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A COMPARATIVE STUDY OF PREOPERATIVE TRANSARTERIAL EMBOLIZED V/S UNEMBOLIZED CASES OF JUVENILE NASOPHARYNGEAL ANGIOFIBROMA

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ABSTRACT

Aim: This prospective study was conducted to assess and compare the effect of preoperative transarterial embolization v/s non embolization in nasopharyngeal angiofibroma patients on intraoperative blood loss in different stages of tumor and local tumor recurrence. **Patients and Methods:** 40 male patients of diagnosed Juvenile angiofibroma from May 2012 to Sept 2017 were randomly divided into 2 groups. Group A included 20 patients who underwent preoperative transarterial embolization by polyvinyl alcohol particles and underwent surgery 24-72 hours later while Group B included 20 patients who underwent surgery directly without preoperative embolization. Tumors were graded using Fisch classification. We measured intraoperative amount of blood loss and did follow up scans for assessment of tumor recurrence. **Results:** The mean amount of blood loss in Group A patients was 350 ml while in Group B patients was 1000 ml. No residual tumor was seen in Group A patients (0/18) on 6 months follow up while residual tumor was seen in 4 patients in Group B (4/17). The technique of embolization was safe with no procedure related mortality. **Conclusion:** Preoperative embolization of JNA is a safe and effective method to significantly reduce intraoperative blood loss there by making tumor resection easier and complete and reducing the chances of residual disease.

Keywords: Juvenile Nasopharyngeal Angiofibroma, Embolization, Bleeding

INTRODUCTION

Juvenile nasopharyngeal angiofibroma is a highly vascular, benign, non-encapsulated, locally invasive tumor. It accounts for approximately 0.05% of all head and neck tumors with an incidence of 1 in 1,50,000**(1)**. The lesion primarily affects males in the second decade of life with the age ranging from 7 to 29**(1)**. The lesion originates in the lateral nasopharynx adjacent to the superior border of sphenopalatine foramen and is locally aggressive, with extension occurring into the surrounding osseous and soft tissue structures ie. anterior nasal cavity, maxillary sinus, pterygopalatine fossa, pterygomaxillary fissure, infratemporal fossa, orbits, sphenoid sinus, skull base and eventually the cavernous sinus and intracranial compartments. Histopathologically, the tumor is comprised of

haphazardly arranged vascular channels surrounded by dense paucicellular fibroblastic stroma, with the myofibroblast being the principal cell **(2, 3)**. The bleeding tendency of these tumors is because of lack of muscular elastic lamina in the vessels of the lesion, predisposing these vessels without a muscular surrounding layer that may otherwise assist in vasoconstriction to control bleeding **(2)**.

The tumors are highly vascular and predominant blood supply of the tumor is via the branches of external carotid artery, mainly from the internal maxillary artery (IMAX) but can also arise from multiple branches of ipsilateral ECA, branches from contralateral ECA, and even small branches arising from the internal carotid artery (ICA).

Angiofibroma most commonly presents with recurrent unilateral epistaxis, nasal obstruction, nasal drainage and a nasopharyngeal mass. Diagnosis of JNA may originally be suspected from symptoms and plain radiographs but definitive diagnosis can be made from CT and MRI examination. CT helps in better delineation of osseous involvement of tumor while MRI is useful for assessing intracranial extension of tumor. An MR-angiogram can additionally be helpful in defining the arterial supply to the tumor, which can help in planning of preoperative embolization. Biopsy is contraindicated in JNA due to its highly vascular nature **(6)**.

The principal method of management of JNA remains surgical resection, but this can be complicated by massive hemorrhage. Many techniques have been proposed and tried to reduce intraoperative bleeding such as, such as preoperative radiation at a dose of 30 Gy, injections of sclerosing agents into tumor, systemic administration of female hormones, and ligation of the external carotid artery (ECA). However, none of these methods have proven to be effective. An important advancement in treatment is preoperative intra-arterial embolization, which is now widely accepted and used. Embolization leads to occlusion of vascular channels of the tumor leading to significant reduction of bleeding during surgery there by enabling easy removal of tumorendoscopically or by open surgical techniques, decreasing duration of surgery and facilitating complete excision of tumor. Various agents used for embolization are Poly Vinyl Alcohol (PVC) particles, N-butyl cyanoacrylate, lipiodal ethanol, methyl methacrylate, gulielmi detachable, gelfoamtorpedos, etc. In our study we used PVC particles for embolization.

This study aims to evaluate the effectiveness of pre-operative embolization in reducing intraoperative blood loss in JNA patients thereby making tumor resection and disease clearance easier.

MATERIALS AND METHODS

This study was conducted from May 2012 to September 2017 at SMS Medical College & Associated Hospitals, Jaipur.

40 cases were taken from otorhinolaryngology outdoor randomly. All of them were evaluated and divided into following 2 groups:

• Group A: Patients underwent preoperative intra-arterial embolization prior to surgical excision.

• Group B: Patients had only surgical excision without preoperative embolization.

All patients underwent detailed clinical history, routine blood counts and CECTPNS. MRI was advised in those patients suspecting of having intracranial extension. All patients were categorized into different stages according to Fisch classification (Table 1). All patients were operated by same team of surgeons and blood loss was also evaluated by same team of nursing staff alike.

Technique of Embolization: Preoperative angiography and embolization was performed by experienced interventional radiologists. A detailed diagnostic angiography of bilateral external, internal carotid and vertebral angiograms was performed, using right common femoral access prior to embolization procedure. Embolization was done 24 hours prior to surgery under general anesthesia. Unilateral or bilateral selective catheterization of the supplying artery of the tumor as distal as possible was done. Digital subtraction angiography technique

was used for embolization until arterial stasis was achieved. The embolization agent used was polyvinyl alcohol (PVA) particles ranging in size from 150 - 500 mm based on feeding artery. Utmost care was taken to not embolize the branches ofICA. Technical success was determined by maximal safe vascular tumor embolization without evidence of non target embolization or inadvertent vascular occlusion.

Technique of Surgery: Surgery was performed within 24 to 72 hours after the embolization procedure as any further delay will lead to neovascularization and revascularization. Surgical approach depended upon the stage of tumor and approaches used were endoscopic approach, lateral rhinotomy and maxillary swing approach. All stage I & II tumors were resected via endoscopic approach while stage III & IV tumors were resected by open approach (Lateral Rhinotomy / Maxillary swing). The amount of blood loss and the amount of blood transfusion was calculated during the operation. The blood loss was estimated by measuring the total operative fluid collected by suction and subtracting the amount of saline administered during the surgery plus estimating amount of blood absorbed by gauze pieces. Operative time was recorded. Surgical notes were also made for complete or incomplete resection of tumor as determined by the operating surgeon. Routine postoperative CT was performed on 6 months post resection.

RESULTS

This study was conducted on 40 patients of diagnosed JNA. Based on the treatment modality, patients were randomly divided into 2 groups. In Group A, patients underwent preoperative embolization before surgical excision while in Group B, patient underwent surgery directly without preoperative embolization.

All the patients in both the groups were males. The median age group in Group A was 18 years and in Group B was 16 years. Common clinical presentations were recurrent attacks of severe epistaxis in 39 patients (97.5%), nasal obstruction in 35 patients (87.5%), unilateral cheek swelling in 13 patients (32.5%), unilateral proptosis in 4 patients (10%) and headache in 10 patients (25 %). The total duration of symptoms before the diagnosis was within 6 months.

Tumor staging was determined by review of the imaging studies and physical examination including CT and MRI for all patients. The tumors were classified according to the Fisch classification.

In Group A, 3 patients belonged to Stage I (15%), 10 patients were in stage II (50%), 4 patients were in stage IIIA (20%), 2 patients were in stage IIIB (10%) and 1 patient in stage IVA (5%). In Group B, 5 patients were in stage I (25%), 6 patients were in stage II (30%), 7 patients were in stage IIIA (35 %), 1 patient was in stage IIIB (5%) and 1 patient was in stage IVA (5%). None of the cases were in stage IVB. (Table 2)

Through digital subtraction angiography, major feeding vessel to the tumor was identified. Major feeding vessel to the tumor was internal maxillary artery (IMAX) in 7 patients (35%); ascending pharyngeal artery in 1 patient (5%) and both internal maxillary and ascending pharyngeal in 12 patients (60%). Bilateral supply was found in 4 patients (20%) and unilateral supply in 16 patients (20%). Blood supply from ICA was found in 5 patients.

• The internal maxillary artery (IMAX) was embolized in 7 patients, ascending pharyngeal artery (APA) in 1 patient and both IMAX and APA in 12 patients. Ipsilateral embolization was done in 16 cases and bilateral embolization was done in 4 cases. There was no intra or post procedural related mortality related to embolization in our study. Minor complication were seen nearly all patients. It included mild to moderate pain in the embolized vascular territory and slightly elevated temperature which were treated by simple analgesics. Other complications were nausea in 3 patients, focal small necrosis in ear pinna which was treated conservatively and local subcutaneous edema in 1 patient. One patient had a major complication in the form of temporary visual loss which improved gradually and the patient fully regained vision after 1 month. Review of the pre-embolization angiogram of

this patient showed aberrant left ophthalmic artery arising from the left middle meningeal artery.

Surgical approaches for JNA were based on the stage of tumor. Endoscopic resection was done in 24 patients while open approach (Lateral rhinotomy or maxillary swing) was used in 16 patients. The average amount of blood loss was calculated during the surgery.

In Stage I tumors, mean blood loss in Group A patients was 120 ml while in Group B patients, it was 500 ml. In Stage II tumors, mean blood loss in Group A patients was 290 ml while in Group B patients it was 700 ml. In Stage IIIAtumors, mean blood loss in Group A patients was 480 ml while in Group B patients, it was 1300 ml. In Stage IIIBtumors, mean blood loss in Group A patients was 550 ml while in Group B patients, it was 1700 ml. In Stage IVA tumors, mean blood loss in Group A patients was 720 ml while in Group B patients, it was 2500 ml.

Therefore in Group A, mean blood loss was 350 ml which is not significant (p value > 0.05) while in Group B, mean blood loss was 1000 ml (p value < 0.05) which is significant (Table 3).

Postoperative imaging was done on 6 months of follow up. 5 patients were lost to follow up. In Group A, 2 patients were lost to follow up, rest of the 18 patients showed no residual disease. In Group B, 3 patients were lost to follow up, out of 17 patients 4 patients had residual disease on postoperative scans (Table 4).

DISCUSSION

Juvenile nasopharyngeal angiofibromas are benign, highly vascular tumors predominantly occurring in adolescent males with propensity of intra-cranial extensions. These are most commonly supplied by internal maxillary artery.

In the early stage of the disease, the ipsilateral internal maxillary artery is the main feeding vessel. With progressive enlargement of tumor, other arteries such as the ascending pharyngeal artery, greater palatine artery and rarely, the occipital artery may also contribute to blood supply. The external facial artery and the superficial temporal artery may also participate in the tumor supply when tumor grows into the infra temporal fossa. On entering the inferior orbital fissure or central nervous system, it can also be fed by branches from the internal carotid system. Bilateral supply from the external carotid arteries is not common in JNAs crossing the midline. Even in the absence of intracranial extension, tumor can be supplied by branches from the internal carotid system **(7)**.

Various modalities for treatment of JNA have progressed from waiting for spontaneous regression of tumor, to radiation of tumor, injection of sclerosing agents and surgical resection . Surgical resection is currently the most widely accepted method of treatment throughout the world. Surgery is often hampered by significant intraoperative hemorrhage, which can contribute to incomplete removal of neoplasm resulting in a higher recurrence rate. As diagnosis is often delayed, these tumors may lie adjacent to several critical neurovascular structures **(8, 9)**.

Temporary or permanent ligation of ECA was used to decrease intraoperative blood loss during JNA resection before the advent of preoperative embolization (11). Various studies have reported intraoperative blood loss ranging from 915 to 3000 ml from JNA resection without preoperative embolization **(14 - 18)**.The embolization of JNA was first reported by Robertson et al **(12)** as a method to reduce the intraoperative blood loss. Preoperative embolization has been proven to be effective in decreasing intraoperative blood loss when compared to surgery without embolization **(11, 15, 19 - 25)**. Antonelli et al **(13)** reported an average reduction of intraoperative blood loss by 60 %. In a study by Moorthy et al **(2)**, eight patients that underwent pre-operative embolization of the ipsilateral maxillary artery utilizing absorbable gel foam, six experienced considerably less bleeding during surgical resection. Moulin et al **(36)** reported mean blood loss of 5380 ml in patients without embolization in comparison to 1037.5 ml in those with embolization. Boghani et al **(1)** in a systematic analysis of 131 cases within 57

studies over 21 years showed that the average blood loss in patients that underwent pre-operative embolization before endoscopic surgical resection was 406.7 ml compared to 828.3 ml in non-embolized patient undergoing endoscopic resection alone.

In our study of 40 patients, in which 20 patients underwent preoperative embolization, the average blood loss during operation was 350 ml, while the rest 20 patients who underwent surgery directly the average blood loss was 1000 ml. Blood loss also depends upon the stage of tumor, higher stage tumors are amenable to greater blood loss. There was significant difference in the amount of blood loss in different stages of tumor in pre-operatively embolized v/s non-embolized group. In Group A patients due to significant reduction in blood loss during surgery, clear visualization of operative field was obtained which helped in proper assessment of extent of tumor, tumor resection was easier and duration of surgery was reduced in contrast to Group B patients. No Group A patents had residual tumor on 6 month follow up while 4 patients of Group B had residual tumor on scans. Several previous studies have reported lower recurrence rate in patients who underwent preoperative embolization **(11, 14, 15, 19).** A dry surgical field enables complete removal of tumor especially in unreachable areas which decreases the rate of recurrence **(10, 21, 26, 27).** Total or near total devascularization is an important factor to achieve the aforementioned results while tumors which have supply from internal carotid artery have suboptimal devascularization which contributes to increased intra-operative blood loss.

Serious complications are sometimes possible in embolization procedure, including stroke or blindness from migration of particles into the middle cerebral artery or ophthalmic artery. These complications are rare and do not outweigh the substantial benefits of embolization **(4)**. However in our study, no patient had any serious long term complication post embolization.

PVA particle size was based on published data determining the ideal particle penetration of JNAtumor tissue which was approximately 200 mm particulate size **(28)**. A novel approach to JNA embolization recently described in the literature involves direct puncture embolization using a combination of an endoscopic and percutaneous approach **(29 - 35).**

CONCLUSION

In conclusion, preoperative embolization of JNAtumors is a safe procedure without any substantial risk of neurological complications. The present study identified a statistically significant difference in intraoperative blood loss between those lesions which were preoperatively embolized in comparison to those that underwent surgery directly. Pre-operative embolization of juvenile nasopharyngeal angiofibromas reduces intraoperative blood loss thereby lessening the risk of massive hemorrhage, shortening operation times, increasing intra-operative visibility, and allowing for easier and complete resection of tumor which contributes in lower rate of recurrence. In light of these findings, pre-operative embolization is a safe and effective method to reduce the risk of massive, sometimes fatal, hemorrhage that occurs with these highly vascular tumors. We recommend it as a routine preoperative adjunct in all patients of JNA.

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Table 1: **Fisch Staging of JNA**

Stage I	The tumor is limited to the sphenopalatine foramen, nasopharynx and nasal cavity without bone destruction
Stage II	The tumor invades the nasal sinuses or the pterygomaxillary fossa with bone destruction
Stage IIIa	The tumor invades the infratemporal fossa or orbit without intracranial involvement
Stage IIIb	The tumor invades the infratemporal fossa or orbit with intracranial and extradural involvement
Stage IVa	The tumor shows intracranial, extradural and/or intradural invasion, without invasion of optic nerve, sella, or cavernous sinus
Stage IVb	The tumor in stage IVa with invasion of optic nerve, sella and/or cavernous sinus

Table 2: **Distribution of cases in various age groups**

Age (years)	Group A		Group B	
	Number of cases	Percentage	Number of cases	Percentage
0-5	0	0	0	0
6-10	0	0	0	0
11-15	9	35	5	25
16-20	11	55	13	65
21-25	2	10	1	5
26-30	0	0	1	5

Table 3: **Distribution of cases with various symptoms**

Symptoms	Group A		Group B	
	Number of cases	Percentage	Number of cases	Percentage
Epistaxis	**19**	**95**	**20**	**100**
Nasal obstruction	**18**	**90**	**17**	**85**
Nasal obstruction	**6**	**30**	**7**	**35**
U/L Cheek swelling	**10**	**50**	**9**	**45**
A headache	**2**	**10**	**2**	**10**

Table 4: **Distribution of cases according to stages (Fisch Classification)**

Stage	Group A		Group B	
	Number of cases	**Percentage**	**Number of cases**	**Percentage**
I	3	15	5	25
II	10	50	6	30
IIIA	4	20	7	35
IIIB	2	10	1	5
IVA	1	5	1	5
IVB	0	0	0	0

Table 5: **Distribution of cases according to the embolized feeding vessel in Group A**

Embolized feeding vessels	**No. of cases**	**Percentage (%)**
InternalMaxillaryArtery (IMAX)	7	35
Ascending Pharyngeal Artery (APA)	1	5
Both APA and IMAX	12	60

Table 6: **Distribution of cases according to ipsilateral and bilateral embolization of vessels**

Embolization	No. of cases	Percentage
Ipsilateral	16	80
Bilateral Supply	4	20

Table 7: Complications of Embolization

Conplication	No. of patients
Temporary visual loss	**1 patient (5%)**
Local pain	**20 patients (100%)**
Nausea	**3 patients (15%)**
Local subcutaneous edema	**1 patient (5%)**
Ischemic necrosis in ear pinna	**1 patient (5%)**

Table 8: **Analysis of blood loss in different stages of JNA operated in Embolized v/s Unembolized case**

Stage	Group A Mean Blood Loss (ml)	Group B Mean Blood Loss (ml)
I	120	500
II	290	700
IIIA	480	1300
IIIB	550	1700
IVA	720	2500

Table 9: **Mean blood loss and the p-value of both groups**

	Mean Blood Loss (ml)	p-value
Group A	350 ml	> 0.05
Group B	1000 ml	< 0.05

Table 10: **Follow up (on six months)**

Outcome	Group A	Group B
Residual Disease	0	3
No Residual Disease	18	14
Mortality	0	0
Total	18	17