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1 **Intraoperative vertebroplasty during surgical decompression and**
2 **instrumentation for aggressive vertebral hemangiomas: A retrospective study of**
3 **39 patients and review of the literature**

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2

3 Keywords: Aggressive Vertebral Hemangioma; Decompression Surgery;
4 Intraoperative Vertebroplasty; Blood loss; Enneking Stage; Surgical
5 Management.

6

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1 **Abstract**

2

3 **Background Context:** Aggressive (Enneking Stage 3, S3) vertebral hemangiomas
4 (VHs) are rare, which might require surgery. However, the choice of surgery for S3
5 VHs remains controversial because of the rarity of these lesions.

6 **Purpose:** We reported our experience of treating S3 VHs, and evaluated the
7 effectiveness and safety of intraoperative vertebroplasty during decompression
8 surgery for S3 VHs.

9 **Study Design:** This is a retrospective study.

10 **Patient Sample:** Thirty-nine patients with a definitive pathological diagnosis of
11 aggressive VHs who underwent primary decompression surgery in our department
12 were included in this study.

13 **Outcome Measures:** Basic data such as surgical procedure, surgical duration,
14 estimated blood loss during surgery, pathology were collected. The modified Frankel
15 grade was used to evaluate neurological function. Enneking staging was based on
16 radiological findings.

17 **Methods:** We retrospectively examined aggressive VHs with neurological deficits.
18 Surgery was indicated if the neurological deficit was severe or developed quickly or if
19 radiotherapy was ineffective. Decompression surgery was performed. Intraoperative
20 vertebroplasty during posterior decompression has been used since 2009. If
21 contrast-enhanced CT revealed a residual lesion, we recommended adjuvant

1 radiotherapy with 40–50 Gy to prevent recurrence. Patients' basic and surgical
2 information was collected. The minimum follow-up duration was 18 months. This
3 study was partially funded by XXXXXX (Blinded).

4 **Results:** Average age of the 39 patients with S3 VHs who underwent primary
5 decompression surgery was 46.2 (range, 10–69) years. All patients had neurological
6 deficits caused by aggressive VHs. Aggressive VH lesions were located in the
7 cervical, thoracic, and lumbar spine in two, 32, and five patients, respectively. The
8 decompression-alone group had 17 patients and the decompression plus intraoperative
9 vertebroplasty groups had 22. There were no statistically significant intergroup
10 differences in preoperative information ($P > 0.05$). The average estimated blood
11 losses were 1764.7 mL (range, 500–4000 mL) and 1068.2 mL (range, 300–3000 mL)
12 in the decompression-alone and decompression plus vertebroplasty group,
13 respectively ($P = 0.017$). One patient who underwent primary decompression alone
14 without adjuvant radiotherapy experienced recurrence after the first decompression.
15 The average follow-up was 50.2 (range, 18–134) months, and no cases of recurrence
16 were observed at the last follow-up.

17 **Conclusions:** Our results suggest that posterior decompression effectively provides
18 symptom relief in patients with aggressive (S3) VHs with severe spinal cord
19 compression. Intraoperative vertebroplasty is a safe and effective method for
20 minimizing blood loss during surgery, while adjuvant radiotherapy and/or
21 vertebroplasty help in minimizing recurrence after decompression.

1 **Introduction**

2

3 Hemangiomas, which present as benign tumors comprising newly formed blood
4 vessels, are a type of vascular malformation [1]. Vertebral hemangiomas (VHs) are
5 the most common benign tumors involving the spinal column and frequently affect
6 the thoracic spine. The incidence of VHs is 10%–26%; most cases are asymptomatic
7 (Enneking stage 1[2], S1), with only 0.9%–1.2% symptomatic cases [1, 3-6].
8 Approximately 55% symptomatic VHs present with pain as the only symptom
9 (Enneking stage 2, S2). The other 45% are aggressive, with possible invasion of the
10 spinal canal and/or paravertebral space, which leads to neurological deficits
11 (Enneking stage 3, S3) [3, 6-13].

12

13 Asymptomatic VHs (S1) are generally found incidentally and require only
14 observation, whereas S3 VHs might require surgery. However, the choice of surgery
15 for S3 VHs remains controversial because of the rarity of these lesions.
16 Decompression with laminectomy and debulking is relatively less technically
17 demanding [3-5, 11, 14]. Japanese surgeons have reported total en bloc
18 spondylectomy to achieve wide oncological margins [9]. Acosta et al. and Goldstein
19 et al. recommended intralesional vertebrectomy because of the benign nature of these
20 lesions [6, 10]. Moreover, Doppman et al. suggested direct intralesional injection of
21 ethanol [15]. VHs are highly vascular lesions and can cause intraoperative excessive

1 hemorrhage during surgery. Preoperative embolization is often mandatory to
2 minimize blood loss [9-11, 16].

3

4 At our institution, we performed intraoperative vertebroplasty for external
5 embolization and learned that it can effectively minimize blood loss. In the present
6 study, we retrospectively evaluated the effectiveness and safety of vertebroplasty
7 during decompression surgery for S3 VHs.

8

9 **Materials and methods**

10

11 *General information*

12 This study was approved by our hospital's ethics committee and conducted according
13 to the principles of the Declaration of Helsinki.

14 We reviewed our spinal tumor database and identified a total of 61 patients with
15 aggressive (S3) VHs who had undergone treatment or consultation with the spinal
16 surgery team at our hospital between 2001 and 2016. Patients treated before 2001
17 were lost to follow-up because of frequent changes in addresses and telephone
18 numbers. Eventually, we identified 39 patients with a definitive pathological diagnosis
19 of aggressive VHs who underwent primary decompression surgery in our department.

20

1 Hospital charts, operating room reports, anesthesia reports, office charts, pathology
2 reports, and radiographs of the included patients were retrospectively evaluated. Data
3 pertaining to patient age, sex, symptoms, underlying diseases, smoking habits, body
4 mass index (BMI), neurological function, radiological features, Enneking stage,
5 surgical procedure, surgical duration, estimated blood loss during surgery, pathology,
6 time between surgery and discharge, and treatment complications were collected. The
7 modified Frankel grade was used to evaluate neurological function. Enneking staging
8 was based on radiological findings.

9

10 *Imaging and biopsy*

11

12 We routinely performed posteroanterior and lateral spinal radiography, computed
13 tomography (CT), and magnetic resonance imaging (MRI) for all patients. Typical
14 lesions exhibit a honeycomb appearance on CT and a salt-and-pepper appearance on
15 MRI. For patients with atypical images, CT-guided biopsy was indicated and
16 performed by our interventional radiologists.

17

18 *Treatment protocol*

19

20 In our practice, radiotherapy is generally the first choice of treatment, particularly for
21 patients with mild or slowly developing neurological deficits, including those with

1 multiple-level VHs and/or massive soft tissue invasion. Indications for surgery at our
2 institute include ineffective radiotherapy and/or severe or rapidly developing
3 neurological deficits (muscle strength grade of <3/5 and rapid deterioration of
4 neurological function within 2 weeks).

5 Four experienced surgeons performed all decompression surgeries, and the surgical
6 techniques were chosen according to each surgeon's personal preference. Two
7 surgeons began performing vertebroplasty during posterior decompression since 2009,
8 while the other two used the conventional decompression procedure.

9

10 *Surgical techniques*

11

12 Posterior decompression was performed in the prone position under general
13 anesthesia. After the pedicle screws were in place, the adjacent cranial and caudal
14 laminae were removed for direct visualization of the normal dural sac. Bilateral
15 transpedicular cement (normal viscosity) was injected with slight pressure to shrink
16 the vessels in the affected vertebral body (VB). Under fluoroscopic guidance, the tip
17 of the cannula was inserted at the ventral edge of the lesion to fill the affected VB
18 with as much cement as possible. The volume of the epidural tumor may decrease
19 after cement filling because of the decreased blood supply. Direct visualization of the
20 adjacent dural sac and the decreased blood loss permitted the safe performance of
21 laminectomy through the affected lesion. The interior pedicles were removed using a

1 burr. Before resection, the epidural tumor could be further decreased in size using
2 bipolar coagulation; this resulted in the achievement of ideal decompression. Further
3 bony curettage of VB was generally not necessary, with the exception of patients
4 exhibiting obvious bony compression. After instrumentation, allograft was used to
5 achieve posterolateral fusion.

6

7 *Follow-up*

8

9 We obtained roentgenograms at 3, 6, and 12 months after the index procedure and
10 annually thereafter. At the 3-month follow-up, if contrast-enhanced CT revealed a
11 residual lesion, we recommended adjuvant radiotherapy with 40–50 Gy to prevent
12 recurrence. MRI was performed at the 3-month follow-up and annually thereafter. If
13 the patient displayed symptoms indicative of local recurrence, immediate MRI was
14 indicated. The minimum follow-up duration was 18 months.

15

16 To evaluate the cement filling rate after surgery with intraoperative vertebroplasty, the
17 maximum area of bone cement and the lesions were measured on axial CT images
18 obtained after surgery. AutoCAD 2014 software (AUTODESK Inc., San Rafael, CA,
19 USA) was used to calculate the area. (Figures 1-H, 2-G, and 3-J)

20

21 *Statistical analysis*

1

2 SPSS version 18.0 (SPSS Inc., Chicago, IL, USA) was used to analyze all collected
3 data. The Kolmogorov–Smirnov test was used to identify whether the data were
4 normally distributed. Measurable variables are presented as means and standard
5 deviations if the data were normally distributed and median and maximum\minimum
6 values if the data were not normally distributed. Student's t-test and the
7 Mann–Whitney U test were used to compare differences in normally and abnormally
8 distributed data, respectively. Immeasurable variables are presented as percentages,
9 with the use of the chi-squared test or Fisher's exact test for comparisons. A P-value
10 of 0.05 was considered statistically significant.

11

12 **Results**

13

14 There were 14 men and 25 women (including two pregnant women) in this study. The
15 average age was 46.2 (range, 10–69) years at the time of diagnosis.

16

17 All patients exhibited neurological deficits caused by aggressive VHs. In total, 31
18 patients exhibited myelopathy (Frankel grade B, C, and D in four, four, and 23
19 patients, respectively). Four and three patients exhibited cauda equina syndrome and
20 radiculopathy, respectively. Eighteen patients also complained of pain. The average
21 time between symptom onset and surgery was 5.14 (range, 0.25–26) months.

1

2 The aggressive VHs were located in the cervical, thoracic, and lumbar spine in two,
3 32, and five patients, respectively. Four patients had multiple lesions, although only
4 one vertebra contained a symptomatic S3 lesion. In three patients, VHs were located
5 only in VB. The lesions in the remaining patients involved the posterior arches, with
6 24 involving the bilateral pedicles and 12 involving a unilateral pedicle. All these
7 lesions exhibited epidural extensions, while 13 patients exhibited paraspinal
8 extensions. Neurological compression was caused by soft masses in 25 patients and a
9 combination of soft and hard masses in 14 patients.

10

11 Twelve patients with atypical radiological findings underwent percutaneous
12 CT-guided biopsy. A definitive pathological diagnosis could be established for only
13 seven (58.3%) patients; the results were not diagnostic for the remaining five,
14 including two with only connective tissue cells, two with only peripheral blood cells,
15 and one with suspicious results that needed to be distinguished from those for
16 malignant vessel tumors. Thirteen patients underwent preoperative embolization.

17

18 *Decompression alone vs. decompression with vertebroplasty*

19

20 In total, 17 patients underwent only decompression and 22 underwent decompression
21 with vertebroplasty. There were no statistically significant intergroup differences in

1 sex, age, BMI, underlying diseases, smoking habits, VH location, and the use of
2 embolization ($P > 0.05$; Table 1).

3

4 In the decompression group, the average estimated blood loss was 1764.7 (range,
5 500–4000) mL. The average surgical duration was 270.0 (range, 180–420) min and
6 the average time to discharge was 8.3 (range, 3–16) days after the index surgery. In
7 the decompression with vertebroplasty group, the average estimated blood loss was
8 1068.2 (range, 300–3000) mL. The average surgical duration was 249.5 (range,
9 150–360) min and the average time to discharge was 7.0 (range, 4–12) days after the
10 index surgery. There was a statistically significant intergroup difference in the
11 estimated blood loss ($P = 0.017$; Table 2).

12

13 One dural sac tear was identified during surgery and successfully repaired. There
14 were no severe intraoperative complications other than massive intraoperative
15 bleeding. Eight and four patients in the decompression and decompression with
16 vertebroplasty groups, respectively, underwent adjuvant radiotherapy after surgery.
17 All lesions were pathologically confirmed as VHs after surgery.

18

19 *Follow-up and recurrence*

20

21 All patients were followed up. The average follow-up duration was 50.2 (range,

1 18–134) months. All patients were symptom-free without any neurological deficits at
2 the last follow-up visit. One of nine patients (11.1%) who underwent primary
3 decompression alone without adjuvant radiotherapy experienced recurrence after the
4 first decompression. This patient underwent a second decompression procedure with
5 adjuvant radiotherapy and did not exhibit recurrence at 64 months after the revision
6 surgery.

7

8 For the 22 patients who underwent decompression with vertebroplasty, the mean
9 cement filling rate was 77.0% (range, 54.1%–93.8%), with no recurrence observed at
10 the last follow-up; this included the 18 patients who did not receive radiotherapy, with
11 a mean bone cement filling rate of 80.0% (range, 64.1%–93.8%).

12

13 **Discussion**

14 Since the vast majority of VHs are asymptomatic and found incidentally (Enneking
15 stage 1, S1), they do not require treatment. However, aggressive VHs (Enneking stage
16 3, S3) may lead to spinal cord compression, vertebral bony destruction, and/or
17 neurological deficits. Surgery is usually indicated for patients with severe
18 neurological deficits and/or marked instability.

19

20 **Surgery.** Different surgical techniques, namely decompression surgery, intralesional
21 vertebrectomy, and total en bloc spondylectomy, have demonstrated acceptable results

1 (Table 3)[3, 4, 6, 8-10, 15, 17-19]. However, there is no consensus on the best
2 treatment strategy for symptomatic VHs.

3

4 Vertebrectomy or en bloc resection for aggressive VHs are associated with low
5 recurrence rates, although they are more technically demanding and accompanied by
6 greater blood loss and higher morbidity [4, 9, 10]. Japanese surgeons (Tomita et al. [9]
7 and Ogawa et al. [12]) reported that radical total en bloc spondylectomy for VHs was
8 time consuming, often hemorrhagic, and quite technically demanding. In their cases,
9 even after preoperative embolization, the estimated blood loss was 2420 (range,
10 1580–3400) mL and the surgical duration was 608 (range, 480–700) min. Vasudeva et
11 al [18] stated that en bloc resection provided benefits similar to those of gross total
12 resection or subtotal resection, although it was associated with higher morbidity rates.
13 Acosta et al. [10] reported intralesional vertebrectomy, which was also associated
14 with a low recurrence rate. However, in their cases (n = 10), the average blood loss
15 after embolization was 2.1 (range, 0.8–5) L. In a multicenter study by Goldstein et al.
16 [6], the rate of VH recurrence after intralesional vertebrectomy was 5.4% (2/37), with
17 no recurrence after other procedures, including decompression (n = 17) and en bloc
18 resection (n = 7). They concluded that formal en bloc resection is not required, and
19 that excellent rates of local control and long-term survival can be achieved with
20 aggressive intralesional resection during the index surgery.

21

1 Decompression surgery is widely used because it is less technically demanding [3-5,
2 11, 14]. Combined with spinal fixation, decompression is reliable for achieving
3 neurological recovery and spinal stability, while vertebroplasty and/or radiotherapy is
4 mandatory to prevent local recurrence [3-6, 11, 14].

5

6 **Intraoperative Vertebroplasty.** VHs are highly vascular lesions that can result in
7 significant intraoperative hemorrhage. Preoperative embolization can decrease this
8 blood loss [14]. In the present study, intraoperative vertebroplasty decreased blood
9 loss through the injection of bone cement into VB, which could obliterate and shrink
10 the vessels in VHs. To our knowledge, the technique of intraoperative vertebroplasty
11 with bone cement has only been reported in small case series [18, 20]. Similarly,
12 Singh et al. [17] reported that intraoperative alcohol injection into VB achieved ideal
13 blood loss control. However, the injection of alcohol is associated with a higher risk
14 of complications such as Brown–Séquard syndrome and pathological fracture [15, 21,
15 22].

16 To avoid recurrence, complete obliteration of the lesion with bone cement is indicated.
17 Of the 22 patients treated with decompression plus vertebroplasty in our study, 18
18 with a relatively higher bone cement filling rate did not receive radiotherapy after
19 surgery and did not exhibit any recurrence.

20

1 **Radiotherapy.** Radiotherapy is also widely used for the treatment of VHs [13, 23, 24].
2 Fractionated doses under 40 Gy spread out over a 3- to 4-week period are associated
3 with minimal risk. Heyd et al. [24] from Germany reported radiotherapy treatment for
4 84 patients with VHs. Fox and Onofrio [3] showed that 50% (3/6) patients
5 experienced recurrence of neurological deficits after subtotal tumor removal plus
6 radiotherapy with ≤ 10 Gy (average time to recurrence was 9.3 years). However, no
7 recurrence was observed in patients who underwent subtotal tumor removal plus
8 radiotherapy with 26–40 Gy or gross total tumor excision. The most severe
9 complication of radiotherapy is the malignant transformation of VHs and nearby
10 tissues[24-26]. However, the cancer risks of radiotherapy are extremely low. In our
11 study, there was no malignant transformation due to radiotherapy.

12

13 *Limitations*

14

15 The major limitations of our study include its retrospective design and the inclusion of
16 data from a single center. In addition, there may be some bias during our data analysis.
17 Future prospective multicenter studies are needed to verify our results.

18

19 *Financial associations*

20

21 This study was partially funded by XXXXXX (Blinded).

1

2 **Conclusions**

3

4 In conclusion, our results suggest that posterior decompression effectively provides
5 symptom relief in patients with aggressive (S3) VHs with severe spinal cord
6 compression. Intraoperative vertebroplasty is a safe and effective method for
7 minimizing blood loss during surgery, while adjuvant radiotherapy and/or
8 vertebroplasty help in minimizing recurrence after decompression.

9

10

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1

2

3

4

5 **Figure Legends**

6 **Figure. 1. Illustrated Case1.** A 34-year-old female suffered from myelopathy and
7 pain for 6 months. Frankel D. A.B. Sagittal and axial CT showed a lesion in T10. C.D.
8 Sagittal and axial MRI. E to H. She underwent decompression and intraoperative
9 vertebroplasty without adjuvant radiotherapy. The filling rate of bone cement is 90.2%.
10 At the 60 months' follow-up, the patient was symptom-free with no recurrence.

11

12 **Figure. 2. Illustrated Case2.** A 69-year-old female suffered from myelopathy for 10
13 months. Frankel D. A.B. Sagittal and axial CT showed a lesion in T7. C.D. Sagittal
14 and axial MRI. E to H. She underwent decompression and intraoperative
15 vertebroplasty without postoperative adjuvant radiotherapy. The filling rate of bone
16 cement is 90.6%. At the 12 months' follow-up, the patient was symptom-free and
17 showed no recurrence.

18

19 **Figure. 3. Illustrated Case3.** A 25-year-old female suffered from myelopathy and
20 pain for 4 months. Frankel C. Radiotherapy was ineffective and neurological function
21 got worse. She underwent surgery. A.B. Sagittal and axial CT showed a lesion in T5.

1 C She underwent CT-guide biopsy with negative result. D.E. Sagittal and axial MRI.
2 F.G. Intraoperative injection of bone cement. H to J. She underwent decompression
3 and intraoperative vertebroplasty without adjuvant radiotherapy. The filling rate of
4 bone cement is 71.4%. At the 70 months' follow-up, the patient was symptom-free
5 and without recurrence.

Table 1. Comparison of detailed information in both groups

Factors	Decompression Group (n=17)	Decompression+VP Group (n=22)	P
Sex (Female)	8 (47.1%)	17 (77.3%)	0.091
AGE	57 (10, 67)	43.5 (21, 69)	0.340
BMI	24.21 (19.73, 32.15)	23.37 (18.75, 36.73)	0.850
Preoperative embolization	6 (35.3%)	7 (30.4%)	1.000
Location			
Cervical	1 (5.9%)	1 (4.5%)	
Thoracic	14 (82.4%)	18 (81.8%)	1.000
Lumbar	2 (11.8%)	3 (13.6%)	
Smoking	1 (5.9%)	2 (9.1%)	1.000
HBP	2 (11.8%)	2 (9.1%)	1.000
DM	1 (5.9%)	2 (9.1%)	1.000

HBP, high blood pressure; DM, diabetes mellitus; VP, vertebroplasty

Table 2. Comparison of the surgical information in the two groups

Factors	Decompression Group (n=17)	Decompression+VP Group (n=22)	z	P
Blood Loss (mL)	1500 (500, 4000)	725 (300, 3000)	-2.386	0.017
Surgery time (min)	270 (180, 420)	240 (150, 360)	-1.072	0.284
Time to discharge after surgery (day)	7 (3, 16)	7 (4, 12)	-1.022	0.307

VP, vertebroplasty

Table 3. Literature review of surgical management of vertebral hemangiomas

Authors	No. of Pts	Treatment	Surgery Time	Blood Loss	Follow-up	Recurrence	Complications
Fox et al. (1993)	59	1 total resection 10 subtotal resections 2 preoperative embolizations 5 adjuvant radiotherapies	—	—	8.7 (1-17) yrs	2/10 in subtotal resection without radiotherapy 1 in subtotal resection and low dose radiotherapy.	2 profuse intraoperative bleeding 2 arachnoiditis 1 epidural hemorrhage
Pastushyn et al. (1998)	86	64 laminectomies or extensive laminectomies with adjuvant radiotherapy for subtotal resection cases	—	—	6-180 mos	16 recurrences 7 revisions	No.
Doppman et al. (2000)	11	11 CT-guide injections of ethanol	—	—	15-76 mos	No	2 pathological fractures
Acosta et al. (2008)	22	16 surgeries: 10 preoperative embolizations 7 decompression surgeries 9 intralesional spondylectomies 6 vertebroplastics or embolizations	—	Mean 400 mL in patients who underwent vertebrectomy	2-240 mos	2 recurrences after decompression surgery	1 excessive intraoperative bleeding

Kato et al. (2010)	5	5 preoperative embolizations and total excisions (en bloc or piecemeal)	—	2424 mL (1580-3400 mL)	92-163 mos	No	No
Singh et al. (2011)	10	10 decompressions with intraoperative ethanol embolization	102 ± 22 min	296 ± 90.82 mL	12-26 mos	No	No
Acosta et al. (2011)	10	10 preoperative embolizations and intralesional spondylectomies without adjuvant radiotherapy.	—	2100 mL (800-5000 mL)	2.4yrs (0.8-5.5yrs)	No	No
Song et al. (2012)	9	9 total en blocs	210 min (180-270 min)	1800 mL (1000-5000 mL)	18-60mos	No	No
Goldstein et al. (2015 multicenter)	68	33 preoperative embolizations; 17 palliative decompressions, including 3 with adjuvant radiotherapy; 37 intralesional spondylectomies, including 2 with radiotherapy; 7 en bloc spondylectomies including 1 with radiotherapy; 7 surgeries without details	—	—	Mean 3.9 yrs	Recurrence was found in 2 patients with intralesional spondylectomy, including 1 with adjuvant radiotherapy	—
Vasudeva et al. (2016)	5	4 preoperative embolizations; 1 en bloc spondylectomy; 2 piecemeal gross-total resections; 2 subtotal resections; 3 intraoperative VPs; and 1 adjuvant radiotherapy	—	400-1800 mL (400 and 500 mL for 2 cases of intraoperative VP)	8-43 mos	No	CSF leak, wound infection DVT, and hardware failure in 1 case

No, number; Pt, patient; Yr, year; Mo, month; VP, vertebroplasty; CSF, cerebrospinal fluid; DVT, deep vein thrombosis

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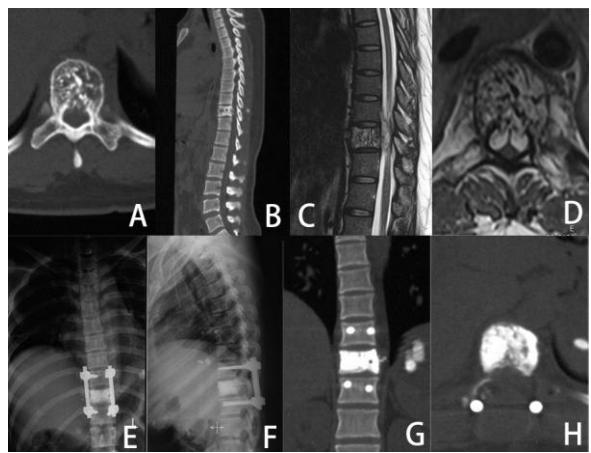


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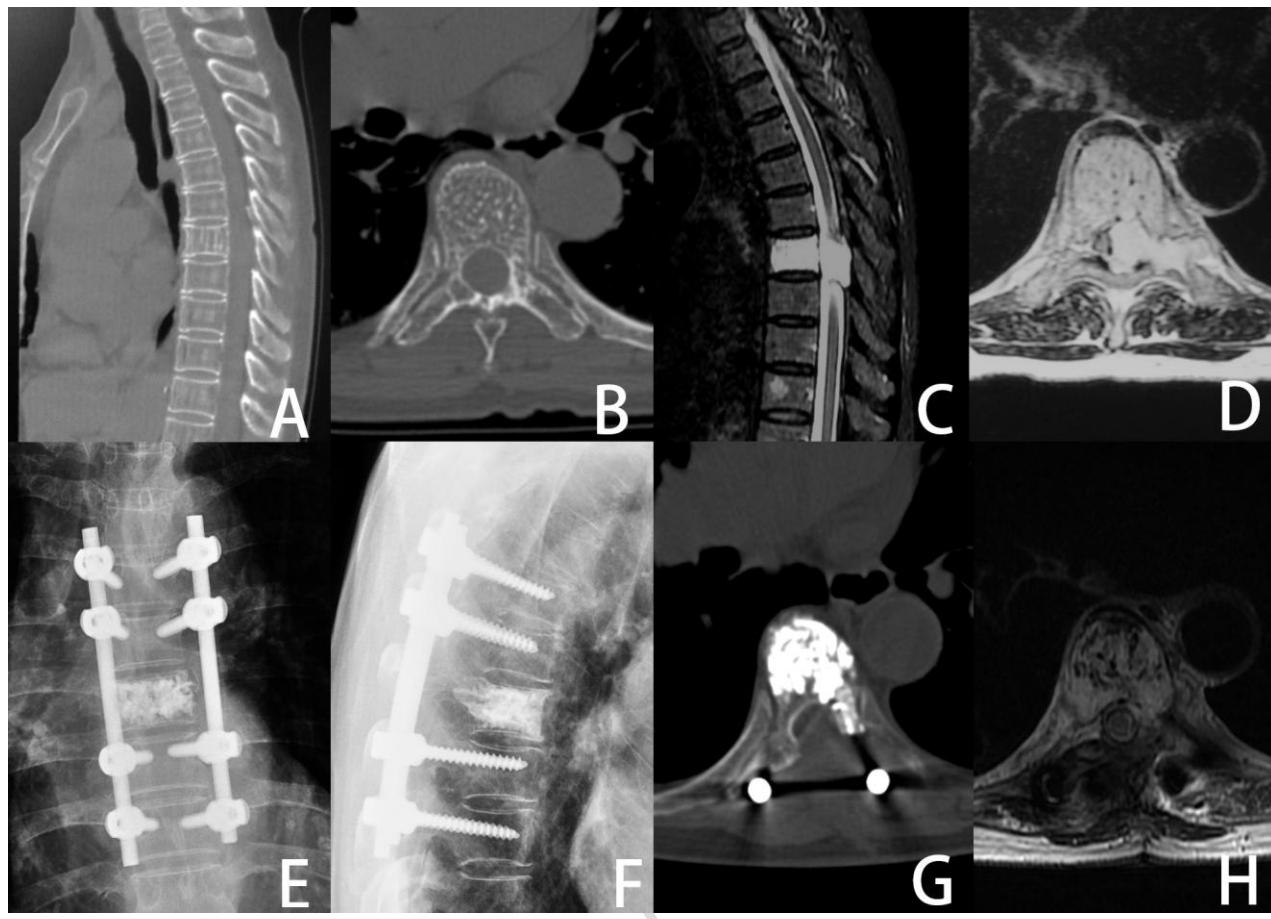


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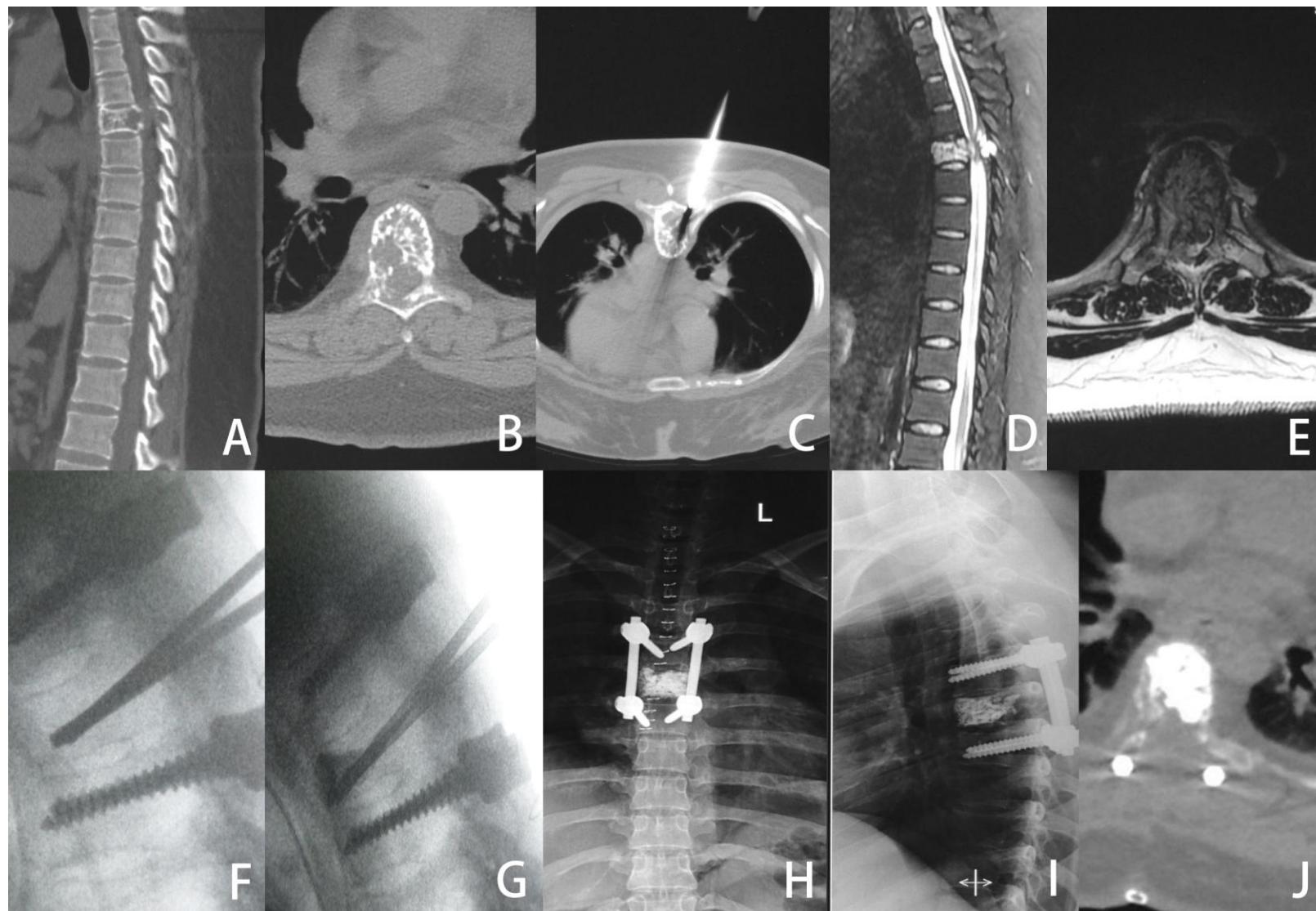


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