Juvenile Nasopharyngeal Angiofibroma
Evaluation and Treatment

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Grand Rounds Presentation
December 29, 2012
Outline

- Fundamentals
- Pathophysiology
- Diagnostics
- Treatment
- Conclusions
Juvenile Nasopharyngeal Angiofibroma (JNA)

- Rare vascular neoplasm
  - Benign
  - Well-circumscribed
  - Locally invasive, submucosal spread
- Posterolateral nasopharynx
- Adolescent males
- Severe morbidity but low mortality
  - Hemorrhage
  - Intracranial extension

(Hauptman 2007)
First described by Hippocrates (Babyn 2005)
- In 5th century BC
- Description with nasal polyps

Chelius, 1847
- Fibrous nasal polyp
- Association with puberty

“Angiofibroma” coined in 1940 by Friedberg (Gullane 1992)
Male predilection

Adolescent
- Average age 14-15 years
- Age range between 10-25 years (Ardehali 2010)

Comprises 0.5% of head and neck neoplasms (Herman 1999, Tewfik 1999)

Indolent course (Radkowski 1996)
- Symptoms for 6-12 months before diagnosis
- Stage II or higher in 70% by diagnosis
Arterial supply
- Internal maxillary most common
- Other sources
  - Ascending pharyngeal
  - External carotid
  - Internal carotid
  - Common carotid

Occasional contralateral supply
- Controversial origin
  - Posterolateral nasal wall at sphenopalatine foramen
  - Vidian canal
- Embryologic chondrocartilage of skull bones (Schiff 1959)
  - Superior margin of sphenopalatine foramen
  - Trifurcation (Neel 1973, Bremer 1986)
    - Palatine bone
    - Horizontal ala of vomer
    - Root of pterygoid process

(Operative Techniques in Otolaryngology 1999; 10(2): 101-106.)
Pituitary androgen-estrogen axis
- Pathogenesis hypothesis (Schiff 1959)

Receptors (Montag 2006)
- Androgen
- Estrogen

(Operative Techniques in Otolaryngology 1999; 10(2): 101-106.)
- Vascular hamartoma  (Girgis 1973)
- JNA stroma cells  (Coutinho-Camillo 2008)
  - Vascular endothelial growth factor receptor-2
  - Transforming growth factor beta 1
  - Insulin-like growth factor 2
- Inflammatory reaction

(Operative Techniques in Otolaryngology 1999; 10(2): 101-106.)
Myofibroblast origin

Fibrous pseudocapsule

Multiple vascular channels
  - Abundant endothelium lining
  - Collagenous tissue network
  - Muscular layer absent  (Liu 2002)
    - Precludes vasoconstriction
    - Contributes to hemorrhage

(Hauptman 2007)

(JNA Histology)

(Intl Arch Otorhinolaryngol Sao Paulo 2008; 12(3):442-449.)
JNA Presentation

- Adolescent male
- Unilateral nasal obstruction most common
- Recurrent epistaxis
- Nasal mass
  - Smooth, lobulated
  - Compressible
  - Purplish or reddish hue

(Hauptman 2007)
Uncommon
- Middle ear effusion
- Dacrocystitis
- Rhinolalia
- Palate deformity
- Hyposmia or anosmia
- Bilateral (Rha 2003)

Advanced
- Facial swelling/mass
- Proptosis
- Cranial neuropathy
- Headaches
- Massive hemorrhage

(J Maxillofac Surg 1986; 14(6):329-31.)
**JNA**

**Natural History**

- **Extension** (Radkowski 1996, Enepekides 2004)
  - Pterygomaxillary fossa
  - Infratemporal fossa
  - Superior orbital fissure
    - Cavernous sinus
    - Orbit
  - Intracranial, 20-36% (Close 1989, Wiatrak 1993)
    - Anterior cranial fossa
    - Middle cranial fossa
    - Pituitary/parasellar

- Dural penetration rare

(Operative Techniques in Otolaryngology 2011; 22(4):281-284.)
(Operative Techniques in Otolaryngology 1999; 10(2): 101-106.)

(adapted from Clin Oncol (R Coll Radiol) 1998; 10(5):330-333.)
- Recurrence secondary to incomplete resection (Fagan 1997)
  - Up to 46% pending surgical technique
  - Extension
    - Sphenoid sinus
    - Base of pterygoid
    - Clivus

- Spontaneous regression (Tosun 2008)
  - After age 25
  - Presumed related to post-pubertal hormonal changes

(J Craniomaxillofac Surg 2012; 40(2):e54-8.)
JNA
Differential Diagnosis

- Vascular fibrosed nasal polyp
- Pyogenic granuloma
- Hemangiopericytoma
- Antrochoanal polyp

- Skull base tumors
  - Craniopharyngioma
  - Chordoma
  - Olfactory neuroblastoma
  - Nasopharyngeal carcinoma
  - Rhabdomyosarcoma
Previous systems
- 1981 - Sessions
- 1983 - Fisch
- 1984 - Chandler
- 1989 - Andrews

Radkowski most recent, 1996
- Posterior extension to pterygoid plates
- Degree of skull base erosion

None is universally accepted

(World Neurosurg 2010; 74(4-5):497-500.)
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(Radkowski 1996)
### Staging

**Radkowski**

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(Radkowski 1996)
Characteristic appearance often makes biopsy redundant
- Location at pterygopalatine fossa
- Pattern of growth
- Flow voids

Diagnostic requirements (Amdur 2011)
- Vascular mass with epicenter at posterior nasal cavity near medial pterygopalatine fossa
- Bony remodeling, not destruction
- No regional or distant metastasis

JNA Radiology (Liu 2002)
Radiology

CT

- Intense homogenous contrast enhancement
- Bony detail
  - Holman-Miller sign: anterior bowing of posterior maxillary wall
  - Widening of sphenopalatine foramen
Intense contrast enhancement with rapid decay

Soft-tissue differentiation
- Mucosal inflammation versus sinus fluid
- T1 Signal
  - Heterogeneous intermediate intensity without contrast
  - Diffuse contrast enhancement
- Similar signal intensity on T2

Intracranial extension

Flow voids within numerous tumor vessels (John 2006)
Angiography

- Not a required diagnostic
- Evaluate source vessel
  - Ipsilateral
  - Contralateral
- Preoperative embolization
- Carotid balloon occlusion test (Danesi 2008)
- Can excise without (Ahmad 2008)
Angiography
Preoperative Embolization

- Performed 24-72 hours before resection
  - Gelfoam
  - Polyvinyl alcohol foam
- Decrease intraoperative blood loss
- Shrink larger tumors
- Complications
  - Cerebrovascular accident
  - Blindness
  - Facial paralysis
  - Skin and soft tissue necrosis
**Angiography**

**Preoperative Embolization**

- **Moulin, 1995**
  - Embolized 7 of 20 patients
  - Less intraoperative hemorrhage, 1037.5mL vs 5380mL
  - Statistically significant for high-grade tumors only

- **Li, 1998**
  - Embolized 11 of 21 patients
  - Less intraoperative hemorrhage, 677mL vs 1136mL
  - Less transfusion, 400mL vs 836mL
Liu, 2002
- Embolized 13 of 34 patients between 1986-1999
  - External carotid ligation in 9
  - No preoperative treatment in 12
- Less intraoperative hemorrhage with embolization
  - 275mL vs 840mL
  - Tumors limited to nasal cavity or nasopharynx
- No hemorrhage difference
  - Larger tumors
  - No difference compared with carotid ligation

Tumor hypoxia may cause radioresistance
(Amdur 2011)
JNA
Treatment

- Surgery
- Radiation (XRT)
- Chemotherapy
- Hormone therapy
- Other
Primary treatment modality (Marshall 2006)

Still viable for intracranial extension (Bales 2002)

Preoperative embolization
  - Decreased hemorrhage
  - Obscure tumor borders for complete resection (Andrade 2007)

Recurrence
  - Most commonly from incomplete resection
Treatment

Surgical Approaches

- Transpalatal
- Lateral Rhinotomy
- Midfacial degloving
- Infratemporal fossa and craniotomy
- Endoscopic transnasal
Surgery
Transpalatal

- Split and retract soft palate
- Exposure with hard palate resection
- Resect palatine bone and inferior pterygoid plate

Complications
  - Palatal dehiscence
  - Oroantral fistula

(Operative Techniques in Otolaryngology 1999; 10(2):98-100.)
Lateral rhinotomy

Weber-Fergusson incision
  - Lynch extension
  - Lateral subciliary extension
  - Subciliary and supraciliary extension
Surgery
Midfacial Degloving

- Facial translocation
- Intercartilaginous and transfixion nasal incisions
- Gingivobuccal incision
- Le Fort I osteotomies

(Operative Techniques in Otolaryngology 2010; 21(3):171-174.)
Surgery
Midfacial Degloving Complications

- Nasal crusting
- Epistaxis
- Nasolacrimal duct obstruction
- Facial paresthesia
- Facial palsy
- Oroantral fistula
- Vestibular stenosis
- Carotid artery rupture

(Radkowski 1996)
Surgery

Infratemporal Fossa and Craniotomy

- Craniotomy not common
- Anterior access often sufficient for intracranial extent
  - Transfacial, transmaxillary approach (Elsharkawy 2010)
  - Endoscopic feasible in select cases (Danesi 2008)
  - May combine both approaches (Douglas 2006)

(Operative Techniques in Otolaryngology 1999; 10(2): 101-106.)
Surgery
Endoscopic

- Middle turbinectomy as needed for exposure
- Middle meatus antrostomy
- Resect posterior maxillary wall
- Sphenopalatine artery ligation
- Tumor resection from pterygopalatine fossa

(Wormald 2003)
Surgery

Endoscopic Complications

- Nasal synechia
- Cheek paresthesia
- Lacrimal duct stenosis
- Vision changes
  - Diplopia
  - Damage to cranial nerves, III and IV
- Sphenoid mucocele
- Cavernous sinus injury

(Wormald 2003)
Surgery

Endoscopic Complications

- Nasal synechia
- Cheek paresthesia
- Lacrimal duct stenosis
- Vision changes
  - Diplopia
  - Damage to cranial nerves, III and IV
- Sphenoid mucocele
- Cavernous sinus injury

(Surgery Endoscopic Complications)
Higher morbidity with extensive resection

Higher recurrence with limited resection, within 6 months (Tyagi 2006)
- Pterygoid fossa
- Clivus
- Basisphenoid
- Sphenoid diploe
- Cavernous sinus
- Intracranial

Lateral rhinotomy and midfacial degloving
- Wide access
- Cosmetic deformity
Medial maxillectomy (Fagan 1997)
- Extension to medial infratemporal fossa or cavernous sinus
- Accesses sphenoid sinus and anterior skull base

Yiotakis, 2008
- Transpalatal approach
  - Extension to sphenoid sinus
  - Limited lateral exposure
- Le Fort I osteotomy
  - Paranasal sinuses
  - Pterygopalatine fossa
  - Infratemporal fossa
Surgery Planning Approach

- Shift toward endonasal approach (Mann 2004)
- Endoscopic considerations
  - Limited simultaneous instrumentation (Wormald 2003)
  - Limited tumor mobilization (Douglas 2006)
  - Limited view with hemorrhage (Yiotakis 2008)
- No consensus on larger tumors

(Am J Otolaryngol 2003; 24(3):149-154.)
Surgery Planning Approach

- Hosseini, 2005
  - 54 patients, 1991-2002
  - Stage I and II tumors
    - Endoscopic
    - Transpalatal
    - Transantral
  - Stage III tumors
    - Lateral rhinotomy
    - Midfacial degloving
  - Less recurrences
    - Transpalatal if nasopharynx only
    - Le Fort I for skull base extension

- Yiotakis, 2008
  - 20 patients, 1998-2007
    - Transpalatal (stage I-II)
    - Midfacial degloving (stage II)
  - Endoscopic, 2001-2007

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<tr>
<th></th>
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<th>Midface</th>
<th>Endoscopic</th>
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<tr>
<td>EBL</td>
<td>925 mL</td>
<td>880 mL</td>
<td>248.8 mL</td>
</tr>
<tr>
<td>Time</td>
<td>260 min</td>
<td>203 min</td>
<td>107.7 min</td>
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<tr>
<td>Hosp</td>
<td>6.8 days</td>
<td>4.4 days</td>
<td>2 days</td>
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EBL: intraoperative hemorrhage
Time: operating time
Hosp: hospitalization duration
Endoscopic appropriate up to stage IIIA tumors (Wormald 2003)

Ardehali, 2010
- 47 patients, 1998-2005
- Endoscopic approach for stage I-IIIA tumors
- Embolization
  - Less intraoperative hemorrhage, 770mL vs 1400mL
  - Less postoperative hemorrhage, 0% vs 11.9%
  - Shorter hospitalization, 1.8 days vs 2.2 days
- Recurrence rate 19.1% within 2.5 years
Treatment

Radiation

- Unresectable or life-threatening tumors
- Dose range: 30-46Gy (McAfee 2006, Chakraborty 2011)
- Reddy, 2001
  - Primary radiotherapy just as effective as surgery
  - Recurrence rate 15%
- Low rate of complications
  - Brain necrosis (Lee 2002)
  - Cataracts (Amdur 2011)
  - Craniofacial growth arrest
  - Induce malignancy (Witt 1983, Makek 1989)
  - Hypopituitarism
  - Osteoradionecrosis (Witt 1983)
Treatment

Radiation

- Control rate 80-85% (Briant 1978, Cummings 1984, Reddy 2001)
- Amdur, 2011
  - 24 patients, 1975-2006
  - Control rate 90% with 36Gy over 20 treatments
  - Adjuvant role
    - No neoadjuvant XRT before subtotal resection
    - No adjuvant XRT if positive microscopic margins
  - Elective nodal irradiation unnecessary
  - Most recurrences by 2 years
  - Tumor decrease less than 50% by 12 months probably not JNA
[Treatment
Chemotherapy

- Recurrent tumors after surgery and radiation
- Side effects
- Rarely used (Lee 2002)
Treatment
Hormone Therapy

- Decrease size and vascularity
  - Estrogens
  - Antiandrogens
- Estrogen therapy
  - Theory
    - Decrease intraoperative blood loss
    - Promote regression
  - Side effects in males  (Briant 1978, Chandler 1984)
    - Physical
    - Psychological
- No efficacy with flutamide  (Labra 2004)
- Coblation (Ruiz 2012)
- Cryotherapy (Witt 1983, Spector 1988)
- Electrocoagulation (Schiff 1959)
- Gamma knife (Dare 2003, Park 2006)
- Harmonic scalpel (Chen 2006)
- Interstitial brachytherapy (Reddy 2001)
- KTP-laser embolization (Hazarika 2002)
- Sclerotherapy (Schiff 1959)
Conclusion

- Rare vascular neoplasm
  - Adolescent males
  - Posterolateral nasopharynx
  - Nasal obstruction and epistaxis

- Surgery is mainstay of treatment

- Radiation is feasible alternative


References


References


