literature on its utilization in this regard is rare.
Methods. A 12-year-old boy with a C2 Ewing sarcoma underwent a staged spondylectomy. Wide resection of the posterior elements was first performed. Two weeks later, a high anterior retropharyngeal approach was taken to remove the remains of the C2 vertebra. A customized artificial vertebral body fabricated according to a computer model using titanium alloy powder was inserted to replace the defect between C1 and C3. The microstructure of the implant was optimized for better biomechanical stability and enhanced bone healing.
Results. Patient had an uneventful recovery and began to ambulate on postoperative day 7. Adjuvant treatment commenced 3 weeks after the surgery. He was tumor-free at the 1-year follow-up. Computed tomography studies revealed evidence of implant osseointegration and no subsidence or displacement of the construct.
Conclusion. This is a case example on the concept of personalized precision medicine in a surgical setting and demonstrates how 3D-printed, patient-specific implants may bring individualized solutions to rare problems wherein restoration of the specific anatomy of each patient is a key prognostic factor.
Key words: C2 reconstruction, Ewing sarcoma, individualized care, patient-specific implants, personalized medicine, porous metal, self-stabilizing artificial vertebral body, spondylectomy, three-dimensional printing, upper cervical spine tumor
Level of Evidence: 5
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Ewing sarcoma is a malignant neoplasm that affects the long bones and the pelvis in most cases.[1] Cervical spine as the primary site of the tumor is considerably uncommon and has been related to a worse prognosis.[2] Three-dimensional (3D) printing, also known as additive manufacturing, refers to a process wherein a 3D object is created from a digital model through successive layering of material under computer control. We herein described a case of primary Ewing sarcoma in the C2 vertebra of a young patient who underwent spondylectomy and reconstruction using the "first-ever 3D-printed vertebra."[3–5]

CASE REPORT

A 12-year-old boy was referred to our institution with severe neck pain that was initially of low-intensity after a minor injury when heading a ball in a soccer game 2 months ago. The pain worsened over time with oral nonsteroidal anti-inflammatory drugs and upon admission, he reported 9 on 10 pain on the visual analog scale and was wearing a cervical collar for head support against gravity. In addition, patient complained of paresthesia and clumsiness of the intermediate and distal phalanges on both hands. Medical history included

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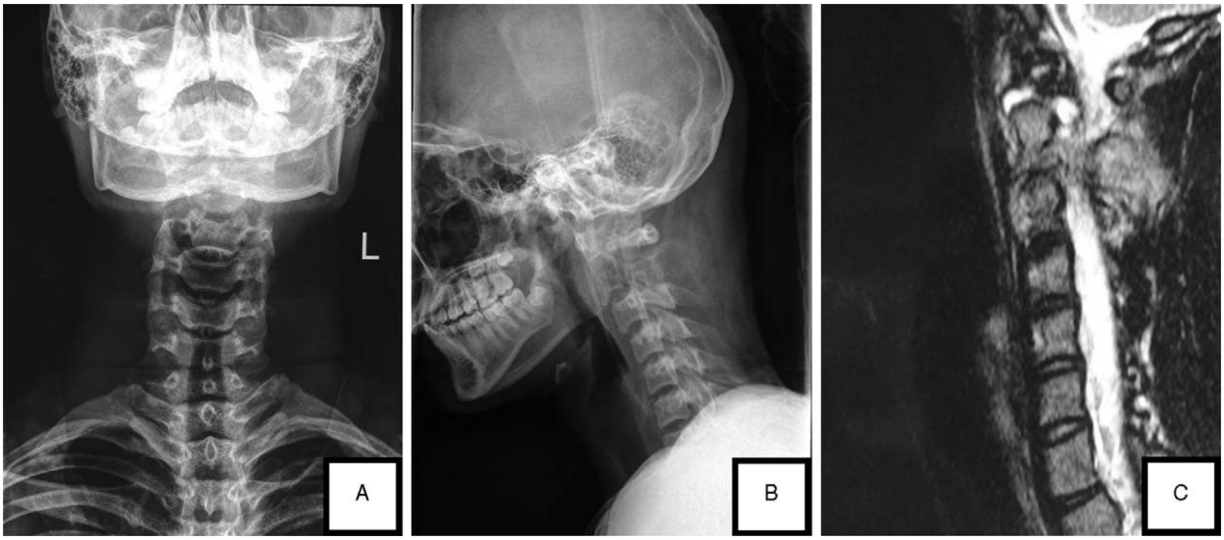

Figure 1. A and B, Preoperative X-rays demonstrated a lytic lesion surrounded by peripheral osteosclerosis involving the entire axial vertebra. C, MRI demonstrated paravertebral soft tissue involvement.

asthma but was otherwise insignificant. On physical examination, decreased muscle strength in the lower limbs was noted (grade III-IV on the Oxford scale) along with hyperactive patellar and Achilles tendon reflexes. No pathological reflexes were elicited. A lytic lesion surrounded by peripheral osteosclerosis involving the entire axial vertebra was found on plain X-rays (Figure 1A, B). Magnetic resonance imaging demonstrated paravertebral soft tissue involvement (Figure 1C). No metastasis was revealed by a whole-body positron emission tomography scan. Immunochemical analyses of computed-tomography–guided percutaneous biopsy samples confirmed the diagnosis of Ewing sarcoma. He was given a score of 13 on the Spine Instability Neoplastic Score[6] scale. Over the course of the evaluation, his neurological function continued to deteriorate with more significant paresthesia and weakness in the upper limbs. His neurological function was rated as 8 on 17 on the Japanese Orthopaedic Association[7] (JOA) scale. The combination of significant pain, worsening neurological function, and local instability prompted the family to a surgical consultation.

METHODS

Surgical Planning

The tumor was staged as IIB according to the Enneking system[8] and Weinstein-Boriani-Biagini 1∼12, A∼D according to the Weinstein-Boriani-Biagini classification.[9] As an extralesional *en bloc* spondylectomy at this level was fraught with complications,[10] the senior author devised a plan for staged intralesional spondylectomy (Fig. 2A, B). Radical excision of the posterior elements of the C2 vertebra along with the involved soft tissue mass would be first performed. The soft tissue mass resection would

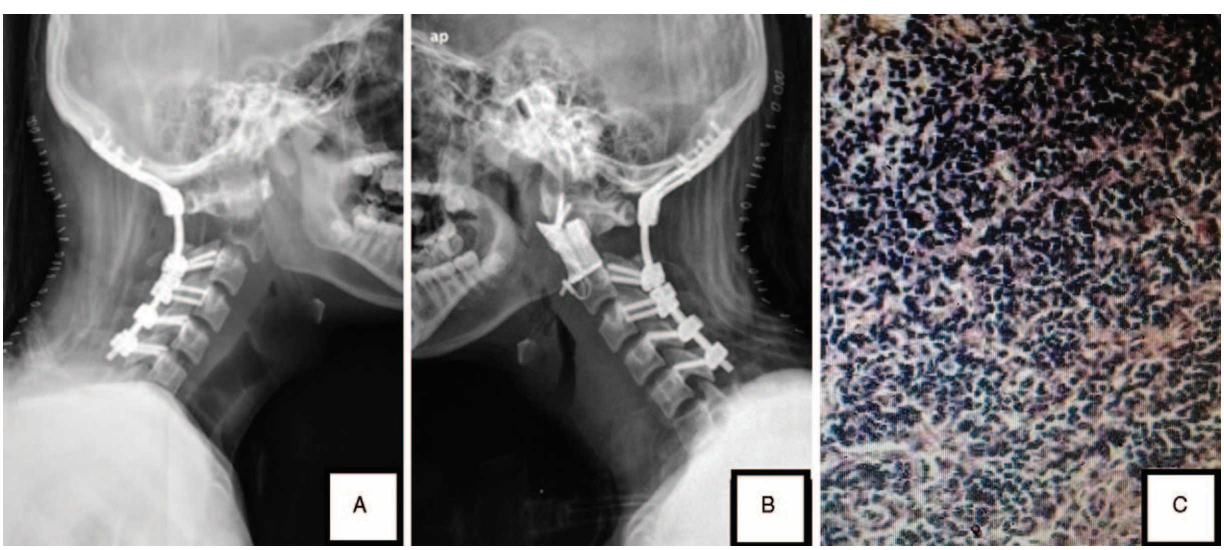

Figure 2. A, Lateral X-ray after resection of the posterior C2 elements and fixation. B, Lateral X-ray after the second surgery. We were not able to put the caudal screws into the C3 body and an ad hoc decision was made to use titanium wire for distal fixation. C, The tumor histology of Ewing sarcoma was confirmed by pathology.

be conducted in an extralesional fashion without violating the tumor capsule. In the surgery, a $7 \times 4 \times 3$ cm-sized mass was resected *en bloc* and the diagnosis of Ewing sarcoma was confirmed by pathology (Fig. 2c). Two weeks later, a high anterior retropharyngeal approach was taken to remove the remains of the C2 vertebra, decorticate the inferior articular surface of C1 and the superior endplate of C3, and insert a customized, self-stabilizing artificial vertebral body (SSAVB) to replace the cancerous vertebral body. No bone grafting was planned thanks to the osteoinduction capability of the SSAVB as described below. Consent was obtained with full disclosure on the potential benefits and risks given to the family.

Design of the SSAVB

We previously reported the first generation of SSAVB in sheep.[11] The design stemmed from the concept of a porous metal scaffold that could provide mechanical support to the anterior spine while conducive to bone in-growth into the trabecular pores.[12] Electron beam melting, a genre of 3D printing technology, was used in fabrication by successive layering of melted Titanium alloy powder according to a computer-aided design model. In the second-generation described here (Fig. 3A), the size and shape of the pores were fine-tuned based on previous results[13] to achieve an ultrastructural balance between the dimension of the struts and the porosity that facilitates bone in-growth, while remaining similar to normal cancellous

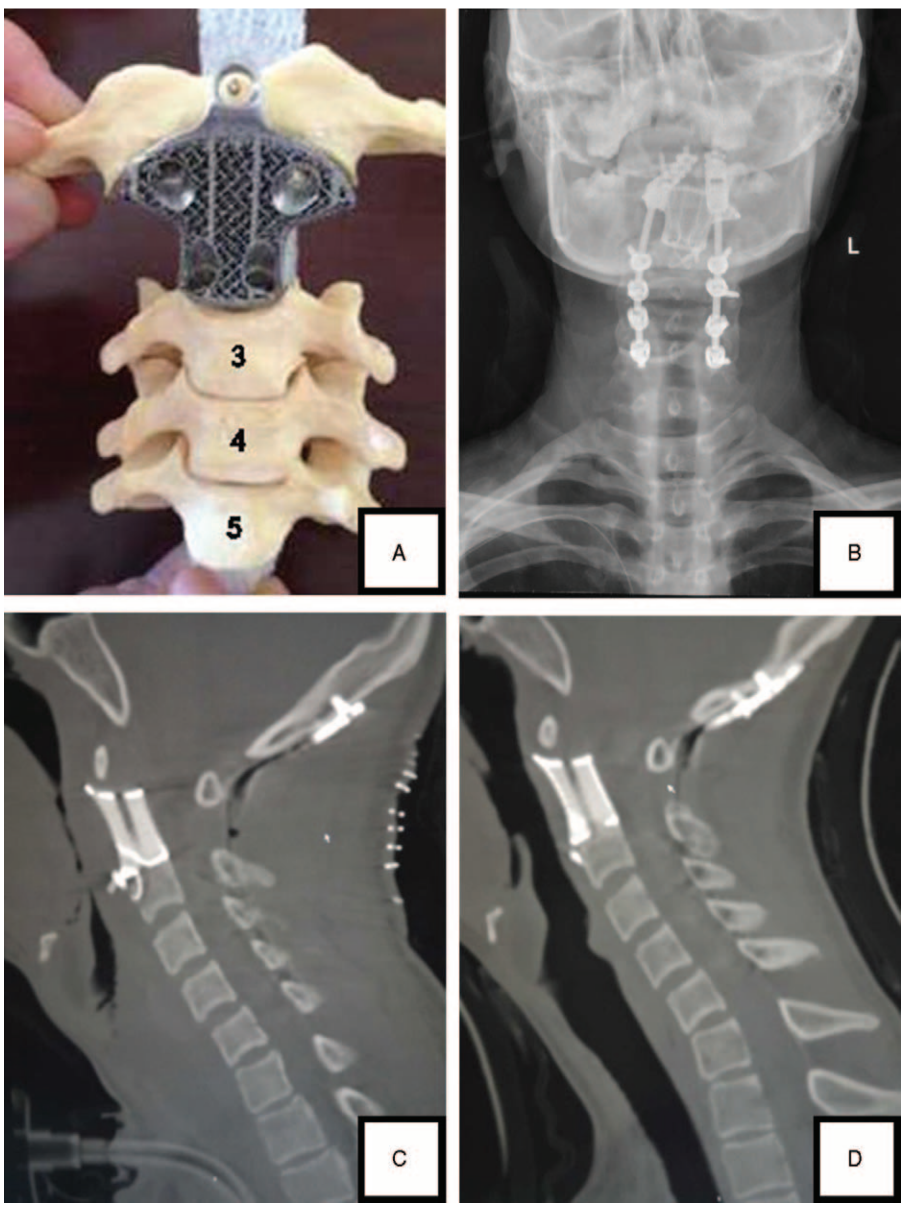

Figure 3. A, Model and B, postoperative X-ray demonstrating how the self-stabilizing artificial vertebral body was inserted between C1 and C3. C, Sagittal reconstruction immediately postoperatively and D, at the 1-year follow-up showing evidence of implant osseointegration, no subsidence or displacement of the construct, and no local recurrence of the tumor.

bone biomechanically. The SSAVB was customized with proximal wings (Fig. 3B) according to the contour of the inferior articular surface of the C1 vertebra, allowing greater proximity and maximal surface area between the two and providing easier access for lateral mass screw insertion. The anterior surface displayed a zero profile on the ventral structures to prevent dysphagia.[14] The bottom of the SSAVB was tailored into a tilted surface based on the angulation of the upper endplate of C3 to further reduce the chance of implant subsidence.[15]

RESULTS

Staged surgeries were performed according to the plan; however, in the second surgery, we were not able to drill the caudal screws into the C3 body as the screwdriver was blocked by the mandible with the head of the patient in hyperextension. An *ad hoc* decision was made to use titanium wire for distal fixation. (Research work is underway to develop a new screwdriver similar to the universal joint screwdrivers used in hip arthroplasty to work around the mandible in upper cervical spine tumor reconstruction in the future.) Before the second-stage surgery, a tracheostomy tube was placed out of concerns of the high incidence rate of pharyngeal complications and respiratory compromise associated with the anterior approach.[16] History of asthma was also taken into account in making this decision. After the surgery, patient was transferred to the intensive care unit and remained ventilator-dependent until postoperative day (POD) 4. His neurologic function improved after the surgery and he was able to ambulate on POD 7 with a sternal-occipital-mandibular orthosis that was replaced by a cervical collar 1 month later. A nasogastric tube was placed on POD 8 to prevent aspiration from coughing that started a few days ago and had worsened. On POD 12, he was extubated and transferred to the oncology unit with the nasogastric tube, which was removed on POD 17 after coughing had been controlled. Considering the extremely high incidence of complications after upper cervical spine tumor surgeries,[16] our patient had a relatively smooth clinical course of recovery. His neurological function was rated as 10 on 16 on the JOA scale at this point. Multiagent chemotherapy and local radiotherapy ensued once the wound had healed and the patient had recovered from the surgery. He was followed 3 months, 6 months, and 1 year after the surgery. No signs of metastasis were present on a positron emission tomography scan at the latest follow-up. Sagittal reconstruction images immediately after the surgery and 1 year later revealed evidence of implant osseointegration (indicated by bone in-growth into the built-in vertical slit in the center), no subsidence or displacement of the construct, and no local recurrence of the tumor (Fig. 3C, D). His neurological function had improved to 16 on 17 on the JOA scale. Overall, the patient felt significantly better than before the surgery without any residual neurologic deficits. He is planning on going back to school after his next cycle of radiation therapy.

DISCUSSION

Although the utilization of multimodal, integrated therapies has led to an impressive improvement in the prognosis of Ewing sarcoma,[17] location of the primary site is still the single most important predictor of its clinical behavior.[18] Extensive tumor resection in the upper cervical spine in accordance with oncological principles increases patient survival[19] but can result in some of the most difficult cases of spinal reconstruction. Studies on the biomechanics of the optimal reconstruction technique after a C2 spondylectomy using conventional implants showed that both ventral cages and bone grafting were necessary to supplement dorsal instrumentation in this region.[20] Local instability, however, remains a major concern with the conventional titanium mesh cages,[21] as the anterior arch anchor provides minimal cancellous bone purchase and only limited area of contact between the cage and the atlas. Bone graft is typically obtained either from autogenous iliac crest harvest, which is associated with additional morbidities, such as persistent pain and functional limitations,[22] or through the use of bone substitutes (allogenous/xenogenous/synthetic), which are related to increased health care costs. As a result, further improvement on the reconstruction technique for the post-resection defect in these patients is predicated on a paradigm shift in the design of the cervical implant. To that end, we investigated a new design of precise and personalized spinal implant made using 3D-printing technology.

Studies have suggested porous metal as a candidate biomaterial for anterior cervical implants thanks to its biochemical stability, biocompatibility, and osteoinduction capability.[23] There are several methods to produce porous metal implants,[24] and SSAVB, the first of such implants made by 3D printing, was described here. The following four major features exist that distinguish a SSAVB from others fabricated using conventional techniques:

- The microstructure is highly organized, as shown by the uniformity of the size and shape of the pores and the continuity of the struts.[11]
- Such microstructure displays biomechanical properties (resistance to compressive strength and Young modulus) that are associated with less stress shielding effect and can better prevent implant subsidence.[15]
- The greater pore density results in an increased area of rough bone-metal interface covered by melted Titanium alloy particles conducive to bone in-growth,[25] potentially obviating the need for bone grafting.[13]
- Based on computer-aided design models that are digitalized to reflect the actual size and unique geometry of the graft site, increased contact area and greater proximity between the implant and the graft site provide additional stability and may help reduce endplate fracture and implant collapse.[26]

Specialized implants are sometimes required to address the need of reconstruction in less common conditions but most device companies are rightfully not incentivized to invest in the development of such products, as they are typically publicly held and accountable to the financial interest of their shareholders. With the dawn of 3D-printing technology, real-time creation of specialized implants has become an option for orthopedic surgeons. This case report lends itself is an example on how 3D-printed, patient-specific implants may bring personalized solutions to a rare problem and has implications for other niche-market conditions wherein restoration of the unique anatomy of each individual patient is a key prognostic factor.

Due to limitations inherent to a case study, more research is warranted to validate the use of 3D-printed implants in extensive spinal reconstruction and beyond. Utilization of the large surface area inside the SSAVB for elution of chemotherapeutic agent or placement of radioactive nanoparticles represents another avenue for future studies.

➢ Key Points

- This study serves as a proof-of-concept demonstration that 3D printing can be used to build precise and personalized implants for patients requiring complex spinal reconstruction surgeries.
- Extensive tumor resection in the upper cervical spine in accordance with oncological principles increases patient survival but can result in some of the most difficult cases of spinal reconstruction.
- Studies have suggested porous metal as a candidate biomaterial for anterior cervical implants thanks to its biochemical stability, biocompatibility, and osteoinduction capability.
- The SSAVB was the first porous metal implant made by 3D printing, and can be distinguished from conventional implants in several different aspects as detailed in the article.

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