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The Effectiveness of Endoscopic Surgery of Juvenile Angiofibroma Using Surgical Glue

Seyed-Hadyi Samimi Ardesan[1], Mojtaba Mohammadi Ardehali[1], Najmeh Doustmohammadian[2]*

[1]Department of Otorhinolaryngology, School of Medicine, Tehran University of Medical Sciences, Amiralam Hospital, Tehran, Iran; [2]Department of Otorhinolaryngology, School of Medicine, Semnan University of Medical Sciences, Semnan, Iran

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***Correspondence:** Najmeh Doustmohammadian, Department of Otorhinolaryngology, School of Medicine, Semnan University of Medical Sciences, Semnan, Iran. Tel.: 02333437842. E-mail: n_dostmohammadin@yahoo.com
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Abstract

AIM: The current study aimed to provide a method for juvenile nasopharyngeal angiofibroma embolization using Glubran glue in patients with low stage tumor. This method not only has less blood loss and good visualization but also impose a low cost, where no pre-operative embolization complications were found for this procedure.

METHODS: Between 2012 and 2014, 30 patients with angiofibroma undergoing endoscopic surgery. Age, sex, tumor stage, average blood loss, complications, length of hospitalization, and recurrence rate of the tumor were the main measured outcomes. Furthermore, 30 patients were divided into three groups with matched age, sex, and tumor staging. Group 1 received glue (Glubran), while Group 2 selected for study without glue and embolization and pre-operative embolization was considered for Group 3.

RESULTS: Based on the amount bleeding, the mean blood hemorrhage in Groups 1, 2, and 3 was 510, 1655, and 800 ml, respectively, the difference of hemorrhage between Groups 1 and 2 was found to be statistically significant ($p = 0.007$). Blood loss in Group 1 was found to be less than Group 3, but the difference of hemorrhage between Group 1 and 3 was not statistically significant ($p = 0.678$). No blood transfusion and complication were recorded for individuals in Group 1. The recurrence was found in 1 patient (10%) in both groups of 2 and 3, and no patient (0%) in Group 1.

CONCLUSIONS: The direct intraoperative embolization technique with glue was capable of providing a more complete and targeted embolization of the tumor. Some advantages can be mentioned for this technique, including decreased blood loss, less radiation exposure, lower rates of complications, and recurrence, as well as shorter hospitalization time, the ease of procedure with a spinal needle and low cost.

Introduction

Juvenile nasopharyngeal angiofibroma (JNA) is defined to be benign and locally aggressive vascular tumor, affecting adolescent males [1]. JNA is responsible for 0.5% of head and neck tumors. Although this tumor is considered to be commonly occurred in nasopharynx, there are reports of its presence in the nasal septum, inferior and middle turbinate, hard palate, and alveolar ridge [2], [3], [4], [5], [6]. The prevalence of JNA is estimated to be 1/150,000–1/1,500,000 individuals [7], [8], [9], [10]. Previous studies indicated that disease was more prevalent in the Indian and Middle Eastern populations as compared to European populations [11]. Diagnosis of the tumor is usually based on the location of origin, post-contrast hypervascularization, and growth patterns [12], [13]. JNA typically receives vascular nutrition from the external carotid system, especially the internal maxillary, ascending pharyngeal, and vidian arteries [14], where vessels from the branches of the internal carotid artery, such as the Inferior hypophyseal artery, are commonly found in lesions involving the cranial base [15].

Many therapeutic modalities have been applied for treating this tumor. Non-surgical treatments include the use of hormones (estrogen and testosterone), radiotherapy, chemotherapy, and more recently embolization. Surgery and radiotherapy are among the most effective procedures [16], [17], [18]. Surgery is the therapeutic choice based on the stage of the tumor and the patient's general condition. For many years, several acceptable numerous approaches have been applied for decreasing morbidity and mortality of tumors. There are various opinions regarding the pre-operative embolization in the surgical treatment of this tumor; some surgeons believed that embolization was acceptable method, while others oppose it [19], [20], [21], [22], [23]. Pre-surgical tumor embolization for hypervascular neoplasms results in improved surgical outcomes reduced intraoperative bleeding and facilitating tumor resection [24]. Polyvinyl alcohol is the most commonly used embolization material that should be performed 24–48 h before surgery for avoiding revascularization [15].

Studies have shown that bilateral embolization of the internal maxillary artery was capable of improving treatment efficacy when the tumor received blood from bilateral external carotid artery [25]. In the past, to

control bleeding originating from the internal carotid artery in a lesion with extensive skull base involvement, a direct transcutaneous lateral embolization technique with a combination of cyanoacrylate, lipiodol, and tungsten powder was proposed [26].

Some recent reports have introduced embolic agent Onyx with a non-migratory and bleeding-reducing property that has significant therapeutic performance, where the interest in this new treatment has increased [27], [28]. Due to the complications of pre-operative embolization, this study aimed to reduce the amount of bleeding during surgery and improve visual acuity, and to minimize the complications of pre-operative embolization and costs.

Materials and Methods

Between 2012 and 2014, 30 patients with angiofibroma undergoing endoscopic surgery in ear, nose, and throat department of Amir A'lam Hospital were enrolled in the study.

Exclusion criteria included pregnancy, history of malignancy, history of previous surgery, patients with Stage IIc above, and patients with other systemic diseases such as Wagner's disease. All patients were included in the study with written consent. However, due to ethical considerations, patient information was kept confidential. All patients were radiologically and surgically classified with Radkowski staging system.

Thirty patients were divided into three groups. The patient group (Group 1) consisted of 10 patients who underwent endoscopic surgery with surgical Glubran glue. The control group (Group 2) consisted of 10 patients without surgical glue and embolization. The third group (Group 3) consisted of 10 patients who underwent embolization surgery. Groups were matched for such factors as sex, age range, and stage of the tumor by propensity score matching method.

Methods

After the patients under hypotensive anesthesia, 0.5 cc glue was injected with normal saline for the patients group. It is worth noting that 0.5 cc surgical glue Glubran in combination with n-butyl 2-cyanoacrylate adhesive was used. Subsequently, tumor bulk was pushed into the nasopharyngeal space by a medium-sized FREER Septum Elevator and adrenaline soaked on gauze. Then, the surgical process continued, depending on the tumor spread. For example, in the case of tumor expansion to the pterygomaxillary fissure, surgery was performed by removing the posterior wall of the maxillary sinus and pushing it toward the medial side. If the tumor had a lateral extension to infratemporal fossa, force was applied from the lateral to the medial with the freer and gauze. Surgical meshes were used for cavernous sinus bleeding while the anesthesia team was ready to treat severe bleeding. The mass was completely removed by the use of DAVIS Mouth Gags and large-size forceps after pushing the bulk of the tumor into the nasopharynx and the oropharynx. Suction electrocautery and bipolar were used for homeostasis. These tumors were never resected in a piecemeal manner. At the end of the operation, an examination of the remaining tissues and sites of abnormal bleeding was performed. In addition, all surgeries are performed by one surgeon.

Prophylactic drilling of the clivus or pterygoid root and sphenoid diploe and vidian canal was also performed on patients who had obvious bone involvement in these locations.

Evaluation of bleeding rate, injection blood, and duration of hospitalization

All patients were compared regarding the amount of intraoperative bleeding, the amount of tumor bleeding based on the surgeon's opinion, the amount of blood transfused the length of stay after surgery, complications, amount of residual tumor, and recurrence. The volume of intraoperative bleeding was calculated based on the counting number of blooded gauze and the volume of suctioned blood. All patients undergoing endoscopic angiofibroma surgery were evaluated endoscopically 2 weeks after surgery, and then evaluated for the first 6 months monthly and then annually. A computed tomography (CT) evaluation was performed in the 3rd month after surgery. If endoscopic abnormalities were seen during the examination of recurrent patients, the findings were confirmed by contrast-enhanced CT (CECT). Diagnosis of recurrent angiofibroma was also assessed based on clinical symptoms and CECT scans and sometimes magnetic resonance imaging. The mean follow-up period was 8.8 ± 3.16 for Group 1 followed by 24.3 ± 17.56 months for Group 2 and 10 ± 7.53 months for Group 3.

Statistical analysis

After data collection, the Data Bank was prepared by SPSS software version 19 and the data were entered. T-test was used to compare the results. In all cases, $p < 0.05$ was considered statistically significant.

Results

In this study, 30 patients underwent surgery, all of whom were male. The mean age of Group 1 was 18.5 ± 5.56 followed by 18.2 ± 5.56 for Group 2 and 17.5 ± 4.10 for Group 3. Patients in each group had

Stage IIc (9 patients) and IIb (1 patient). The three groups were matched for age, sex, and stage of the disease (Table 1).

Table 1: Characteristics of the three groups of patients with angiofibroma according to sex, sex, and stage of disease

Character	Group 1		Group 2		Group 3		p-value
Age	18.5±5.56		18.2±5.06		17.5±4.10		0.907
Sex	Female	Male	Female	Male	Female	Male	1
	0	10	0	10	0	10	
Disease stage	IIc	IIb	IIc	IIb	IIc	IIb	1
	9	1	9	1	9	1	

As can be seen in Table 2, the most common symptom was a nasal obstruction in 29 patients (96.7%) followed by epistaxis in 18 patients (60%). One patient also had a headache (3.3%).

Table 2: The most common clinical symptoms of angiofibroma patients at the time of referral based on the three groups

Frequency of clinical symptoms at the time of referral			
Studied groups	Frequency of nasal obstruction (%)	Epistaxis frequency (%)	Headache Frequency (%)
The first group (surgical technique using glue)	10 (100)	6 (60)	0
The second group (surgery without the use of glue and embolization)	9 (90)	7 (70)	1 (10)
The third group (surgery with pre-operative embolization)	10 (100)	5 (50)	0
All patients	29 (96)	18 (60)	1 (3.3)

The number of people with mild, moderate, and severe bleeding is shown in Figure 1. In terms of bleeding rates, the average bleeding in Groups 1, 2, and 3 was determined as 510 cc, 1655 cc, and about 800 cc, respectively. There was a significant difference in the amount of bleeding between Groups 1 and 2 ($p = 0.007$) and Groups 2 and 3 ($p = 0.048$). Bleeding in Group 1 was lower than in Group 3, but there was no significant difference between Groups 1 and 3 ($p = 0.678$). In Group 1, no blood unit was injected. The difference between Group 1 and 2 was significant ($p = 0.004$).

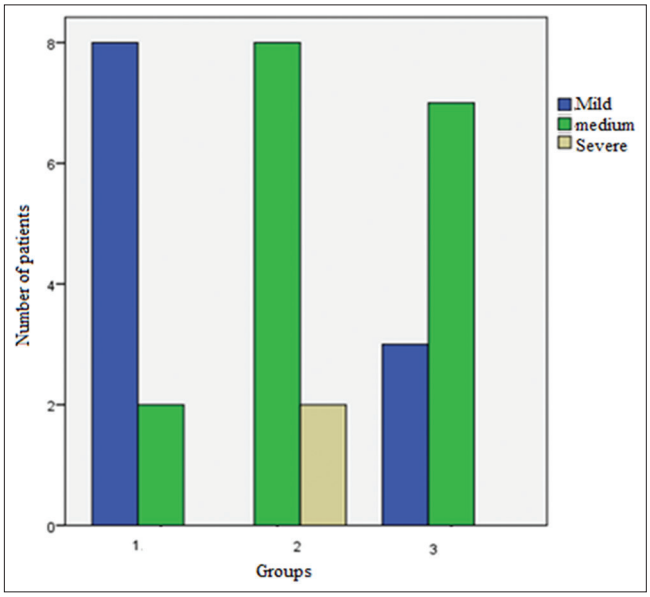

Figure 1: Number of people with mild, moderate, and severe bleeding depending on the surgeon's view for severity of bleeding

Analysis of hospital stay variables showed no significant difference between groups (Table 3). Mean days of hospitalization in Group 1 were 2.1 ± 0.32 followed by 2.4 ± 0.84 in Group 2 and 2.3 ± 0.48 days in Group 3. The mean days of admission were lower in Group 1.

Table 3: Number of admission days after surgery in three groups of angiofibroma patients

Patients	The number of hospitalization days	
	1–2 day	>2 day
Group 1	9	1
Group 2	6	4
Group 3	8	3
Significant	p=0.09	

The mean follow-up period for Group 1 was 8.8 ± 3.16 months followed by 24.3 ± 17.56 months for Group 2 and 10 ± 7.53 months for Group 3. The recurrence rate in Group 1 was 0% and Groups 2 and 3 each had one recurrent patient (10%). An 18-year-old patient was recorded for Group 2 and a 13-year-old patient for Group 3, both of whom were in Stage IIc. There was no significant difference in the recurrence rate between Groups 1 and 2 and 3 ($p = 0.754$).

Discussion

The direct percutaneous approach using liquid embolic materials such as glue or onyx is the most widely used approach. The benefits of onyx over glue are primarily due to the slower rate of polymerization which allows deeper penetration within the tumor vasculature, in contrast to the instant polymerization of glue on contact with blood that prevents uniform and controlled penetration of the tumor vasculature [27], [29].

Another liquid embolic agent commonly used in practice is Fibrin. Fibrin glue has been used in neurosurgery, pharmacology, vascular surgery, pre-operative embolization of the patient with intracranial meningioma, closure of the dura, and prevention of spinal fluid leaks [30]. In addition, fibrin glue spray has been effective in fixing mucoperichondrium to cartilage instead of suture [31]. The present study investigated the effect of glue on post-operative health factors of patients. According to our findings, the amount of bleeding was lowest in the group with glue, where the complications of blood transfusion were minimal.

Intraoperative use glue appears to block intratumor vessels and reduces intraoperative hemorrhage while it may be a useful measure to reduce bleeding in tumors with bilateral blood supply and internal carotid blood supply. The use of embolic agents has played an important role in the treatment of patients [27], [28]. Elhammady *et al*. have compared pre-operative transarterial embolization and embolization with onyx via direct tumoral puncture [32].

However, it should be noted that complications after the use of embolic agents are

important, and all studies on embolization have not been fully successful [26]. Ethylene-vinyl alcohol copolymer embolic agent has been studied for the direct percutaneous embolization of angiofibroma with complications such as trigeminal cardiac reflex [33], [34], [35]; however, the advantage of onyx is the absence of side effects and a positive effect on bleeding [29]. The success criteria for any tumor surgery is depend on the recurrence rate. The recurrence rate of angiofibroma has been reported in some studies (7–39.5%) [36] and some studies have reported a recurrence rate of 25–46%, where a rate of 25% was reported for Stage IIc and 40–50% for Stage III [37], [38], [39], [40]. In our study, no recurrence was seen in Group 1 that is different from other studies; this difference may be related to the selection of patients with Stage IIc (below). In a recent study, three factors were predictive of a recurrence rate that including patient under 18 years of age at diagnosis, tumor size >4 cm, and advanced stage of disease, according to Radkowski's classification [41].

Our findings should take into consideration in light of limitations regarding a relatively short follow-up period of patients after surgery. Although most symptomatic relapses are expected to occur during the first 12 months after treatment [42], this can certainly be debated. Fibrin glue had a positive effect on reducing bleeding and requiring blood transfusion, which has been the main finding of our study.

There are a number of limitations to our study. In the first place, the number of cases included in this study is somewhat small which makes the generalization of results not possible. There is also some minor inaccuracy in estimated intraoperative blood loss due to the fact that adjustment is made for the surgical effluent containing both fresh blood and operative irrigation fluid.

Finally, it may be suggested that comprehensive studies are required with longer follow-up, and it is hoped that this method will be used as a routine technique in future angiofibroma operations.

Conclusions

The direct embolization technique using surgical glue allows for more complete and targeted tumor embolization. The main advantage of this technique is the ease of procedure with a spinal needle which was associated with reduced exposure to radiation, less intraoperative bleeding, and lower cost. In addition, surgical glue injection can be used in all vascular tumors of the sinus cavities as a research and its application in tumor recurrence and advanced stages of angiofibroma tumor can also be evaluated.

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