

Aphagia Strongly Suspected to Be Caused by an Allergic Reaction to a Gelatin-based Hemostatic Agent after Anterior Cervical Decompression and Fusion for Central Cervical Cord Injury

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Abstract

Gelatin-based hemostatic agents are widely used in neurosurgery. This is a case of postoperative aphagia strongly suspected to be caused by an allergic reaction to a gelatin-based hemostatic agent after anterior cervical decompression and fusion for central cervical cord injury. A 55-year-old man underwent cervical anterior decompression and fusion at the C3/4 and 4/5 levels for central cervical cord injury. Immediately after the surgery, he could not swallow saliva at all, but his voice was not hoarse. Postoperative cervical computed tomography and magnetic resonance imaging showed significant edema from the post-hypopharynx wall to the front of the vertebral body. The retropharyngeal space was remarkably enlarged to 15.8 mm with cervical spine X-rays. Without neurological symptom improvement, his condition was diagnosed as marked edema of the area where Surgiflo (porcine-derived gelatin-based hemostatic agent; Johnson & Johnson Wound Management, Somerville, NJ, USA) had been applied during the operation. It was strongly suspected to be caused by an allergic response to the porcine-derived gelatin. When methylprednisolone 1000 mg was administered for 3 days from the 5th postoperative day, swallowing became almost normal within a few hours after the initial administration, and his neurological symptoms improved. The patient left the hospital on the 12th day after the operation. Before using porcine-derived gelatin products during surgery, special consideration should be given to patients with an allergy history before surgery.

Keywords: gelatin-based hemostatic agent, central cervical cord injury, anterior cervical decompression and fusion, Surgiflo, allergy

Introduction

Central cervical cord injury refers to damage to the spinal cord center caused by hyperextension of the cervical spine. In these cases, upper-limb paralysis is more severe than that of the lower limbs due to the location of the conduction path in the cervical transverse surface.¹⁾ For central cervical cord injury, the acute-phase operation is often advanced from the short of the morbidity period.²⁾ On the other hand, patients with galactose- α -1,3-galactose (α -gal) syndrome, which is associated with red meat allergies, may develop an allergic reaction to gelatin of animal

origin that is contained in hemostatic agents used during surgery.³⁻⁹⁾ We experienced a case of severe dysphagia after anterior cervical decompression and fusion (ACDF) for central cervical cord injury strongly suspected to be caused by an allergic reaction thought to be caused by a gelatin-containing hemolytic agent derived from porcine collagen called Surgiflo (Johnson & Johnson Wound Management, Somerville, NJ, USA).¹⁰⁾ All participants included in the case report provided written informed consent.

Received January 27, 2022; Accepted April 6, 2022

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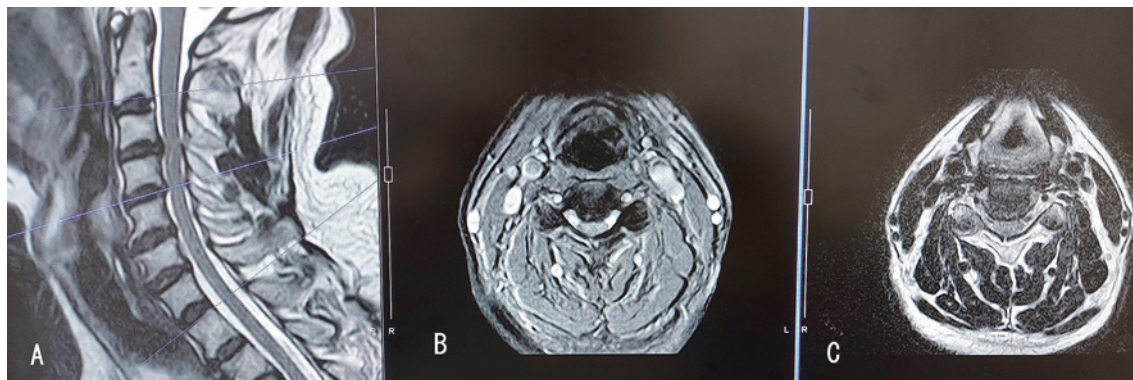


Fig. 1 Sagittal (A) and transaxial (B, C) T2-weighted MRI showed the development of cervical spinal canal stenosis at C3/4 (B) and C4/5 (C).

Case Report

A 55-year-old man fell from his bicycle after drinking alcohol and was taken to our hospital by ambulance. He claimed to have no memory of the injury. His consciousness level was I-2 (Japanese Coma Scale), 3+4+5 (Glasgow Coma Scale) and both upper limbs were difficult to move. There were no visual acuity problems or eye movement disorders. He complained of severe pain in both shoulders. A 4 cm-long cut in his upper left eyelid was closed by suture. His grasping forces were 19.0 kg in the right hand and 19.0 kg in the left hand, but bilateral skillful movement disturbance was obvious and he could not use chopsticks. The preoperative Japan Orthopedic Association (JOA) score was 8.5/17.¹¹⁾ Fifteen years ago, he had an autologous toxic dermatitis history. He had no history of drug allergy, but he had a strong allergy to mackerel and a mild allergy to shrimp and crab. Computed tomography (CT) scans at the time of his hospitalization revealed fractures to the left temporal bone and the posterior lateral wall of the left orbit. There were no bone wounds on the cervical spine. Cervical magnetic resonance imaging (MRI) revealed spinal canal stenosis at the C3/4 and C4/5 levels (Fig. 1A-C).

C3/4 and C4/5 ACDF was performed with two M-cages-SR (Ammtec, Tokyo, Japan). A 4 cm-long transverse linear incision was made within the transverse skin fold on the right side. The operative approach was performed through a triangle made by the sternocleidomastoid and omohyoid muscles. A knife incised the surface of the C4/5-disk. The nucleus pulposus with a fibrous annulus were removed piece by piece with a rongeur and curettes. A Casper spreader widened the disk space with two burrs. The posterior spur of the vertebral body was shaved slightly with a 3 mm diamond burr and a curette. The dural surface was exposed by resection of posterior longitudinal ligaments. The same procedure was performed at the C3/4 level. Two 6 mm-high M-cages-SR were inserted into the C3/4 and C4/5 disc spaces and locked. Surgiflo was used for hemosta-

sis of the epidural space before the cage insertion and the front of the vertebral body after the cage insertion. Surgiflo was thoroughly washed and removed with artificial cerebrospinal fluid 1 minute after topical administration. A significant change in the amplitude of transcranial motor evoked potential monitoring was not seen throughout the operation.

He was easily aroused from anesthesia, but he could not swallow saliva, even though there was no hoarseness immediately after the operation. He still could not swallow the day after the operation. CT-scan on the day after the operation revealed swelling of the front of the vertebral body from the post-pharyngeal wall (Fig. 2). The diameter of his retropharyngeal space in the lateral view of the cervical spine X-rays showed a marked enlargement to 15.8 mm it was 3.3 mm preoperatively (Fig. 3A, B).¹²⁾ Although the postoperative JOA score showed a slight improvement to 10 points, pain in both shoulders, numbness and skillful movement disorders in both hands remained. There was no recurrent nerve paralysis. Based on an otolaryngology examination, his inability to swallow after the operation appeared due to esophageal trismus because of strong edema in the front of the vertebral body as shown by laryngoscope (Fig. 4).

Postoperative serum tests showed a marked increase in non-specific IgE antibodies to 1671 U/mL (the normal range is 0-170 U/mL). This retropharyngeal edema seemed to be an allergic response to the gelatin-based Surgiflo which had been widely used in the front of the vertebral body during the operation. There was no improvement in swallowing or upper-limb nerve symptoms with prednisolone 40 mg. Therefore, steroid pulse therapy for 3 days, consisting of methylprednisolone 1000 mg/day by intravenous injection, was started on the 5th postoperative day. Swallowing became possible within 3 hours of the initial methylprednisolone administration, and normal eating became possible the next day. The pain in both shoulders also disappeared, and skillful movement disorder in both hands improved remarkably. The retropharyngeal space in

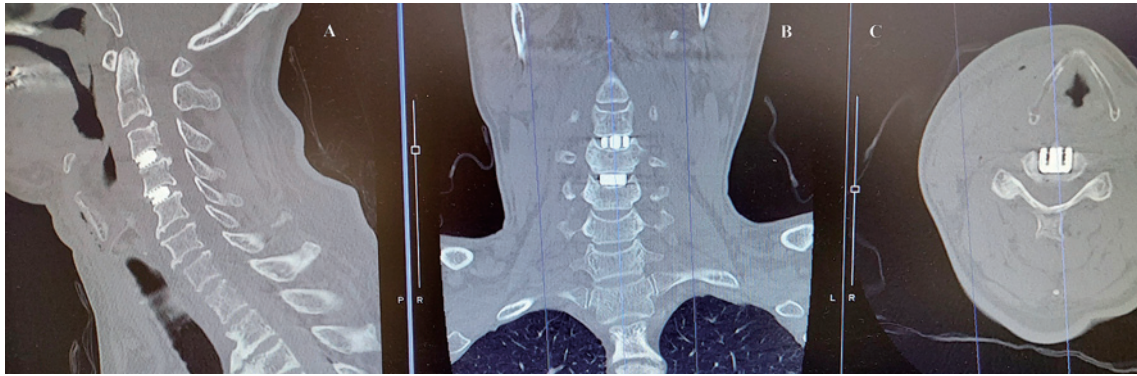


Fig. 2 CT scans of the sagittal (A), coronal (B) and axial views on the day after the operation revealed swelling of the front of the vertebral body from the post-pharyngeal wall.

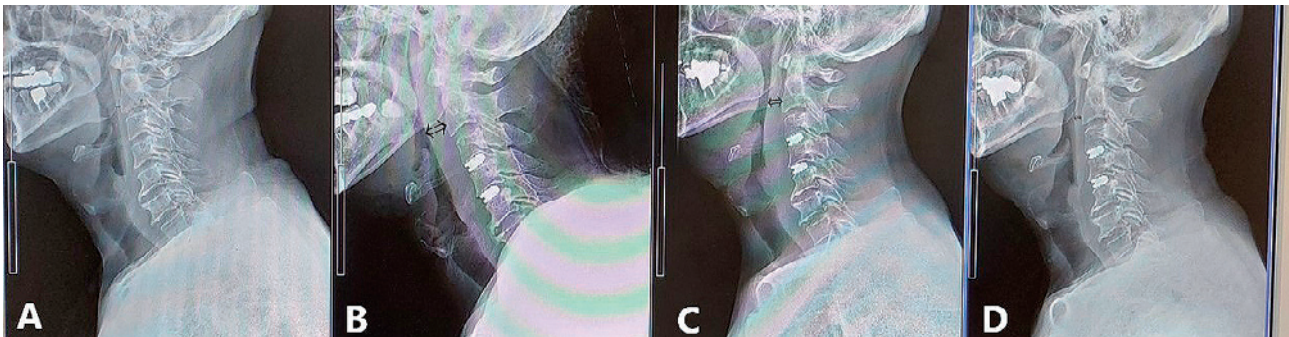


Fig. 3 The diameter of the retropharyngeal space (\Leftrightarrow) at the C2 vertebral body in the lateral view of cervical spine X-rays was 3.3 mm on admission (A), 15.8 mm a day after the operation (B), 10.7 mm 7 days after the operation, and 4.5 mm at discharge (12 days after the operation).

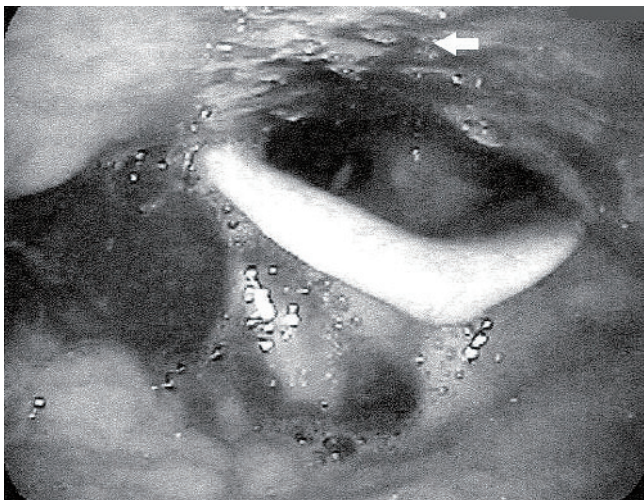


Fig. 4 Laryngoscope finding disclosed the retropharyngeal strong edema in the front of the vertebral body (arrow).

the cervical X-rays was 10.7 mm 7 days after the operation (Fig. 3C). The JOA score recovered to 15 points. The patient could use chopstick, and the retropharyngeal space

in the cervical X-rays was reduced to 10.7 mm seven days after the operation (Fig. 3C). In View-39, a radioallergen sorbent test (RAST, BML, Tokyo Japan) was performed on the 9th day after surgery. Moths, cockroaches, house dust 1, and shrimp were positive as allergens, but pork was negative.¹³⁾ On the 12th day after the operation, he could walk home. When he was discharged from the hospital, the only neurological symptom was mild numbness in both hands, the JOA score was 16 points, and the retropharyngeal space in the cervical X-rays was reduced to 4.5 mm (Fig. 3D).

Discussion

In this case, otolaryngology revealed that the inability to swallow after an ACDF operation was due to esophageal trismus resulting from strong edema in the front of the vertebral body. Even asymptomatic patients may have soft tissue swelling in the front of the vertebral body after ACDF, with X-rays showing an enlarged retropharyngeal space at the C2 level. It has been reported that the postoperative 1 to 2 days may peak and increase by about 10 to 15 mm from preoperative levels.¹⁴⁾ However, even if thick-

ened soft tissue in the front of the vertebral body may cause dysphagia, swallowing rarely becomes impossible.¹⁵⁾ In this case, the retropharyngeal space the day after the operation increased to 15.8 mm, so the aphagia was due to the esophageal trismus.

In this case, the cause of aphagia is an allergic reaction because of the clinical course, the increase of nonspecific IgE, swelling in the posterior pharynx and front of the vertebral body, and significant improvement by large doses of steroids. As an allergen, Surgiflo used during surgery is strongly suspected from the site of the edema. View-39 RAST did not prove allergies to pork, but Surgiflo including gelatin derived from porcine collagen, was considered different in antigenicity from pork. In addition, no other drugs or devices were used that caused allergic reactions during surgery.

In the brain and spinal surgery, gelatin-containing hemostatic agents such as Floseal (Baxter International, Inc., Deerfield, IL, USA) and Surgiflo are often used for hemostasis.¹⁰⁾ Floseal is made from gelatin derived from collagen in bovine, and Surgiflo is made from gelatin derived from collagen in porcine. Allergies to gelatin are called galactose- α -1,3-galactose (α -gal) syndrome, or red meat allergies.³⁻⁹⁾ Since the reported case was not allergic to pork in the View-39 RAST, it should not be called α -gal syndrome or red meat allergy. Neurological complications during spinal surgery due to allergy to Floseal have been reported previously.¹⁶⁾ An example of an anaphylactic reaction using Floseal in ACDF in 2012 has been reported.¹⁷⁾ Surgiflo has also been associated with an intraoperative anaphylaxis reaction.^{7,8)}

In the past, gelatin was considered to be a substance that did not present allergens to people. However, in 1991, a patient was shown to exhibit anaphylaxis symptoms in response to a vaccination (mumps, measles) containing gelatin, and the IgE antibody to gelatin was found to be the causative agent.¹⁸⁾ Before 1988, Japanese children were given a mixture of three vaccines (diphtheria, whooping cough, and tout) at 2 years of age. However, since 1989, the vaccination age has been changed to 3 to 24 months due to the successful detoxification of the vaccine in Japan. Some cases of very young infants who were sensitized to gelatin in the vaccine were thought to have been allergic reactions caused by gelatin. In Japan, by 1996, measures were taken to remove gelatin from the three mixed vaccines as a countermeasure against gelatin allergy, and no new anaphylaxis cases due to gelatin-containing vaccinations have been reported since then. Of course, the conditions that induce gelatin allergy are not limited to gelatin-containing vaccination. However, after gelatin was removed from the vaccines, there have been very few cases in which gelatin is sensitized for other reasons. In addition, there have been a few cases in which gelatin induced a food allergy.¹⁹⁾ An immediate food allergy to gelatin within 1 hour after meals is rare because the allergen of

gelatin is decreased by digestion.

An allergic reaction to α -gal, i.e., red meat allergy, may develop due to a bite by a chigger, a type of tick. For the past 5-10 years, it has been recognized that ticks, which are also a type of mite, can produce a similar allergic reaction. A common allergic reaction develops in a few minutes, but the reaction to the sugar chain α -gal, the causative agent of this allergy, is very slow after 3-6 hours.^{5,16)}

We reported a case of dysphagia strongly suspected to be caused by an allergic reaction to Surgiflo. This is the first report of an allergic reaction to Surgiflo that causes postoperative dysphagia. In addition to postoperative recurrent nerve neuropathy, mild dysphagia is also often experienced after ACDF surgery. In this case, if dysphagia had been mild, it may not have been noticed that an allergic reaction to Surgiflo caused it. Surgiflo or Floseal may be rarely used during ACDF surgery, but Gelform (Pfizer, NY, USA), often used in neurosurgery, is a gelatin preparation, and Aviten (Davol Inc., MA, USA) also uses bovine collagen. In addition, bovine lung extracts are also used in Beriplast P (CSL Behring K.K., Tokyo, Japan), a fibrin glue most commonly used as a topical hemostasis agent, which can be an allergen. When using a gelatin-based hemostatic agent during surgery, it is necessary to ask for an allergy history before surgery.

Conflicts of Interest Disclosure

There are no conflicts of interest.

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