Nasopharyngeal Angiofibroma-changing Trends in the Management

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Abstract Juvenile nasopharyngeal angiofibroma is a rare high-risk tumor of adolescent males. To present the experience of managing extensive angiofibroma at a single institution. A retrospective analysis of patients with nasopharyngeal angiofibroma between 1980 and 2009. 150 patients have been included in the analysis. The patients have been divided into two groups depending on diagnostic and therapeutic protocols into two groups. A 1980–1990 and B from 1990 to 2009. The disease pattern, surgical approaches and outcome in the two groups have been analyzed. Surgery has been the main modality for management of this tumor. Preoperative embolization and open surgical approaches results in less blood loss and favourable outcome.

Keywords Angiofibroma · Surgical approach · Embolization

Introduction

Juvenile nasopharyngeal angiofibroma is a rare high-risk tumor of adolescent males. It is the most common benign neoplasm of the nasopharynx. Most of patients present with

nasal obstruction and bleeding from nose which can be life-threatening also. Incidence of juvenile nasopharyngeal angiofibroma is less than 0.5% of head and neck tumors [1]. The most common presenting symptoms are severe, recurrent epistaxis with persistent nasal obstruction. As the disease progresses, facial deformities, proptosis, blindness, and cranial nerve palsies may occur. The diagnosis of JNA is essentially based on a careful history and nasal endoscopic examination, supplemented by imaging studies using computed tomogram (CT) and Magnetic Resonance Imaging (MRI). MRI is more accurate than CT in assessing intracranial extension [2]. Biopsies to establish histological diagnosis are contraindicated and definitive diagnosis is established by angiography which also serves as therapy since embolization of the tumor feeding vessels may be performed at the same sitting. Surgery is the main modality for this tumor. The treatment for the nasopharyngeal angiofibroma can present formidable problems for the surgeon. These most notably are concerned with the management of bleeding during extirpation of the lesion and because of these problems, the subject has stimulated a great deal of interest among otolaryngologists and Head & neck surgeons. Current concern with the hazards of multiple transfusions of whole blood and blood products has prompted a continued search for additional strategies to decrease intraoperative blood loss.

The aim of this paper is to present our experience of managing extensive angiofibroma at a single institution.

Materials and Methods

This is a retrospective observational analysis whereby the medical records of 150 patients treated for JNA between 1980 and 2009 were reviewed to see the ongoing changes

This material has never been published and is not currently under evaluation in any other publication.

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in diagnosis and management of patients with juvenile nasopharyngeal angiofibroma. The patients have been divided into two groups depending on diagnostic and therapeutic protocols into two groups. A 1980–1990 and B from 1990 to 2009. The disease pattern, surgical approaches and outcome in the two groups have been analyzed.

Result

Data of 150 patients was retrospectively reviewed. Age of 150 patients ranged from nine to twenty-seven years.

Epistaxis and nasal obstruction were the chief symptoms. Between 1980 and 1990, four patients also presented with ophthalmoplegia and decreased vision and one patient presented with bilateral temporal hemianopia.

There remains always a concern of surgical blood loss in patients of nasopharyngeal angiofibroma. Different modalities to reduce blood loss include use of hypotensive anesthesia and preoperative embolization. In a study of 90 patients done in our department done between 1980 and 1990, the average blood loss with hypotensive anesthesia was 800 ml as compared to 1300 ml without hypotensive anesthesia which is highly significant ($P = 0.000$). Pre operative embolization also has become a main tool in the last decade particularly in tumor removed by endoscopic approach (Table 1; Fig 1).

Surgery remains the definitive treatment modality for the treatment of nasopharyngeal angiofibroma but there has

been marked shift in the approaches used for excision of this tumor. In the ninth decade majority of the cases were performed by transpalatal approaches while in the next 20 years there is a shift toward transmaxillary and endoscopic approach (Table 2). Transmaxillary approach enables us to resect the lateral most extension of the tumor while endoscopic approach results in precise complete excision and minimal morbidity (Fig 2). Types of complications also changed in frequency as the surgical approaches. Between 1980 and 1990 the main complications were nasal crusting and palatal fistulas while these complications could be avoided in recent past with the use of anterior transfacial approaches (Table 3). Follow up of patients after surgery and early detection of recurrence have also been facilitated greatly by outdoor endoscopic examinations and easy availability of imaging tools as CT and MRI (Fig 3).

Discussion

Juvenile angiofibroma is a histologically benign, highly vascular tumor of the nasopharynx, which commonly presents in male teenagers. Morbidity from JNA is due to progressive obstruction of nasal respiration, bleeding, obstruction and invasion of paranasal sinuses, and in advanced cases, intracranial extension leading to blindness or other cranial neuropathy. The tumor grows slowly at a rate that has not been determined accurately. Extensive growth is not uncommon because of the silent area of origin. 10–20% of cases have intracranial invasion at the time of initial presentation, the rate being higher the younger the age of symptom onset. Intracranial extension may be unsuspected clinically since neurologic findings are often minimal in spite of massive size. We have analyzed the data of our 150 patients to see the changing trends in management of juvenile angiofibroma in terms of diagnosis and treatment for this tumor.

Table 1 Blood loss and recurrence with hypotensive anesthesia

	With hypotensive anaesthesia $n = 50$	Without hypotensive anaesthesia $n = 40$
Average blood loss	800	1,300
Recurrence	14%	25%

Fig. 1 Pre and post embolization scans showing disappearance of tumor blush

Table 2 Surgical approaches in 150 patients

S. No.	Surgical approaches	1980–1990	1990–2009
1	Transpalatal	43	8
2	Transpalatal + lateral rhinotomy	13	–
3	Transpalatal + sublabial	13	–
4	Transpalatal + transzygomatic	7	–
5	Transpalatal + sublabial + transzygomatic	5	–
6	Midfacial degloving procedure	5	1
7	Trans maxillary	4	26
8	Lateral rhinotomy	–	13
9	Transnasal endoscopic	–	10
10	Transcervical	–	2
	Total	90	60

Bold values indicate most commonly used surgical approach

Table 3 Complications following excision of nasopharyngeal angiofibroma

Complications	1980–1990
Nasal crusting	43
Flap tear	05
Oronasal fistula	07
Dural exposure	15
Cavernous sinus bleeding	02
Meningitis	01
Unsightly scar	02
Anosmia	01

These complications were significantly less during 1990–2009

Diagnosis

Diagnosis of juvenile angiofibroma is based on its typical presentation, clinical examination and radiological investigations. The typical patient of angiofibroma is a young boy who has the history of recurrent nasal bleed and nasal obstruction. Majority of the patient in our series also presented with the same complaints. In the analysis of patients, the duration of symptoms before treatment has decreased. This probably reflects both increased awareness

and improved diagnostic methods. In nineties the main radiological investigation available was plain X-ray. With the advent of computed tomography (CT) scan, there was a revolutionary change in the diagnosis and management. Nasal endoscopy, CT scan and MRI are helpful to delineate the exact location of the lesion, to show any intracranial or infratemporal spread, and to determine the relationship between the tumor and vital structures [3]. Through improved radiography in the form of computerized tomography & MRI, it has been seen that some 20% of the more advanced lesions exhibit intracranial extension. Definitive diagnosis is established by angiography, which also serves as therapy, since embolization of the tumor-feeding vessels may be performed at the same sitting. Characteristic angiographic appearance in JNA is characteristic ‘TUMOR BLUSH’ and absence of venous filling. The major arterial supply to these tumors is typically the ipsilateral internal maxillary artery, with occasional additional vessels from branches of the internal carotid or contralateral external carotid system [4].

Zhang et al. [5] described 99mTc-MIBI as a noninvasive, effective and preoperative method of diagnosis for nasopharyngeal angiofibroma. They stated that 99mTc-MIBI imaging of the angiofibroma was significantly different from that of malignant and benign tumors, and

Fig. 2 Pre and postoperative CT scan (coronal section) of juvenile angiofibroma excised by transmaxillary approach

Fig. 3 Pre and postoperative CT scan (coronal and axial section) showing tumor free cavity on follow up

concluded that ^{99m}Tc -MIBI oncotrophic imaging is of qualitative diagnostic value for nasopharyngeal angiofibroma before operation.

Treatment

Surgical excision is the gold standard in the management of juvenile nasopharyngeal angiofibroma. The decision regarding approach is usually made after reviewing radiographic studies to assess tumor extent, blood supply, and presence or absence of intracranial extension. Radiotherapy is the second main modality of treatment in JNA. Now a day, this treatment modality is kept reserved for the large unresectable tumors with intracranial extension or it is given in post operative period where part of tumor is left behind. The main concerns with radiotherapy, which is delivered by external beam, are malignancies in the irradiated field and the danger of inhibiting normal facial growth in younger patients.

Some reports are there in the literature with use of chemotherapy [6] but at present its use as a treatment modality is not established. JNA is a hormone dependent tumor as suggested by its sex selectivity and presentation at younger age. So, hormonal therapy in form of androgens and estrogens has been tried in the past. Two reports are there in the literature using flutamide, an antiandrogen compound to decrease the tumor volume [7, 8].

Surgical Management open approaches can be used for tumors of all stages and certainly were the only option

before the application of endonasal endoscopic techniques became more widespread. Data reveal that during the last 15 years, there has been a marked shift toward endonasal procedures while the tumor stages of the patients treated remained the same [9, 10].

Surgical excision is the gold standard in the management of juvenile nasopharyngeal angiofibroma. Irrespective of the extent of disease, certain principles are applicable to all cases of nasopharyngeal angiofibroma. These principles include selection of appropriate approach for adequate exposure of the tumor, vascular control of the tumor and dissection in subperiosteal plane. There are several surgical approaches described in the past each having its advantage and disadvantage. The *transpalatal approach* is somewhat limited to tumors confined to the nasopharynx and the nasal cavity and the sphenoid sinus. This approach was a midline approach in an anteroposterior direction but Wilson [11] popularised the transverse incision. With the popularization of endoscopic approaches, use of transpalatal approach has gone into oblivion. As in our study where majority of the surgeries in ninth decade used this approach, in next 20 years use of this approach remained limited to only eight surgeries.

Midfacial degloving is also an excellent approach for tumors not having large lateral extensions. This carries the advantage of an excellent exposure of the lesion and direct control of the internal maxillary artery in the pterygopalatine fossa and it provides a very satisfactory cosmetic outcome. *Lateral rhinotomy approach* has also its distinct

advantages. This approach provides excellent surgical exposure of the tumor and its extensions.

Transmaxillary (transantral) approach remains the most widely used approach in last two decades. Transmaxillary approach via a Weber-Fergusson incision has advantage of providing a wide surgical field exposure. What is more important is that a wide lateral exposure be obtained by adequate removal of the anterior and lateral wall of the maxilla. In cases where the pterygopalatine fossa is involved, the posterior antral wall is also removed, thus converting into a single cavity the entire passage taken by the tumor.

When transfacial and midfacial degloving have been used for angiofibroma excision in the past, *transnasal endoscopic tumor resection* has been established as the mainstay of surgical resection in the present era. The main advantage of the endoscopic approach is the possibility of obtaining a magnified view of the lesion and related anatomical structures from multiple angles, enabling better identification of the interface between the lesion and soft tissues or adjacent bone structures, thus allowing a more accurate and complete dissection and better control of bleeding [10]. There is a changing trend toward transnasal endoscopic approach as it avoids the facial scar and this trend is also evident in our series. Endoscopic excision of JNA is safe and effective in our experience and can be performed for selected lesions, including Sessions classification stage IIC lesions. Preoperative embolization minimizes intraoperative blood loss while planning for endoscopic resection.

Intracranial Extension

With the advent of newer diagnostic methods it is prudent that intracranial extensions are much more common than initially believed, and reported in as many as 10–30% of cases [12]. Majority of these intracranial extensions are extradural and only few reports are available in the literature regarding intradural extension [13]. The size and the route of intracranial invasion may influence the surgical choice. A tumor that extends intracranially and remains lateral to the cavernous sinus is accessible through either a lateral skull base or an anterior approach. When a tumor extends intracranially and remains medial or inferomedial to the cavernous sinus, it is more readily removed through the anterior approach [14]. Some of these lesions may well receive substantial blood supply from large branches of the internal carotid artery. At this point, the otolaryngologist may have reached the outer limits of his capacity to manage these advanced lesions. Under these circumstances, a combined approach utilizing the expertise of the neurosurgeons has been advocated.

Adjuvant Therapies

Other techniques which have proven effective in the management of this lesion are hypotensive anesthesia, transantral ligation of the internal maxillary artery, use of cryoprobe, hormonal therapy & pre operative arterial embolization. In the past radon seeds, cryotherapy, electrocoagulation and injection of sclerosing agents were also tried in juvenile nasopharyngeal angiofibromas with variable results.

Preoperative Embolization

The vast majority of series reviewed employ pre-operative tumor embolization 24–48 h prior to surgery. The majority of authors feel that the addition of preoperative embolization in the management of these tumors has diminished vascularity to the extent that surgery has been relatively bloodless in some hands [15, 16]. More extensive tumors acquire a blood supply from other vessels, branches of both external and internal carotid circulations. Surgical resection of these tumors can be formidable and preoperative selective embolization, some day before surgery can be very helpful [17]. Some authors have raised concerns about increased recurrence following embolization [18]. They have attributed it to the shrinkage of tumor into the inaccessible bone and thus lead to greater residual disease. Tranbahuy et al. [19] described the technique for intratumoral embolization. An injection made slowly with an intranasal or lateral percutaneous route with either a mixture of cyanoacrylate, lipiodol and tungsten powder. This technique induced a marked devascularization and necrosis of the tumor. The technique provided useful perioperative visualization of the tumor.

Hypotensive Anesthesia

This modality of treatment remains an essential tool in the armamentarium of the surgeon. As the prime concern in surgery of these tumors is the high vascularity and intraoperative bleeding, hypotensive anesthesia provide a relative bloodless field to the surgeon and the tumor removal is easier, quicker and satisfactory. In a study of 90 patients done in our department done between 1980 and 1989, the average blood loss with hypotensive anesthesia was 800 ml as compared to 1,300 ml without hypotensive anesthesia. This series also revealed less recurrence rate in surgeries done with hypotensive anesthesia (14% Vs 25%).

Hormonal Therapy

Hormonal therapy has been explored as adjuvant therapy to primary surgical treatment. Clinical studies have demonstrated tumor enlargement with the administration of testosterone and shrinkage with estrogen therapy [20]. Flutamide (2-

methyl-*n*-[4-nitro-3-(trifluoromethyl)phenyl]propanamide), is an orally active non-steroidal androgen antagonist (NSAA). Unlike the previously used di-ethyl stilbesterol, flutamide is a pure anti-androgen compound, and therefore causes no suppression of gonadotropin or testosterone levels [21]. Clinical literature regarding the use of Flutamide is limited to two studies and 11 cases. Gates et al. [7] observed an average tumor reduction of 44% in 4 of 5 cases receiving a 6 week treatment course, and Labra et al. [8] observed a maximum tumor reduction of only 11.1% in 6 cases receiving a 3 week treatment course. Currently recommendation include 6 week course of flutamide as adjuvant therapy in the post-pubertal patient, so as to bring about pre-surgical volume shrinkage and facilitate surgical excision.

Radiotherapy for JNA

These are the tumors where radiation therapy might offer an advantage as an adjuvant therapy. It is justified in saying that many of us remain reluctant to administer radiation therapy for the routine case. This modality should not be the treatment of choice primarily because of its late effects. However in advanced lesions in which there is intracranial extension, the risks of radiation therapy are less than those of surgery. External beam radiation is delivered in several fractions to achieve a total tumor dose of 30–55 Gy. All series report that regression of angiofibromas after radiotherapy is very slow indeed, often taking 2–3 years before ‘radiological stabilization’ is achieved. Intensity-modulated radiotherapy has been used to deliver 3,400–4,500 cGy to patients with extensive disease involving the cavernous sinus and skull base [22]. Gamma knife therapy has also been tried in patients of nasopharyngeal angiofibroma but there is no conclusive data available till date regarding its use.

Recurrence

The principal cause of post surgical recurrence is incomplete tumor excision. Appropriate and adequate surgical exposure is therefore the prime intervention to decrease recurrence rates. Recurrence of juvenile angiofibroma after surgical removal is common ranging from 20 to 50% [23]. Some studies have found encouraging results in reducing recurrence by meticulously drilling out the pterygoid base, the pterygoid canal and the basisphenoid [24]. Such drilling may remove microscopic residual disease and can be very useful in decreasing recurrence.

Conclusion

Juvenile nasopharyngeal angiofibroma presents a treatment challenge to surgeons, owing to its high vascularity and

high recurrence rates following surgery. Surgery remains the main modality for management of this tumor and there has been changing trends toward anterior transfacial and endoscopic approaches. Intraoperative uses of hypotensive anesthesia and preoperative embolization have proven to be a useful tool in managing these tumors.

Conflict of interest There is no conflict of interest or financial disclosure to be made.

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