Juvenile Nasopharyngeal Angiofibroma

**DEFINITION**
- Benign, biologically progressive, highly vascular, high incidence of persistence and recurrence.
- 0.5% of all neoplasms of head and neck.
- Hippocrates described a polyp in the nose which weeped blood. Finally Friedberg in 1940 used the term Angiofibroma.

**SITE OF ORIGIN**
- Sphenopalatine foramen (Usually Superior lip of the sphenopalatine foramen at the junction of the Pterygoid Process of the Sphenoid Bone and the Sphenoid Process of the Palatine Bone)
- Exclusively in Juvenile males (7 to 21 years). Rarely seen below 7 yrs of age.
- Extranasopharyngeal angiofibroma is extremely rare and tends to occur in older patients, predominately in females, but the tumor is less vascular and less aggressive than juvenile nasopharyngeal angiofibroma (JNA).
May regress in late teens but may persist into adulthood.

**PATHOGENESIS**

- **RCB BMW HOD MSG –**
  - Ringertz theory – JNA arises from ventral periosteum of posterior pharyngeal wall
  - Coenes theory – Chondrocranium formed the matrix of tumour
  - Bensch theory – *(fibroblast theory)* – Abnormal growth of CT like embryonic occipital plate.
  - Brunner Hypothesis – origin from fascia basalis
  - Martin and able theory – oestrogen antrogen imbalance decreased androgen and increased estrogen
  - Willi’s theory – Form of immune response
  - Harma theory – Hyperplastic tissue response
  - Osbornes Hamartoma hypothesis – Hamartomatous origin
  - Danes theory – Androgen estrogen imbalance with increased androgen and decreased estrogen.
  - Mild and Mauris hypothesis *(New concept)* – from midline erectile tissue and is a hamartoma. Period of development of tumour coincides with erectile tissue of penis i.e. androgen dependent hamartoma having vascular and stromal component both having androgen receptors.
  - Sciffs theory – Pituitary androgen estrogen axis causes over activity of pituitary i.e. increased oestrogen levels but seldom to produce feminizing effects. Even androgen increases leading to proliferation of tumour cells
  - Girgis and Fahmy theory – relation with paragangliomata – JNA arises in relation to large arteries. Nutrient artery of JNA is terminal part of Internal Maxillary artery. Paraganglionic cells are site of origin and explain extrapharyngeal extension of tumour. Zellbalan cells is suggestive of paraganglioma relation
  - Som & Neffson
  - Sternberg – Hamartoma

- May be caused by ectopic nidus of cells which are androgen dependent
- **Androgen receptors** are present in both Vascular and Stromal components
A much smaller proportion of tumours also have some **Progesterone receptors**. In contrast, oestrogen receptors have not been demonstrated.

**VEGF** has been found localized on both endothelial and stromal components.

Overexpression of insulin-like growth factor II (IGFII) has also been found in a large number of juvenile angiofibromas. The IGFII gene is situated on the short arm of chromosome 11. It is thought that overexpression of IGFII might be associated with a tendency to recurrence and poorer prognosis.

JNA 25 times more common with **APC mutation** i.e. FAP (Familial adenomatous polyposis)

Mutations of **beta-catenin** have been found in sporadic and recurrent juvenile angiofibromas

**HISTOPATHOLOGY**

**Macroscopy**

- Rounded, Spongy, Nodular (nodularity increases with age), Non Encapsulated tumour, red pink or tan grey in appearance covered by nasopharyngeal mucosa. The intact membrane covering the tumour is deep red in colour as usually seen in younger patients.

**Microscopy**

- Connective Tissue with Immature fibroblasts (myofibroblasts) and thin walled blood vessels usually with single layer of endothelium (lacking smooth muscles and elastin fibres) throughout most of the tumour.
- It could also be seen that, as one strays away from the heart of the tumor the fibrous tissue element overshadows vascular element
- Lacunar spaces filled with blood. Vascularization noted mostly in the periphery where growth is most active.
- A specific dehydrotestosterone receptor in **JNA cytosol**
- Sphenopalatine foramen is situated in nasopharynx midway between the posterior ends of middle and superior meatus. Rather than invading surrounding tissue, this tumour displaces and distorts, relying on pressure necrosis to destroy and push through its bony confines
- Tumour has 2 components – Vascular and Fibrous :: 2 types of vessels – larger arterial and small thin walled capillary vessels (embryonic and lack contractile elements)
Fibrous more in elder children and vascular more in younger.

**CLINICAL FEATURES**

- In most cases, there is a **delay** of at least **6-7 months** between the onset of symptoms and presentation.
- Nasal obstruction (**earliest presentation**), intermittent unprovoked epistaxis, facial deformity, eye signs, neck mass, headache, cranial nerve involvement, ET dysfunction with CHL, otitis media with effusion, rhinolalia clausa.
- If the swelling enlarges to force the soft palate down, the voice may become plummy.
- Diplopia may occur secondary to the erosion of the mass into the cranial cavity and causing pressure on the **optic chiasma**.
- Anterior rhinoscopy shows the presence of abundant purulent nasal secretions together with bowing of nasal septum to the uninvolved side. Posterior rhinoscopy in a cooperative patient shows a **pink or red mass filling the nasopharynx**.
- The most common deformity referred to as the "**frog face"** is due to the forward spread involving the **ethmoidal region**.
- It may have two components, one filling the nasopharynx and the other extending out into the pterygopalatine and infratemporal fossa. It can encroach into the orbit by passing through the infra orbital fissure. It can erode the skull base and cause intracranial problems.
- Several staging systems have been proposed but that of **Fisch** is the most robust and practical. Others include **Sessions Staging System**, **Radkowski's staging system**, **Chandler's staging system**.

**FISCH STAGING CLASSIFICATION:**

- **TYPE I** : Tumour limited to the nasopharyngeal cavity; bone destruction negligible or limited to the sphenopalatine foramen.
- **TYPE II** : Tumour extension into the pterygopalatine fossa, or maxillary, sphenoid or ethmoid sinuses with bone destruction.
- **TYPE III** : Tumour invading the infratemporal fossa or orbital region.
IIIa ➔ without intracranial involvement
IIIb ➔ with intracranial extradural (parasellar) involvement

**TYPE IV**

- Intracranial intradural tumour:
  - IVa ➔ without infiltration of the cavernous sinus, pituitary fossa or optic chiasm
  - IVb ➔ with infiltration of the cavernous sinus, pituitary fossa or optic chiasm

Surgery is usually recommended for stages up to IVa while for stage IVb radiotherapy is advisable.

**DIFFERENTIAL DIAGNOSIS**

- JNA should be differentiated from:
  - 1. Pyogenic granuloma
  - 2. Choanal polyp
  - 3. Angiomatous polyp
  - 4. Nasopharyngeal cyst
  - 5. Chordoma
  - 6. Carcinoma (Nasopharyngeal, rhabdomyosarcoma, lymphoma)
  - 7. Neurofibroma
  - 8. Adenoidal hypertrophy

**MANAGEMENT**

**INVESTIGATIONS**

- **X Ray** ➔ **Holman Miller Sign** aka **Antral Sign** ➔ the plain lateral skull radiographic appearance that would show anterior bowing of the posterior wall of the maxillary sinus

- **Hondousa Sign** – X ray finding indicating infratemporal fossa involvement characterised by widening of gap between ramus of mandible and maxillary body.

- **Dodd’s Sign/Crescent Sign (Negative)** – X-ray finding Crescent of air between the mass and posterior pharyngeal wall. **Positive in AC polyp. Negative in Angiofibroma.**

- **CT scan**

- **MRI** – Indicated to delineate and define the extent of the tumor, especially in cases of intracranial involvement

- **CAROTID ANGIOGRAM**
1. Surgery
2. Irradiation
3. Hormonal (purely supportive in nature)

**SURGERY**

- Nowadays, stage Fisch I, 2 and some type 3 tumours are suitable for endoscopic resection using one or two surgeon techniques:
- There is much to be gained by endonasal endoscopic techniques, for example, reduced intraoperative blood loss, fewer postoperative complications and a reduced length of hospital stay.

**Endoscopic Endonasal Techniques**

- Preoperative embolization is usually undertaken (not thinking of its drawbacks).
- The anterior end of the middle turbinate is resected at the outset of the procedure.
- An anterior ethmoidectomy together with removal of the medial wall of the maxillary sinus gives access to the posterior wall of the antrum.
- This is then removed to achieve complete lateral exposure of the tumour.
- Dissection then continues into the sphenoid until its rostrum is reached following which the tumour can be peeled inferiorly.
- Throughout this process it is necessary to use bipolar diathermy and ligacips to control the feeding blood vessels.

**Tumor Removal - Via Naturalis**

This approach is preferred for very small tumors confined to nasopharynx. The tumor can be removed by subperiosteal dissection after soft palate retraction. Access is limited in this approach.

**Denkers Approach**

Wide anterior antrostomy done, Removal of ascending process and maxilla, Removal of inferior half of lateral nasal wall.
Wilsons Trans Palatal Approach

Wilson in 1951 described this approach. This approach gives exposure to nasopharynx as well as extensions into the sphenoid sinus and choana. It gives no visible scar and post op healing is good. This approach is useful in dealing with masses in the nasopharynx with minimal extension into the choana and sphenoid sinus.

Lateral Rhinotomy Approach (Moure's incision)

Round This approach is suited for smaller growth restricted to the nasal cavity. It is contraindicated for larger masses and whose extensions and attachments cannot be ascertained

Trans Hyoid Approach

Round This is suitable for tumours localised to nasopharynx without any extension into the surrounding structures. The major disadvantage is that it requires a temporary tracheostomy

Transmandibular Approach: (Kermen)

Sublabial Midfacial Degloving Approach (Conley 1979)

Round Most Common open approach. Mainly used for bilateral tumours.
Round The complication of this procedure is vestibular stenosis

Trans zygomatic approach (Sami & Girgis 1965)

This approach is useful for removal of Tumor involving the temporal and infra temporal regions.

COMBINED APPROACHES

Trans Palatal Sublabial Approach (Sardana’s Approach)

This approach is useful for tumors extending into pterygoid and infratemporal fossa

Combined Transpalatal & Lateral Rhinotomy Approach

Triple Approach of Hiranandani
Transpalatal and Lateral Rhinotomy are combined along with Caldwell Luc Extensive juvenile angiofibromas are better resected through skull base approaches, preferably undertaken by a combined otorhinolaryngological and neurosurgical team.

However, the components of tumour in the cavernous sinus and any intradural disease demands adequate exposure and this can only be achieved with a Pre-Auricular Infratemporal Fossa Approach, usually Combined With A Modified Middle Fossa Craniectomy

RADIOThERAPY

- External beam radiation was delivered in several fractions to achieve a total tumour dose of 30-55 Gy.
- Radiotherapy can produce some amount of tumour regression by radiation vasculitis and occlusion of vessels by perivascular fibrosis.
- All studies report that regression of angiofibromas after radiotherapy is very slow indeed, often taking two to three years before 'radiological stabilization' is achieved.
- Treatment failure was apparent, usually within the first two to three years, and surgical salvage was generally successful in all these patients

ADJUNCTIVE TREATMENT

HORMONAL THERAPY

- Oestrogens have been reported to induce shrinkage in some but their effect is variable and not without complications. At the very least, oestrogen therapy delays surgery and the secondary feminizing effects are certainly unwanted by an adolescent boy. In a small series of patients given the nonsteroidal androgen receptor blocker, Flutamide, tumour shrinkage of up to 44 percent was reported by Gates. But hormones could even act as carcinogens.

EMBOLISATION

- Usually not required as the blood supply is predictable, usually the terminal branches of the internal maxillary artery (ascending pharyngeal or vidian arteries may contribute to the blood supply), and these can be controlled easily at the time of surgery.
On the contrary, recurrence rates seem to be increased by preoperative embolization.
Ideally carried out a few days before surgery.
Material Used: **Autologous substances like fat, blood clot, or chopped muscle fragments**
Artificial materials: **Gelfoam, Oxidised Cellulose, Tantalum Powder, Glass Beads, Polyvinyl Alcohol etc.**
Embolization should always be preceded by angiography.
Immediate complications of embolization are pain, embolization of normal vessels, hypersensitivity. Delayed complications include fever, pain and infections.
Cryosurgery and Lasers can also be used during surgery to minimise bleeding.

**COMPLICATIONS**

- **Recurrence** (more in younger individuals). Disease-free status 5 years after primary surgery probably represents cure.
- Surgically induced **Infraorbital Nerve Sensory Deficits**
- Complication of Mid-Facial Degloving, as is **Nasal Vestibular Stenosis**.
- **Fistula of the palate** at the junction of the soft and hard palate may occur with the Transpalatal Approach.
- **Transient blindness** has been reported as a result of embolization, but it is a rare occurrence. **Osteoradionecrosis and/or blindness** due to optic nerve damage may occur with radiotherapy.
- Prolonged **Nasal Crusting** is also common and this may well develop into **Ozaena**.

**RADIATION COMPLICATION**

- Growth Retardation, Panhypopituitarism, Temporal Lobe Necrosis, Cataracts, Radiation Keratopathy, together with Skin, Thyroid & Nasopharyngeal Malignancies were the most common problems encountered in the first 10-15 years after treatment.