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# **Treatment of Aggressive Vertebral Hemangiomas with Poly Vinyl Alcohol (PVA) Microparticles Embolization, PMMA, and Short Segment Stabilization: Preliminary Results with at Least 5 Years of Follow-up.**

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## **Objective**

Vertebral hemangiomas (VHs) are the most common incidental lesions of vertebral body, but they are very challenging to treat if they become symptomatic. Several treatments have been proposed but none was superior to others. The aim of this study is to analyze blood loss and long-term clinical and neurological results of aggressive VHs treated with arterial embolization the day before operation, followed by vertebroplasty, posterior decompression, and short segment stabilization.

## **Methods**

Ten patients (4 males and 6 females) were treated for aggressive VHs with polyvinyl alcohol microparticles embolization, posterior short segment stabilization, and poly methyl methacrylate. Clinical and neurological outcomes were assessed with visual analog, Nurick, and American Spinal Injury Association (ASIA) scales.

## **Results**

At last follow-up mean, visual analog scale was  $1.8 \pm 1.3$ , with a significant difference with preoperative values ( $P = 0.00018$ ). Neurological deficits persisted in 4 patients (ASIA scale: C in 1 patient [10%], D in 3 patients [30%]), but they improved from baseline in all cases. Also, Nurick scale rating improved in all patients (0 in 3 patients [30%], 1 in 4 patients [40%], 2 in 2 patients [20%], and 3 in the last one [10%]). A statistically significant difference between pre- and postoperative values was observed for both scores (ASIA,  $P = 0.0102$ ; Nurick,  $P = 0.026$ ). Relapse of pathology was recorded in 2 patients.

## **Conclusions**

Polyvinyl alcohol microparticles embolization, short segment fixation, and vertebroplasty is an effective treatment option for aggressive VHs, with a fast surgical time, poor blood loss, and improvement of preoperative clinical and neurological outcomes.

## **Introduction**

Vertebral hemangiomas (VHs) are the most common incidental lesions of vertebral body; however, they are very challenging to treat if they become symptomatic (0.9%–1.2% of cases).<sup>1, 2</sup> VHs are most common in women, with a preference for thoracic spine. Sometimes they can become aggressive and may involve more than 1 vertebra, even if the involvement of more than 2 levels is rare.<sup>3</sup>

Several treatments have been proposed in the literature, including embolization and vertebrectomy,<sup>4, 5</sup> vertebroplasty,<sup>4, 5</sup> and radiotherapy.<sup>6, 7</sup> Despite vertebrectomy being the most radical approach, this type of surgery is extremely complex and with high morbidity and mortality. On the other hand, selective embolization and vertebroplasty with poly methyl methacrylate (PMMA) are less invasive but they could temporarily reduce vascularization with high risk of recurrence. Moreover, if vertebroplasty could increase the risk of adjacent vertebral fracture is still far from being solved.

Selective ethanol embolization<sup>8, 9</sup> is reported to be effective; however, some studies reported a high incidence of subsequent vertebral collapse. To avoid this risk, some authors have proposed using short segment posterior stabilization with pedicle screws.<sup>10, 11, 12, 13</sup>

To avoid ethanol toxicity, some articles proposed using polyvinyl alcohol (PVA) microparticles instead of ethanol, which is less detrimental for vascular endothelium.<sup>14</sup> Because decompression creates an area of spine instability,<sup>15</sup> vertebroplasty alone is not able to properly avoid myelopathic compression.<sup>16</sup> Embolization alone reported poor decompressive features and a not-negligible risk of recurrence.<sup>17</sup> A combined approach with preoperative embolization, vertebroplasty, posterior stabilization, and decompression was proposed instead.

The aim of our study is to analyze intraoperative blood loss and long-term clinical and radiological results of aggressive VHs treated with preoperative arterial embolization, followed by vertebroplasty and short segment stabilization.

## ***Patients and Methods***

### **Patient Selection**

All patients with aggressive VH treated by our department from 2007 to 2013 were retrospectively reviewed. All of them had spinal cord compression and myelopathic features or lumbar spinal stenosis with compression of neurological elements, with or without neurological deficit. Patients with affected vertebral fracture and kyphotic deformity were also included.

The presence of pure ventral compression, severe systemic injury, or von Hippel disease was considered as exclusion criterion. All patients lost at follow-up, with incomplete data or without 5 years of minimum follow-up, were excluded.

Preoperative assessment was performed with a visual analog scale (VAS), American Spinal Injury Association (ASIA), and the Nurick scale; radiological evaluation was performed with conventional x-ray, computed tomography, and magnetic resonance imaging and lesions classified according to the Tomita classification ([Figure 1](#)).

Informed consent was provided by the patients and the study followed the principles laid down by declaration of Helsinki.

### **Arterial Embolization with PVA Microparticles**

The day before surgery, patients underwent selective arterial embolization with PVA microparticles in neuroradiology department under angio-computed tomography control. After about 24 hours, patients underwent surgical treatment in the operating theater with an open approach (with pedicle screw and PMMA of affected vertebra).

### **Surgical Treatment**

VH level was confirmed by fluoroscopy. Pedicle screws were inserted in the level above and below in vertebral pedicles with a standard technique through an open approach. If more than 1 level was involved and a lesion located at the thoracolumbar junction or an impending fracture is highly likely to occur, the stabilization was extended cranially and caudally. During surgery and before cement injection, biopsies were performed through a Jamshidi needle to confirm the radiological diagnosis. If present, a rapid oozing from the needle also confirmed the presence of hemangioma. After that, vertebroplasty was performed under fluoroscopic guidance and pedicle screws were connected with bars and inner in order to stabilize the system ([Figure 2](#)). Posterior decompression of the involved segment was always performed.

### **Follow-up**

After hospital discharge, the patients were followed with magnetic resonance imaging and computed tomography scans every 6 months. Clinical examination was performed every month for the first 3 months, and then at 6 and 12 months. A subsequent evaluation was performed yearly with x-rays. Clinical and neurological outcomes were assessed with VAS, Nurick, and ASIA impairment classifications. All radiological features were reviewed to find any sign of recurrence, implant loosening, or adjacent vertebral fractures.

### **Statistical Analysis**

The analysis was performed through STATA13 software (StataCorp LLC, College Station, Texas, USA). Categorical variables were reported as frequency by percentage, whereas quantitative

variables were reported as mean  $\pm$  standard deviation. Differences between quantitative variables were assessed through Mann-Whitney *U* test, whereas differences between categorical data were performed through Wilcoxon matched-pairs signed-ranks test.

## Results

From 2008 to 2013, 14 patients were treated for aggressive VHs with PVA microparticle embolization, short segment stabilization, and PMMA. According to inclusion and exclusion criteria, the study sample was composed of 10 patients (4 males and 6 females), mean age  $50.6 \pm 17$  years (Table 1). Of 4 excluded patients, 2 females had pure ventral compression and incomplete data (mean age,  $48.5 \pm 2.12$  years), a 45-year-old male had von Hippel disease, and a 51-year-old female was first treated with radiotherapy without satisfactory response. VHs were all located in the thoracic spine (T11, T8, T9) with the exception of the patient with von Hippel disease because he had multiple localizations (T12, L1).

All patients were affected by significant pain, mean VAS  $6.5 \pm 1.4$ ; 7 patients had neurological deficit (ASIA scale: 1 grade A [10%], 1 grade B [10%], 3 grade C [30%], 2 grade D [20%], and 3 grade E [30%]). Nurick scale was 0 in 2 patients (20%); 1 in 1 patient (10%); 2, 3, or 4 in 2 patients, respectively (20%); and 5 in 1 patient (10%). Seven patients had only 1 level involved, whereas 3 patients had multiple VH localizations. Mean follow-up was  $7.2 \pm 2.3$  years.

Mean operation time was  $91.5 \pm 36.7$  minutes, whereas mean intraoperative blood loss was  $261.5 \pm 76$  mL. At the last follow-up, no loosening of pedicle screws, adjacent vertebral fracture, or junctional instability was recorded. Mean VAS was  $1.8 \pm 1.3$ , with a significant difference with preoperative values ( $P = 0.00018$ ).

Neurological deficits improved in all cases, although they persisted in 4 patients (ASIA scale: C in 1 patient with a preintervention A score [10%], D in 3 patients [30%], 2 of whom with preintervention score C and 1 with B). Nurick scale improved in all patients, except for 1 who went from a preintervention Nurick score of 2 to a postintervention score of 3 and had a recurrence.

The equality of matched pairs of observations for both the ASIA and the Nurick scores before and after the surgical intervention was tested through the Wilcoxon matched-pairs signed-ranks test. A statistically significant difference between pre- and postoperative scores was observed for both ASIA score ( $P = 0.0102$ ) and Nurick score ( $P = 0.0260$ ).

Recurrence was recorded in 2 patients. One reported relapse of pathology at 4 years' follow-up that was treated with corpectomy; the other showed recurrence of collateral pathological circulation after 3 months. A second selective embolization was resolute.

## Discussion

Aggressive VH is a challenging pathology because of the high risk of uncontrolled bleeding, pending fracture, and invasion of the spinal canal with spinal cord compression and neurological deficit.<sup>18</sup>

Because of its vascular nature, selective embolization of pathological blood vessels is 1 of the first-line treatments used to treat this pathology. Preoperative embolization, as adjuvant therapy, proved to be useful in reducing surgical bleeding and thus operative risks.<sup>19</sup> In the literature, however, only short-term follow-up data are reported.<sup>8,20, 21</sup> The most commonly used embolization agent for intravascular or intraoperative vascular sclerosing is pure ethanol. Ethanol causes tissue infarction and denaturation of vascular and tissue proteins, with resultant acute vessel thrombosis and fibrosis. Actually, intralesional<sup>10, 22</sup> use of ethanol embolization through pedicles has replaced trans catheter arterial embolization, which is still used for other pathologies.<sup>23</sup> The use of ethanol selective embolization through arterial catheter is limited because of its toxicity on vascular endothelium, difficult-to-control placement because rapid drainage from a lesion could disperse and dilute in neighboring districts, and lack of opacity under radiological guidance. Moreover, the risk

of damaging the spinal cord or nerves is not negligible. Ethanol injection into hemangioma through pedicles or directly intralesional seems to be less dangerous. The amount of alcohol injection is lower and tissue diffusion and dilution could be better controlled during operation, making it also more accurate.<sup>14</sup> However, the direct intralesional injection of ethanol exposes the vertebra to a risk of pathological fracture.<sup>24</sup>

PVA microparticles are derived from a PVA foam sheet that is vacuum dried and rasped into particles, ranging in size from 100 to 1100  $\mu\text{m}$ . PVA microparticles are slightly irregular in size and shape because of the preparation process. For this reason, the aggregation of particles is enhanced. The particles promote permanent occlusion, adhering to vascular walls and causing a blockage of blood circulation.<sup>25</sup> They also stimulate local inflammatory reaction and angionecrosis, resulting in vascular fibrosis over time. PVA particles are biocompatible, so they have no toxicity of surrounding tissues; however, they tend to aggregate, occluding vessels more proximally than desired. Particle aggregation may also cause catheter occlusion resulting in incomplete injection, or they can accumulate in catheter hub and cause casual embolization during catheter flushing.<sup>14</sup> A possible alternative to PVA embolization in those patients with contraindications is the use of temporary arterial occlusion by aneurysm clip. In this way, it is possible to directly evaluate tumor blood supply and prevent any damage to surrounding healthy tissues.<sup>26</sup>

Vertebroplasty was proposed as an effective treatment, alone<sup>27, 28</sup> or in combination with alcohol embolization or posterior decompression and instrumentation.<sup>22, 29</sup> Despite sole vertebroplasty being reserved for patients without neurological impairment, Omidi-Kashani et al<sup>29</sup> reported that vertebroplasty of affected vertebra promotes little improvement in neurological deficit. Another study confirmed that the posterior wall involvement is not a contraindication for vertebroplasty.<sup>30</sup> PMMA has a great benefit in terms of pain relief. It offers mechanical stability to load, preventing any subsequent vertebral collapse, and it has an analgesic effect, acting on pain termination of the periosteum. On the other hand, cement leakage into the spinal canal or blood vessels are some of the most frequent complications reported.<sup>31</sup>

Short segment fusion was also proposed in literature to adjuvate other procedures. It offers stability and protection of the affected vertebra. As after ethanol embolization, the treated vertebra is more prone to collapse from a weakening of trabecular structure and lower mechanical strength.<sup>10, 22</sup> Moreover, vertebroplasty makes the spine segment stiffer and could cause adjacent segment fracture. This risk was more frequent with older generations of bone cement; with the new generation of PMMA, the risk is more theoretical and not supported by clinical data.<sup>32, 33</sup> Vertebral augmentation also offers primary stability of affected vertebra, which allows a very short segment stabilization, with few vertebrae involved. The association of posterior decompression creates an area of instability that needs to be protected to prevent further segment instability.<sup>34</sup> Based on these premises, the association of short segment stabilization to vertebroplasty and embolization guarantee a more gradual transition between regions with different stiffness. In this way, upper and lower vertebrae are protected from excessive loads,<sup>35, 36</sup> with the risk of losing segment mobility.

Posterior decompression effectively provides symptoms relief in patients with aggressive hemangiomas and intraoperative vertebroplasty could help in reducing recurrence after decompression. Our outcomes, with preoperative embolization, support these results.<sup>37</sup>

En bloc resection or subtotal resection with vertebroplasty or adjuvant radiotherapy is a possible alternative treatment for aggressive vertebral hemangiomas. It must be noted however that this is a highly demanding surgery with high morbidity for patients.<sup>38</sup>

Comparing our results with those in similar articles, we found them to be comparable in term of clinical and neurological scores and relapse of pathology. On the other hand, the use of preoperative embolization ensures a small reduction of blood loss ( $274 \pm 80 \text{ mL}$  vs.  $261.5 \pm 76 \text{ mL}$ ) compared with the study of Chandra et al<sup>22</sup> but a great reduction ( $511.1 \pm 279.3 \text{ mL}$ ) if compared with the study of Singh et al.<sup>10</sup>

A greater surgical time saving was reported in our series if compared with the surgical time of the 2 previous articles ( $124 \pm 39$  minutes or  $292.1 \pm 101$  minutes vs.  $91.5 \pm 36.7$  minutes).<sup>10, 22</sup> This result could be explained by our choice of performing embolization the day before surgical treatment, making the procedure more simple by reducing bleeding during operation and saving the time of direct ethanol injection. Our approach could appear more aggressive than others proposed in the literature, but we did not record any case of adjacent vertebral fracture or junctional instability. It is also important to note that a prompt and fast approach is important to treat those cases with acute compressive myelopathy before symptoms became irreversible. With these premises, our treatment can be completed within 24 hours, preventing excessive blood loss with a reasonable surgical time.<sup>39</sup>

Some limitations to this work must be acknowledged. Some are intrinsic to the rarity of pathology itself and study design because of its retrospective nature and the lack of a control group or randomization. Furthermore, the low number of patients and the lack of a priori sample size calculation could be a source of potential bias. Giving that, this is a long-term study showing the recurrence of pathology at 4 years of follow-up, whereas the majority of other studies has a mean follow-up of 2 years. This outcome raises the risk of recurrence after a short follow-up period, which could also be possible and change the results of other studies, making them less exciting.

## Conclusions

PVA microparticles embolization, short segment fixation, and decompression along with vertebroplasty is an effective treatment option for aggressive VHs, with a short surgical time, low blood loss, and improvement of preoperative clinical and neurological outcomes.

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