PROTEUS SYNDROME

AlShabib Abdulrahman
PROTEUS SYNDROME

Rare, progressive disorder that is manifested as asymmetric, disproportionate overgrowth affecting tissues derived from any germline layer.
HISTORY

- Joseph Merrick, was born in 1862.
- He developed severe abnormalities of the skin and bones; multiple exostoses; an enlarged skull; and subcutaneous thickening of the skin.
- His right arm and one leg were asymmetric. A plaster cast of his foot showed a cerebriform connective tissue nevus on the plantar surface.
HISTORY

- He was diagnosed as having neurofibromatosis and he exhibited himself as ‘an elephant man’, but in fact had Proteus syndrome,
- several articles, two books, and the play about ‘The Elephant Man’ preceded the movie about him.
BACKGROUND

- Cohen and Hayden first described the syndrome in 1979
- Less than 100 cases have been recorded in the literature
- activating \textit{AKT1 mutation}, c.49G>A, p.Glu17Lys is thought to be the cause of Proteus syndrome.
Children diagnosed PS are usually normal at birth or have mild-to-moderate alterations, hamartomas, or vascular malformations.

It appears to be more common in males than females, with a ratio of 2:1

It does not seem to have a preference for any particular ethnic group.
CLINICAL MANIFESTATIONS

GENERAL CRITERIA
Sporadic occurrence
Progressive course

SPECIFIC CRITERIA
Category A
Two from category B
Three from category C
CLINICAL MANIFESTATIONS

GENERAL CRITERIA
Sporadic occurrence
Progressive course

SPECIFIC CRITERIA
Category A
Two from category B
SPECIFIC CRITERIA

Category A

1. Cerebriform connective tissue

Proteus syndrome review

Fig. 1. Cerebriform connective tissue nevus. Left: at age of 51/2 years. From Cohen (2). Right: another patient at age of 12 years. From Cohen and Hayden (14).

Epidermal nevi and other skin lesions

Epidermal nevi are etiologically heterogeneous (3, 4, 16, 17). In Proteus syndrome, such nevi are evident in early life and may occur on the neck (Fig. 4), trunk, or extremities. Histopathological findings consist of acanthosis and hyperkeratosis. Patchy areas of dermal hypoplasia and hypopigmentation have also been observed. Figure 5 shows dermal hypoplasia of the leg which demonstrates the underlying venous pattern (3, 4, 17).

Vascular malformations

Vascular malformations may be of the capillary, venous, or lymphatic types, or may occur as combined channel anomalies, e.g. capillary and venous channels or capillary, venous, and lymphatic channels. They are developmental anomalies lined by flat endothelium exhibiting a normal, slow rate of turnover. They grow proportionately with the patient; they never regress, but they can expand (3, 4, 18, 19).

Dysregulated adipose tissue

Although normal and abnormal adipose tissue can be identified by magnetic resonance imaging (MRI), histopathological study is necessary to determine various subtypes. Apparently, four types of abnormal fat occur in Proteus syndrome: (i) lipomas, (ii) lipohypoplasia, (iii) fatty overgrowth, and (iv) localized fat deposits or partial lipohypoplasia. In the lipohypoplasia of Proteus syndrome, subcutaneous fat may be decreased or absent, but most likely the former (20). It tends to occur on the trunk and limbs, resulting in accentuated bony contours. Dermal hypoplasia with thin skin may involve the lower limbs, resulting in prominently appearing veins (17) (Fig. 5).

'Normal' lipomas are benign tumors of mature fat cells. They may occur in subcutaneous tissue, but may appear elsewhere and, in some cases, they may be multiple. They have increased lipoprotein lipase and a large number of precursor cells. These lipomas may be encapsulated or non-encapsulated (3). In contrast, lipomas in Proteus syndrome may be single or multiple and occur subcutaneously or internally. Those in the abdomen and thorax may be aggressive despite their benign histology. Biopsied material, to date, has demonstrated non-encapsulation, and it is unknown if precursor cells occur more commonly than in normal fat (3).

Pulmonary abnormalities

Bullous lung abnormalities have been discussed by several authors (3, 4, 19, 21–24). Two patients were well-studied by Lim et al. (24), who noted that high-resolution CTs were mandatory during childhood when the diagnosis of Proteus syndrome is made. One patient had bullous lung alterations, but both patients had pulmonary venous dilatation.

Fig. 2. Left: infant. Right: same patient at the age of 41/2 years with a large cerebriform connective tissue nevus involving the whole chest and abdomen. From Cohen (2).
Proteus syndrome review

Fig. 1
Cerebriform connective tissue nevus. Left: at age of 51/2 years. From Cohen (2). Right: another patient at age of 12 years. From Cohen and Hayden (14).

Epidermal nevi and other skin lesions
Epidermal nevi are etiologically heterogeneous (3, 4, 16, 17). In Proteus syndrome, such nevi are evident in early life and may occur on the neck (Fig. 4), trunk, or extremities. Histopathological findings consist of acanthosis and hyperkeratosis. Patchy areas of dermal hypoplasia and hypopigmentation have also been observed. Figure 5 shows dermal hypoplasia of the leg which demonstrates the underlying venous pattern (3, 4, 17).

Vascular malformations
Vascular malformations may be of the capillary, venous, or lymphatic types, or may occur as combined channel anomalies, e.g. capillary and venous channels or capillary, venous, and lymphatic channels. They are developmental anomalies lined by flat endothelium exhibiting a normal, slow rate of turnover. They grow proportionately with the patient; they never regress, but they can expand (3, 4, 18, 19).

Dysregulated adipose tissue
Although normal and abnormal adipose tissue can be identified by magnetic resonance imaging (MRI), histopathological study is necessary to determine various subtypes. Apparently, four types of abnormal fat occur in Proteus syndrome: (i) lipomas, (ii) lipohypoplasia, (iii) fatty overgrowth, and (iv) localized fat deposits or partial lipohypoplasia. In the lipohypoplasia of Proteus syndrome, subcutaneous fat may be decreased or absent, but most likely the former (20). It tends to occur on the trunk and limbs, resulting in accentuated bony contours. Dermal hypoplasia with thin skin may involve the lower limbs, resulting in prominently appearing veins (17) (Fig. 5).

'Normal' lipomas are benign tumors of mature fat cells. They may occur in subcutaneous tissue, but may appear elsewhere and, in some cases, they may be multiple. They have increased lipoprotein lipase and a large number of precursor cells. These lipomas may be encapsulated or non-encapsulated (3).

In contrast, lipomas in Proteus syndrome may be single or multiple and occur subcutaneously or internally. Those in the abdomen and thorax may be aggressive despite their benign histology. Biopsied material, to date, has demonstrated non-encapsulation, and it is unknown if precursor cells occur more commonly than in normal fat (3).

Pulmonary abnormalities
Bullous lung abnormalities have been discussed by several authors (3, 4, 19, 21–24). Two patients were well-studied by Lim et al. (24), who noted that high-resolution CTs were mandatory during childhood when the diagnosis of Proteus syndrome is made. One patient had bullous lung alterations, but both patients had pulmonary venous dilatation.

Fig. 2
Left: infant. Right: same patient at the age of 41/2 years with a large cerebriform connective tissue nevus involving the whole chest and abdomen. From Cohen (2).

SPECIFIC CRITERIA

Category A
1. Cerebriform connective tissue
Disproportionate asymmetric overgrowth and skeletal abnormalities

Overgrowth in Proteus syndrome is disproportionate, asymmetric, distorting, and relentless (Figs 6–11) (3).

SPECIFIC CRITERIA

Category B

1. Epidermal nevus
2. Asymmetric, disproportionate overgrowth
   A. limbs, arms/legs, hands/feet/digits or extremities
   B. hyperostoses of the skull
SPECIFIC CRITERIA

Category B

1. Epidermal nevus

2. Asymmetric, disproportionate overgrowth
   A. limbs, arms/legs, hands/feet/digits or extremities
   B. hyperostoses of the skull
   C. hyperostosis of the external auditory meatus
Proteus syndrome review

Fig. 8. Asymmetric overgrowth of legs with thin cortices and deficiency of the overlying soft tissue. From Cohen (2).

Abnormalities of bone in Proteus syndrome are very different than those observed in various forms of hemihyperplasia. The latter has a ballooning effect of the enlarged soft tissue together with enlargement of the underlying bone (22, 25). In Proteus syndrome, the long bones are overgrown with abnormally thin cortices and deficiency of the overlying soft tissue (22, 25). Table 2 shows the characteristic skeletal abnormalities. Other findings may sometimes include scoliosis and kyphoscoliosis; talipes valgus; megaspondylodysplasia; cervical, thoracic, or lumbar defects; abnormal hands and/or feet; and various other anomalies (3, 4, 22).

Neoplasms

Only lipomas are common. Other reported neoplasms include monomorphic adenoma of the parotid gland (2 cases) (Fig. 12); cystadenomas of the ovary (many cases) (Figs. 13 and 14); testicular tumors (4 cases); meningiomas (several cases); and mesothelioma (1 case) (3, 4, 26, 27). Monomorphic adenomas, unlike the common pleomorphic adenomas, are rare and normally occur in old men. In Proteus syndrome, two monomorphic adenomas have occurred in teenage patients (3, 4). Cystadenomas of the ovary normally occur in adult women, but are common in Proteus syndrome teenagers, and have even occurred bilaterally in two cases. Other unusual tumors as well as patients with multiple tumors are reviewed elsewhere (3, 4).

Facial phenotype

A facial phenotype has been described in Proteus syndrome patients with intellectual disability, and in...
Deep vein thrombosis (DVT) is most common (28–30). Symptoms warranting investigation include calf pain, calf or leg swelling, shortness of breath, and chest pain. Patients undergoing surgical procedures need to make their health-care providers aware of the risk of DVTs. Symptoms warranting investigation include calf pain, calf or leg swelling, shortness of breath, and chest pain. About 20% of patients with Proteus syndrome have premature deaths. DVT is most common (28–30). Two measures are available: anticoagulant prophylaxis with Warfarin and Anticoagulant prophylaxis with Heparin. Heparin can be used because Warfarin is dangerous. Warfarin acts 2–3 days later. In pregnant women, only sometimes at the same time, heparin acting quickly and pathologic potential warrants antithrombotic prophylaxis. To prevent DVTs, Warfarin and heparin may be used, be evaluated by a hematologist to determine if coagulation laboratory values are appropriate.

To prevent DVTs, Warfarin and heparin may be used, to be evaluated by a hematologist to determine if coagulation laboratory values are appropriate. To prevent DVTs, Warfarin and heparin may be used, to be evaluated by a hematologist to determine if coagulation laboratory values are appropriate. To prevent DVTs, Warfarin and heparin may be used, to be evaluated by a hematologist to determine if coagulation laboratory values are appropriate. To prevent DVTs, Warfarin and heparin may be used, to be evaluated by a hematologist to determine if coagulation laboratory values are appropriate.

Table 2 shows the characteristic skeletal abnormalities.

### Table 2. Skeletal abnormalities

- Hyperostoses of the skull
- Arachnodactyly
- Abnormally calcified connective tissue
- Hyperplasia of osteoid with variable calcification, producing abnormal bony edges
- Abnormally overgrown long bones often with abnormally thin cortices
- Abnormal bone that may be difficult to recognize radiologically
- Invasion of joint spaces, eventually resulting in immobility of the knee joint

- Capillary malformations (Table 1) and (ii) immobility of the knee joint by bony invasion (Table 2). Patients with Proteus syndrome and/or their families should be evaluated by a hematologist to determine if coagulation laboratory values are appropriate. To prevent DVTs, Warfarin and heparin may be used, to be evaluated by a hematologist to determine if coagulation laboratory values are appropriate.

- Many other abnormalities may occur in some cases of Proteus syndrome and these have been reviewed elsewhere (3, 4, 22). These may include, among other findings (renal asymmetry, renal cysts, hydroureters, hydronephrosis) (3, 4). Asymmetric overgrowth of legs with thin cortices and deficiency of the overlying soft tissue (22, 25). In Proteus syndrome, the latter has a ballooning effect different than those observed in various forms of hemihyperplasia. The latter has a ballooning effect different than those observed in various forms of hemihyperplasia. The latter has a ballooning effect different than those observed in various forms of hemihyperplasia. The latter has a ballooning effect different than those observed in various forms of hemihyperplasia.
SPECIFIC CRITERIA

Category B

1. Epidermal nevus

2. Asymmetric, disproportionate overgrowth
   A. limbs, arms/legs, hands/feet/digits or extremities
MANAGEMENT

- Initial skeletal survey with targeted follow-up radiographs MRI
- Dermatology consultation; biopsy when indicated
- Orthopedic consultation; operation when indicated
- Ongoing genetic/pediatric management
- Other consultations as indicated
- Referral to family support group
A **reduction osteotomy** may be used to shorten and/or straighten a long bone.

**Shoe lifts** can be used for milder instances of leg length discrepancy.
MANAGEMENT

- **Prosthetic joint replacement** should be considered for joint immobility.
- Surgical considerations include aggressive and early use of **epiphysiodesis, amputation, and spinal bracing**
COMPLICATIONS

- About **20%** of patients with Proteus syndrome have premature deaths.

- **Deep Vein Thrombosis** is most common. Two predisposing factors may play a role, such as large venous and capillary malformations and immobility of the knee joint by bony invasion.

- It is known that **respiratory deaths** have happened in three cases and **central nervous system deaths** in two cases.
Parents of affected patients frequently report feeling isolated because of the rarity of Proteus syndrome and the social stigmata of having a progressively disfiguring condition.

23% of parents of affected children have reported to have symptoms of depression.

They should be able to receive psychological attention if needed, they can be referred to a family support group.
DIFFERENTIAL DIAGNOSIS

- Neurofibromatosis
- PTEN hamartoma syndrome
- Hemihyperplasia-lipomatosis syndrome
CASE REPORT

Radiographic manifestations of the temporomandibular joint in a case of Proteus syndrome

E Yılmaz¹, Ö Kansu*¹, B Özgen², G Akçiçek¹ and H Kansu¹

¹Department of Oral Diagnosis and Radiology, Faculty of Dentistry, Hacettepe University, Ankara, Turkey; ²Department of Radiology, Faculty of Medicine, Hacettepe University, Ankara, Turkey
Purpose

Describe the radiographic manifestations of an asymptomatic condyle malformation and other craniofacial, oral and dental findings in a 33-year-old female patient with known Proteus syndrome.
Extraoral Findings

Pronounced hemifacial hypertrophy, and hyperostosis
A panoramic radiograph revealed mandibular hemihypertrophy of the left side. There was an excessive generalized growth of the left mandibular body and ramus. Hyperostoses in the left condyle and mandible were observed. There was coarse trabeculation of the left angulus mandible. The tuber maxilla of the affected side was also enlarged. More alveolar bone loss in the maxillary left side than the right side was detected. Dilaceration of the roots of both maxillary left canine and mandibular right central incisor was recorded. The panoramic radiograph also showed the left condyle malformation and wide sclerosis in the glenoid fossa (Figure 5). In addition to the panoramic radiograph, the open–closed lateral radiograph of the TMJ, which was obtained using the TMJ-specific program of the panoramic device, was also taken. This radiograph showed a significant limitation of movement of the condyle on the affected side, whereas there was anterior excursion of the unaffected condyle beyond the articular eminence (Figure 6). In order to obtain a more detailed image of the left TMJ morphology, CT was performed obtaining the sagittal and axial slices. CT images also demonstrated extensive degenerative changes of the left TMJ with pseudoarticulation of the coronoid process anteriorly. This pseudoarticulation was due to the hypertrophic changes of the temporal bone and mandibular condyle (Figure 7a,b). Additionally, CT images of the head revealed new bone formation in the occipital and temporal region.

Discussion

PS is a rare complex disorder characterized by asymmetrical and disproportionate overgrowth of various tissues of the body. Since PS is progressive in nature, the craniofacial distortion becomes more evident with age. The disease may slow or stabilize during early adolescence. In our female patient the onset of asymmetrical overgrowth started at the age of 7 years. The clinical manifestations are highly variable, because of multifocal overgrowth affecting any tissue of the body. In this case, extraoral examination revealed several of the previously reported craniofacial features of PS: pronounced hemifacial hypertrophy, macrodactyly and hyperostosis. Both the left tuber maxilla and the mandible were affected. Craniofacial hyperostoses are common in PS. They may occur in the cranium, nasal bones, external auditory meatus, alveolar ridge, maxillary and mandibular bone. In the presented case, hyperostoses in the alveolar bone, condyle and mandible were observed on the affected side. Multiple skull hyperostoses involving the parietal, occipital, temporal and frontal bone were removed surgically 10 years before. The tissue overgrowth may stabilize after adolescence, but in our patient new bone overgrowth has been radiographically observed in the occipital and temporal region following the surgery.

Dental and intraoral manifestations of PS have been described in the literature. A high arched palate and unilateral enlargement of the tongue on the affected side were found in our patient. Most of the teeth on the left side were extracted owing to periodontal disease. There were only three teeth on the affected side.

Intraoral Findings

Intraoral view showing gingival hyperplasia and the high arched palate

High arched palate and gingival hyperplasia.
A panoramic radiograph revealed mandibular hemihyper trophy of the left side. There was an excessive generalized growth of the left mandibular body and ramus. Hyperostoses in the left condyle and mandible were observed. There was coarse trabeculation of the left angulus mandible. The tuber maxilla of the affected side was also enlarged. More alveolar bone loss in the maxillary left side than the right side was detected. Dilaceration of the roots of both maxillary left canine and mandibular right central incisor was recorded. The panoramic radiograph also showed the left condyle malformation and wide sclerosis in the glenoid fossa (Figure 5). In addition to the panoramic radiograph, the open–closed lateral radiograph of the TMJ, which was obtained using the TMJ-specific program of the panoramic device, was also taken. This radiograph showed a significant limitation of movement of the condyle on the affected side, whereas there was anterior excursion of the unaffected condyle beyond the articular eminence (Figure 6). In order to obtain a more detailed image of the left TMJ morphology, CT was performed obtaining the sagittal and axial slices. CT images also demonstrated extensive degenerative changes of the left TMJ with pseudoarticulation of the coronoid process anteriorly. This pseudoarticulation was due to the hypertrophic changes of the temporal bone and mandibular condyle (Figure 7a,b). Additionally, CT images of the head revealed new bone formation in the occipital and temporal region.

Discussion

PS is a rare complex disorder characterized by asymmetrical and disproportionate overgrowth of various tissues of the body. Since PS is progressive in nature, the craniofacial distortion becomes more evident with age. The disease may slow or stabilize during early adolescence. The disease process is not usually apparent at birth; the onset of overgrowth commonly occurs in childhood. In our female patient the onset of asymmetrical overgrowth started at the age of 7 years. The clinical manifestations are highly variable, because of multifocal overgrowth affecting any tissue of the body. In this case, extraoral examination revealed several of the previously reported craniofacial features of PS: pronounced hemifacial hypertrophy, macrodactyly and hyperostosis. Both the left tuber maxilla and the mandible were affected. Craniofacial hyperostoses are common in PS. They may occur in the cranium, nasal bones, external auditory meatus, alveolar ridge, maxillary and mandibular bone. In the presented case, hyperostoses in the alveolar bone, condyle and mandible were observed on the affected side. Multiple skull hyperostoses involving the parietal, occipital, temporal and frontal bone were removed surgically 10 years before. The tissue overgrowth may stabilize after adolescence, but in our patient new bone overgrowth has been radiographically observed in the occipital and temporal region following the surgery. Dental and intraoral manifestations of PS have been described in the literature. A high arched palate and unilateral enlargement of the tongue on the affected side were found in our patient. Most of the teeth on the left side were extracted owing to periodontal disease. There were only three teeth on the affected side.
In addition to the panoramic radiograph, malformation and wide sclerosis in the glenoid fossa were recorded. The left condyle and mandibular right central incisor was also enlarged. More alveolar bone loss in the left angulus mandible. The tuber maxilla of the affected side was observed. There was coarse trabeculation of the ramus. Hyperostoses in the left condyle and mandible were also detected. The generalized growth of the left mandibular body and hypertrophy of the left side. There was an excessive formation in the occipital and temporal region following the surgery. There were only three teeth on the affected side, whereas there was an excessive tissue of the body. Since PS is progressive in nature, the disease process is not usually apparent at birth; the onset of overgrowth commonly occurs in childhood. In our female patient the onset of overgrowth was at the age of 7 years. Asymmetrical overgrowth started at the age of 7 years. The disease may slow or stabilize during early adolescence. The disease may slow or stabilize during early adolescence. The disease may slow or stabilize during early adolescence.

**Discussion**

The clinical manifestations are highly variable, being determined by the site and degree of overgrowth. They include craniofacial hyperostoses, gigantism, macrodactyly, and hyperostosis. Both the auditory meatus, alveolar ridge, maxillary and mandibular bone. Craniofacial hyperostoses are common in PS. They may involve any bones of the skull base, including the frontal bone. In the presented case, hyperostoses involving the parietal, occipital, temporal and frontal bone were removed surgically 10 years before. The disease may slow or stabilize during early adolescence. The disease process is not usually apparent at birth; the onset of overgrowth commonly occurs in childhood. In our female patient the onset of overgrowth was at the age of 7 years. Asymmetrical overgrowth started at the age of 7 years. The disease may slow or stabilize during early adolescence.

Radiographs

A panoramic radiograph revealed mandibular hemihyperplasia and both gingival hyperplasia and alveolar bone degenerative changes detected. There was only dilaceration of the roots of both maxillary left canine and mandibular right central incisor; other dental anomalies and dilaceration of the roots of both maxillary left canine and mandibular right central incisor were recorded. The disproportionate overgrowth was due to the hypertrophic changes of the coronoid process anteriorly. This pseudoarticulation of the coronoid process anteriorly. (b) Axial image of the three-dimensional CT reveals hypertrophic changes of the temporal bone and mandibular condyle with accompanying degenerative changes of the left temporomandibular joint with pseudoarticulation of the coronoid process anteriorly. (a) Sagittal multiplanar reformat demonstrating extensive degenerative changes of the left temporomandibular joint with accompanying degenerative changes of the left temporomandibular joint.
TREATMENT

- There are **no completely satisfactory orthopaedic procedures** to treat these lesions—the therapy should take a multidisciplinary approach owing to the syndrome's complexity.

- The aim of the treatment is **minimization of the disability**, and contributions can be made by plastic, dental and orthopaedic surgeons and physiotherapists.

- Treatment was not necessary owing to the asymptomatic situation but periodic follow-up with clinical and radiographic examination was considered.
REFERENCES


THANK YOU!
Solitary Median Maxillary Central Incisor Syndrome

CBY 579L

Ana Torres

Advanced Orthodontics
1st Year Resident
Contents

1. Introduction
2. Etiology
3. Holoprosencephaly (HPE)
4. Clinical description
5. Diagnosis & Differential diagnosis
6. Treatment
Solitary Median Maxillary Central Incisor

- Definition
- Prevalence 1:50’000
- Scott 1958
- Isolated incident - associated with HPE
- Genetic mutations
- Syndroms: CHARGE, VACTERL, VCF, DiGeorge
• Etiology uncertain: 35th-38th days in utero

• Embryonic development: maxillary dental lamina

• SMMCI: inhibition of the lateral movement of structures

• Premature fusion of the dental lamina
Genetics

Heterogeneous genetic profile:

- Deletion in 7q36
- Deletion/trisomy 13
- Deletion in 18p11 *
- Deletion in 22q11.2
- Deletion in chromosome X

Contain genes that intervene in HPE: SHH, SIX3, ZIC2 y TGIF

Relevance of the association of these mutations to SMMC is unknown

Specific mutation for SMMC in SHH gene

Nanni et al. (2001)
Holoprosencephaly

Introduction

Etiology

Clinical description

Diagnosis

Treatment

Normal development

Holoprosencephaly

Video: https://www.youtube.com/watch?v=BOinh2VcapA
Holoprosencephaly

1:250 early development embryos

1:16’000 live births

Autosomal dominant with incomplete penetrance

Wide phenotypic variability

Alobar HPE $\rightarrow$ SMMCI

One of the major causes of spontaneously aborted foetuses

Consequence: developmental defects in the facial region belonging to the frontonasal field of embryonic development: sella turcica —> dientes

Solitary Maxillary Incisor

- Symmetric crown + root
- Maxillary midline
- Primary + permanent dentition
- + anomalies in the oral cavity
Oral cavity

100% • Solitary maxillary incisor
80% • Undefined labial filtrum
60% • Elevated or arched midline of upper lip
100% • Absence of labial frenum and incisive papilla
100% • Malformation of palatal suture
100% • Vaulted palate
90% • Bony ridge in palate (vomer)
25% • Cleft lip and/or palate

Frequency observed by Kjaer et al. (2001 and 2002)
HPE

Hypotelorism
Anomalies of the nasal cavity
Altered craniofacial + brain morphology
Short stature
Other anomalies
Associated syndromes

Clinical description

Morphologic anomalies of sella turcica
Congenital pyriform aperture stenosis

Charge

Craniofacial dimensions
Diagnosis

Essentially clinical

- Solitary incisor
- Neonatal nasal obstruction

At different points

1. Prenatal
2. Neonatal
3. After 8 months of age
Differential diagnosis

- Trauma
- Agenesis: rare
- Fusion
- Interruption of development of one CI

Medical history: trauma
Exploration: crown symmetry
X-Ray: palatal suture

Images from: Moreira et al. (2012)
Treatment

- Interdisciplinary team
- Individualized treatment
- Based on present anomalies
Dental Management

Primary dentition → Prevention

Mixed - permanent dentition

1. Study of facial growth
2. Photographic series

Orthodontic treatment*

Introductions
Etiology
Holoprosencephaly
Clinical description
Diagnosis


Image from: http://www.ortho-concept.com/quad-helix/orthodontie_en/2.5
References

1. Hall RK. Solitary median maxillary central incisor (SMMCI) syndrome. Orphanet J Rare Diseases 2006;1:12.
References


Gorlin-Goltz Syndrome
Nevoid basal cell carcinoma syndrome (NBCCS)

Haifa Alsobiyl BDS
Advanced Operative Resident
Nevoid basal cell carcinoma syndrome
Gorlin–Goltz syndrome

• A hereditary condition characterized by a wide range of developmental abnormalities and a predisposition to neoplasms.

• It is an autosomal dominant disease.
• **Background**

• This syndrome existed since Dynastic Egyptian times, as shown by findings compatible with the syndrome in mummies dating back to 1,000 b.c.
Nevoid basal cell carcinoma syndrome
Gorlin–Goltz syndrome

- Described by Gorlin and Goltz in 1960
- The classical triad:
  - Multiple basal cell carcinoma
  - Keratocystic odontogenic tumors (KCOTs) in the jaws
  - Bifid ribs
Nevoid basal cell carcinoma syndrome
Gorlin–Goltz syndrome

Several different names:

• Gorlin syndrome
• Gorlin-Goltz syndrome
• Nevoid basal cell carcinoma syndrome (NBCCS)
• Multiple nevoid basal-cell carcinoma syndrome (MNBCCS)
• Multiple basal-cell carcinoma syndrome
• Basal cell nevus syndrome (BCNS)
• Multiple basalioma syndrome
Epidemiology

- The prevalence is about 1 per 60,000
- Affects both men and women in the same way
- Presents in all ethnic groups
Nevoid basal cell carcinoma syndrome
Gorlin–Goltz syndrome

• Diagnostic methods

• Diagnosis can be made in the presence

2 major criteria
1 major + 2 minor criteria
Nevoid basal cell carcinoma syndrome
Gorlin–Goltz syndrome

- **Major criteria**

1. Multiple (>2) BCCs or one under 20 years
2. Odontogenic keratocysts of the jaws
3. Palmar or plantar pits (3 or more)
4. Bilamellar calcification of the falx cerebri
5. Bifid or fused ribs
6. First degree relatives with NBCCS
Nevoid basal cell carcinoma syndrome
Gorlin–Goltz syndrome

**Minor criteria:**

1. Macrocephaly
2. Congenital malformation: cleft lip or palate, frontal bossing
3. Other skeletal abnormalities: sprence deformation, marked pectus deformity, marked syndactyly of the digits
4. Radiological abnormalities
5. Ovarian fibroma
Etiology

• **Genetics**

  • The tumor suppressor gene Patched (PTCH) has been identified as cause Gorlin syndrome

  • The PTCH1 gene is mapped to the long arm of chromosome 9 (q22.3-q31)

  • Data suggest that the product of this gene acts as a tumor suppressor
Nevoid basal cell carcinoma syndrome
Gorlin–Goltz syndrome

- Variety of neoplasms and skeletal anomalies with the universal finding being multiple basal cell carcinomas (BCCs)
Nevoid basal cell carcinoma syndrome
Gorlin–Goltz syndrome

- The classical triad:
  - Multiple basal cell carcinoma
  - Keratocystic odontogenic tumors (KCOTs) in the jaws
  - Bifid ribs
Basal Cell Carcinoma

- Various forms from skin-coloured nodules or papules to ulcerating plaques.
- Located on the face, back and chest, but they may also be found on skin not exposed to the sun.
Nevoid basal cell carcinoma syndrome
Gorlin–Goltz syndrome

- Affected individuals usually present with multiple primary BCCs that pose a therapeutic challenge because of their number, size, and location.

- The goal of therapy is to achieve adequate cancer control while minimizing cosmetic disfigurement.
Treatment:

- Multiple modalities such as surgery, lasers, and topical, injectable or systemic therapy

- Highlight the role of chemoprophylaxis, sun protection, and radiation avoidance.
Nevoid basal cell carcinoma syndrome
Gorlin–Goltz syndrome

- The classical triad:
  - Multiple basal cell carcinoma
  - Keratocystic odontogenic tumors (KCOTs) in the jaws
  - Bifid ribs
Odontogenic Keratocystic lesions

- Benign locally aggressive developmental cystic neoplasm of epithelial origin
Odontogenic Keratocystic lesions

- The first symptom is either an **odontogenic keratocyst** or an odontogenic cyst of the jaws

- OKCs are the most consistent and representative signs of Gorlin syndrome in the **first** and the **second** decades of life
Recurrent jaw cysts present in 90% of patients

Characterized by a thin external fibrous capsule and an internal lining of keratinized stratified squamous epithelium

Keratocysts appear in the tooth-bearing areas of the jaws, and are believed to arise from the dental lamina.
• The epithelial cells of the basal layer show increased mitotic activity, together with a potential for budding and the presence of daughter cysts in the wall.

• It has been reported that the presence of daughter cysts was related to the recurrence of KCOT.
Odontogenic Keratocystic lesions

• It is well circumscribed and has a well-defined **osteosclerotic rim**, which may become less visible while the lesion grows and transforms into a multi-locular form.

• The latter form of the tumour needs to be differentiated from ameloblastoma

• In the course of its growth, the tumour causes **bony expansion** that may result in deformation or asymmetry of the facial structures
Treatment of OKC

The methods of treatment:

- Conservative
- Aggressive
- Radical
Treatment of OKC

- **Conservative**: simple enucleation with or without curettage and marsupialization

- Due to the presence of satellite micro-tumours in the surrounding bone causing recurrence rate.

- Better results can be obtained if enucleation is followed by a chemical or mechanical curettage of the surrounding bone.
• **Aggressive**: include peripheral ostectomy, chemical curettage with Carnoy’s solution, and resection.
Thank you
Syndromic Craniosynostosis
KUANG-LING, OU
Nov. 13th 2015
Synopsis

- Syndromic craniosynostoses have **coexisting anomalies** aside from fused cranial sutures.

- Common features: midface hypoplasia, cranial base growth abnormalities, abnormal facies, and limb abnormalities (except Crouzon)

- Acro–Cephalo-Syndactyly

- Treatment paradigms are best applied according to patient **phenotype**, and not genotype.

- The avoidance of neurocognitive delays requires a focus on the prevention of both **sleep apnea** and chronic elevations in **intracranial pressure**.
Molecular genetics and developmental pathogenesis

- Mutations in fibroblast growth factor receptor (FGFR) genes
- Autosomal dominant skeletal disorders
- FGFR - regulation of cell proliferation, differentiation, migration, and play a role in controlling normal bone morphogenesis via complex cell signaling pathways
- Mutations FGFR genes on chromosomes 8, 10q, and 4p.
- Pfeiffer syndrome: FGFR1 and FGFR2 mutation
- Crouzon, Apert syndromes: FGFR2 mutation
Role of FGF/FGFR signaling in skeletal development and homeostasis: learning from mouse models

Nan Su*, Min Jin* and Lin Chen

Fibroblast growth factor (FGF)/fibroblast growth factor receptor (FGFR) signaling plays essential roles in bone development and diseases. Missense mutations in FGFs and FGFRs in humans can cause various congenital bone diseases, including chondrodysplasia syndromes, craniosynostosis syndromes and syndromes with dysregulated phosphate metabolism. FGF/FGFR signaling is also an important pathway involved in the maintenance of adult bone homeostasis. Multiple kinds of mouse models, mimicking human skeleton diseases caused by missense mutations in FGFs and FGFRs, have been established by knock-in/out and transgenic technologies. These genetically modified mice provide good models for studying the role of FGF/FGFR signaling in skeleton development and homeostasis. In this review, we summarize the mouse models of FGF signaling-related skeleton diseases and recent progresses regarding the molecular mechanisms, underlying the role of FGFs/FGFRs in the regulation of bone development and homeostasis. This review also provides a perspective view on future works to explore the roles of FGF signaling in skeletal development and homeostasis.

Bone Research (2014) 2, 14003; doi:10.1038/boneres.2014.3; Published online 29 April 2014
The diagram illustrates the signaling pathways activated by FGF (fibroblast growth factor) receptors (FGFRs). The FGF binds to the FGFR, leading to the activation of TK (tyrosine kinase) domains. This activation further leads to the phosphorylation and activation of downstream effectors such as PLCγ (phospholipase C gamma), SHC, STAT1, and PI3K (phosphatidylinositol-4,5-bisphosphate 3-kinase). The activated PI3K then phosphorylates AKT (protein kinase B) which can regulate cell proliferation, differentiation, and apoptosis. Additionally, the activated SHC can also interact with ERK1/2 (extracellular signal-regulated kinases) through the MEK1/2 (mitogen-activated protein kinase kinase 1/2) pathway. The p21 protein is also regulated in this pathway, playing a role in cell cycle arrest and apoptosis. Chondrocytes are depicted at the bottom, illustrating the possible biological outcomes such as proliferation, differentiation, and apoptosis.
## Clinical findings

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Skull shape</th>
<th>Midface</th>
<th>Hands and feet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apert</td>
<td>Moderate to severe brachycephaly with occasional severe turribrachycephaly</td>
<td>Moderate hypoplasia</td>
<td>Pansyndactylies of hands and feet (thumbs can be free, and partial syndactylies of small fingers and toes may occur)</td>
</tr>
<tr>
<td>Crouzon</td>
<td>Brachycephaly</td>
<td>Mild to moderate hypoplasia</td>
<td>Generally unaffected</td>
</tr>
<tr>
<td>Muenke</td>
<td>Unilateral or bilateral brachycephaly</td>
<td>Mild to none</td>
<td>Variable carpal and tarsal fusions</td>
</tr>
<tr>
<td>Pfeiffer type I</td>
<td>Brachycephaly</td>
<td>Moderate</td>
<td>Broad thumbs and halluces. Variable limited syndactyly</td>
</tr>
<tr>
<td>Pfeiffer type II</td>
<td>Cloverleaf skull deformity with pansynostoses</td>
<td>Moderate</td>
<td>Broad thumbs and halluces. Variable limited syndactyly</td>
</tr>
<tr>
<td>Pfeiffer type III</td>
<td>Pansynostoses with marked turricephaly</td>
<td>Moderate to severe</td>
<td>Broad thumbs and halluces. Variable limited syndactyly</td>
</tr>
<tr>
<td>NAME OF SYNDROME</td>
<td>RELATIVELY UNIQUE FEATURES OTHER THAN CRANIOSYNOSTOSIS</td>
<td>FREQUENCY</td>
<td>MODE OF INHERITANCE</td>
</tr>
<tr>
<td>----------------------------------</td>
<td>--------------------------------------------------------------------------------------------</td>
<td>----------------</td>
<td>---------------------</td>
</tr>
<tr>
<td>Apert (acrocephalosyndactyly type I)</td>
<td>Severe brachycephaly, moderate hypertelorism, turricephaly, midface hypoplasia often causing airway obstruction, high-arched palate, 30% cleft palate, parrot beak deformity of nose, acne vulgaris, complex syndactyly of fingers and toes, lower than average IQ</td>
<td>1:160,000</td>
<td>AD One of two FGFR-2 mutations</td>
</tr>
<tr>
<td>Crouzon (acrocephalosyndactyly type II)</td>
<td>Most common craniofacial dysostosis, higher potential for increased intracranial pressure, high potential for optic nerve compression, no limb involvement</td>
<td>1:10,000</td>
<td>AD Multiple possible mutations in FGFR-2</td>
</tr>
<tr>
<td>Saethre-Chotzen (acrocephalosyndactyly type III)</td>
<td>Craniosynostosis not obligatory, bicoronal if present, low-set frontal hairline, upper lid ptosis, facial asymmetry, brachydactyly, usually partial simple syndactyly</td>
<td>1:25,000–50,000</td>
<td>AD Mutation in TWIST gene</td>
</tr>
<tr>
<td>Pfeiffer (acrocephalosyndactyly type V)</td>
<td>Broad thumbs and great toes, conductive hearing loss Type I: Mild form, bilateral coronal synostosis, normal intelligence, mild proptosis Type II: Most severe, cloverleaf skull, severe proptosis, hydrocephalus, midface deficiency Type III: Type II without cloverleaf skull, neurologic compromise, limited life span</td>
<td>1:100,000</td>
<td>AD FGFR-1 and FGFR-2</td>
</tr>
<tr>
<td>Carpenter</td>
<td>Tower-shaped skull, short neck, preaxial polydactyly, syndactyly, mild to moderate mental deficiency although may be normal, often associated with cloverleaf skull (pansynostosis), cardiovascular anomalies in up to one third of patients</td>
<td>Very rare</td>
<td>AR</td>
</tr>
</tbody>
</table>
Apert syndrome

- Apert described in 1906
- Craniosynostosis, exorbitism, midface hypoplasia
- Symmetric syndactyly of both hands and feet
- most as brachycephaly (coronal) with short AP dimension – turribrachycephaly/oxycephaly
- Class III malocclusion
- Hand syndactyly most often involves fusion of the 2~4 fingers - mid-digital hand mass
- Increased incidence of delayed mental development, but many of these patients develop normal intelligence (Apert vs. Crouzon)
Apert Syndrome
Defective gene: FGFR2

Normal Cells
Intracellular signal for development

The FGFR2 gene product is a protein receptor in the cell membrane that recognizes fibroblast growth factor [FGF]. FGF plays roles in cell division, cell growth, and embryonic development.

FGFR2
Fibroblast growth factor [FGF]

Mutated Cells
Stronger intracellular signal

The mutated FGFR2 gene produces a protein receptor product that exhibits enhanced functioning. This stronger signal results in primarily misaligned eyes (strabismus) as well as keratitis, corneal scarring, or optic atrophy. Other consequences are premature fusion of skull bones resulting in a misshapen head, distinct facial features, and/or digit abnormalities. Some patients exhibit development delay and cognitive impairment.

Marc E. Tischler, PhD
Dept. of Chemistry & Biochemistry
Univ. of Arizona
Pfeiffer syndrome

- Described by Pfeiffer in 1964
- Craniosynostosis, **broad thumbs** and toes, and partial syndactyly (2-3 digit)
- Type I  Brachycephaly
- Type II  Cloverleaf skull deformity
- Type III  Pansynostoses with Turricephaly / Oxycephaly
- Maxillary hypoplasia, midface deficiency, shallow orbits, exorbitism, hypertelorism and downslanting palpebral fissures
- Intelligence is reported to be **normal** in the more common
### Diagnosis

- PE, X-rays
- Genetic testing

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Gene (% responsible)</th>
<th>Mutations</th>
<th>Mutation Detection Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pfeiffer</td>
<td>FGFR2 (&gt;95%)</td>
<td>Several</td>
<td>67%</td>
</tr>
<tr>
<td></td>
<td>FGFR1 (&lt;5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apert</td>
<td>FGFR2 (100%)</td>
<td>Ser252Trp, Pro253Arg</td>
<td>&gt;98%</td>
</tr>
<tr>
<td>Crouzon</td>
<td>FGFR2 (100%)</td>
<td>Several</td>
<td>&gt;50%</td>
</tr>
<tr>
<td>Crouzon with acanthosis</td>
<td>FGFR3 (100%)</td>
<td>Ala391Glu</td>
<td>100%</td>
</tr>
<tr>
<td>Muenke</td>
<td>FGFR3 (100%)</td>
<td>Pro250Arg</td>
<td>100%</td>
</tr>
<tr>
<td>Saerthre Chotzen</td>
<td>TWIST1</td>
<td>Several mutations &amp; deletions</td>
<td>46% to 80%</td>
</tr>
</tbody>
</table>
Complications

- Airway obstruction
- Feeding impairment
- Raised intracranial pressure
- Visual changes-exposure related
- Hydrocephalus
Treatment

- Fronto-orbital and cranial vault remodeling → midface advancement procedure with or without distraction (Le Fort III or monobloc) → secondary orthognathic surgery to correct any dentofacial deformities (Le Fort I, mandibular osteotomies)

- Early age (4 to 12 months) for suture release, cranial vault decompression, and upper orbital reshaping/advancement

- Later age (4 to 12 years) for midface deformities and jaw surgery (14 to 18 years)

- The exact timing and surgical procedures is dependent on both the functional and the psychological needs of the patient
<table>
<thead>
<tr>
<th>Procedure</th>
<th>Timing (age)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Craniectomy, fronto-orbital advancement</td>
<td>4–12 mo</td>
<td>Repeat procedure may be indicated in childhood or adolescence for continued growth restriction or abnormal growth of the skull.</td>
</tr>
<tr>
<td>LeFort III osteotomy and advancement—conventional or by distraction osteogenesis</td>
<td>4–8 y</td>
<td>If performed in this age group, a secondary LeFort III may be required in teenage years.</td>
</tr>
<tr>
<td>LeFort III osteotomy and advancement—conventional or by distraction osteogenesis</td>
<td>9–12 y</td>
<td>Delaying to this age in less-severe cases may obviate the need for a second major midface advancement.</td>
</tr>
<tr>
<td>LeFort I ± mandibular osteotomy</td>
<td>14–18 y</td>
<td>Required to establish neutral dental occlusion after facial growth has ceased.</td>
</tr>
<tr>
<td>Monobloc frontofacial advancement—conventional or by distraction</td>
<td>4–12 y</td>
<td>Simultaneously improves forehead, orbital, and midface aesthetics. Suitable for a patient whose deformity allows simultaneous advancement.</td>
</tr>
<tr>
<td>Contouring via reduction, onlay bone grafts, bone substitutes, or alloplasts</td>
<td>15–19 y</td>
<td>Performed as the final procedure to enhance aesthetics after all growth has ceased.</td>
</tr>
</tbody>
</table>
References

- Role of FGF/FGFR signaling in skeletal development and homeostasis: learning from mouse models Su N et al Bone Research (2014) 2, 14003; doi:10.1038

Hemifacial Microsomia

Noha Alghobari
Advanced Operative
Hemifacial Microsomia

• A congenital disorder that affects the development of the lower half of the face

• Second most common FACIAL birth defect

• If severe it can lead to difficulties in breathing, obstructing the trachea and requiring a tracheotomy
Other names

- Lateral facial dysplasia
- First and second branchial arch syndrome
- Oral-mandibular-auricular syndrome
- Otomandibular dysostosis
- Craniofacial microsomia
- Goldenhar's syndrome
Prevalence

- 1 in 5600 live births.
- Males appear to be more frequently affected than females.
- It is usually unilateral (70%) and always asymmetrical if it exhibits bilaterality.
- 1-2% of cases report autosomal dominant transmission.
- A few families consistent with autosomal recessive have been reported.
Cause

- Disturbance of the blood supply to the first and second branchial arches in the first 6 to 8 weeks of pregnancy
Common features

Ears

- Microtia (small ear)
- Aural atresia (no ear canal)
- Preauricular tags or facial tags
- Other ear differences
Common features

Face

- FACIAL palsy (difficulty with muscle movement)
- Small cheekbone
- Epibulbar dermoid (pinkish-white growth on the eye)
- Macrostomia
- Cleft lip and palate
Common features

Jaw and teeth

- Trismus (limited opening of the mouth)
- Shortness of lower jaw
- Crooked lower jaw
- Malocclusion (bad bite)
Classification
S. Pruzansky’s mandible hypoplasia classification

• **Type I**: Mild hypoplasia of the ramus, and the body of the mandible is slightly affected.

• **Type II**: Functioning but deformed TM joint with anteriorly and medially displaced condyle.

• **Type III**: Absence of the ramus and glenoid fossa.
Other clinical features

• Mild mental retardation occasionally
• Bony anomalies, especially of the vertebral column
• Congenital heart diseases like VSD and hypoplasia of the lung
• Central nervous system malformation
Craniofacial Microsomia Diagnosis

- No genetic test
- Extra oral examination
- CT scan
• The wide spectrum of anomalies associated with HFM has made systematic and inclusive classification difficult.

• Classification of the disease aids in diagnosis, treatment planning, prognostic predications, and data evaluation.

• Two popular classification systems used for HFM, namely, the skeletal, auricular, and soft tissue (SAT) system, and the orbit, mandible, ear, nerve, and soft tissue (OMENS) system.
<table>
<thead>
<tr>
<th>Skeletal categories</th>
<th>Auricle categories</th>
<th>Soft tissue categories</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1 = Small mandible with normal shape</td>
<td>A0 = Normal</td>
<td>T1 = Minimal contour defect with no cranial nerve involvement</td>
</tr>
<tr>
<td>S2 = Condyle, ramus, and sigmoid notch identifiable but grossly distorted; mandible strikingly different in size and shape from normal</td>
<td>A1 = Small, malformed auricle retaining characteristic features</td>
<td>T2 = Moderate defect</td>
</tr>
<tr>
<td>S3 = Mandible severely malformed, ranging from poorly identifiable ramal components to complete agenesis of ramus</td>
<td>A2 = Rudimentary auricle with hook at cranial and corresponding to the helix</td>
<td>T3 = Major defect with obvious facial scoliosis, possible severe hypoplasia of cranial nerves, parotid gland, muscles of mastication; eye involvement; clefts of face or lips</td>
</tr>
<tr>
<td>S4 = An S3 mandible plus orbital involvement with gross posterior recession of lateral and inferior orbital rims</td>
<td>A3 = Malformed lobule with rest of pinna absent</td>
<td></td>
</tr>
<tr>
<td>S5 = The S4 defects plus orbital dystopia and frequently hypoplasia and asymmetrical neurocranium with a flat temporal fossa</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The skeletal, auricle, and soft tissue (SAT) classification system of HFM
The orbit, mandible, ear, facial nerve, and soft tissue (OMENS) classification system of HFM

<table>
<thead>
<tr>
<th>Orbit</th>
<th>Mandible</th>
<th>Ear</th>
<th>Facial nerve</th>
<th>Soft tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>O0</strong></td>
<td>Normal orbital size</td>
<td>Normal ear</td>
<td>No facial nerve involvement</td>
<td>No obvious soft tissue or muscle deficiency</td>
</tr>
<tr>
<td><strong>M0</strong></td>
<td>Normal mandible</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>E0</strong></td>
<td>Normal ear</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>N0</strong></td>
<td>No facial nerve involvement</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>S0</strong></td>
<td>No obvious soft tissue or muscle deficiency</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>O1</strong></td>
<td>Abnormal orbital size</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>M1</strong></td>
<td>Mandible and glenoid fossa are small with a short ramus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>E1</strong></td>
<td>Mild hypoplasia and cupping with all structures present</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>N1</strong></td>
<td>Upper facial nerve involvement (temporal and zygomatic branches)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>S1</strong></td>
<td>Minimal subcutaneous/muscle deficiency</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>M2</strong></td>
<td>Mandibular ramus is short and abnormally shaped</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>M2</strong> A</td>
<td>Subdivision A and B are based on relative positions of condyle and TMJ</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>M2</strong> B</td>
<td>Subdivision A and B are based on relative positions of condyle and TMJ</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>M3</strong></td>
<td>Complete absence of ramus, glenoid fossa, and TMJ</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>M3</strong> A</td>
<td>Submental vertex views were used to distinguish mandibular type 2A from type 2B</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>M3</strong> B</td>
<td>Submental vertex views were used to distinguish mandibular type 2A from type 2B</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>N2</strong></td>
<td>Lower facial nerve involvement (buccal, mandibular, and cervical branches)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>S2</strong></td>
<td>Moderate between the 2 extremes, S1 and S3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>M3</strong></td>
<td>Complete absence of ramus, glenoid fossa, and TMJ</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>M3</strong> A</td>
<td>Subdivision A and B are based on relative positions of condyle and TMJ</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>M3</strong> B</td>
<td>Subdivision A and B are based on relative positions of condyle and TMJ</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>N3</strong></td>
<td>All branches of facial nerve affected. Other involved nerves were also analyzed; eg, trigeminal N5 (sensory), hypoglossal N12; remaining cranial nerves are signified by the appropriate number in superscript</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>S3</strong></td>
<td>Severe soft tissue deficiency due to subcutaneous and muscular hypoplasia</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Type O, an apparently normal mandible has not been included in previous classification systems.
Treatment

• Depends:

1. Age

2. How much is the patient affected
Treatment

- Lowering of jaw on affected side
- Lengthening jaw
- Addition of bone to build up cheeks
- Soft tissue may be added to face
- 3 to 4 operations to rebuild ear
Treatment

- Treatment of hearing loss or deafness
- Speech therapy
- Managing feeding problems
- Orthodontics
- Treating associated problems like heart or kidney issues
Prognosis

VERY GOOD

Normal Lifespan    Normal Intelligence
Thank you
What is Hemangioma?

- Most common benign tumor → infancy
- Composed of blood vessels that are actively multiplying
- Not hereditary or genetic
- Most are not present at birth → appear within the first two weeks of life
- Commonly on the head and neck area (60%)
- Common in one area (80%)
- Bright red spot → increases in size/volume with time
- More common in girls
What is Hemangioma?

Possibility of shrinkage/regression:
- continue to grow for up to 12 months
- eventually shrink as the blood vessels stop growing
- red color begins to show patches of grey and white, and the hemangioma begins to soften as it becomes less engorged with blood
- most shrink very slowly over the course of 5–7 years.
1.5 years old

5 years old
hemangioma at 15 months old

hemangioma at 5 years old

hemangioma at 9 years old
What is Hemangioma?

- 30% of hemangiomas will leave behind a permanent deformity → redundant skin, fatty scar tissue, and residual vessels.
1 month old

3 years old
hemangiomas located around the eyes or in the airway near the vocal cords are potentially dangerous and require urgent treatment. Hemangiomas that block vision can lead to permanent lazy eyes (amblyopia), and hemangiomas that press on the eye can distort the cornea.

Medical intervention is required.
In Airway

- Hemangiomas in the airway can block breathing → life-threatening
- Medical intervention is required
Hemangiomas in the liver can become very large and stress the heart.

Need medical intervention.
In Parotid Gland

- salivary gland in front of the ear
- can lead to blockage of the ear canal
- both sides are affected → hearing loss
- medical treatment is usually necessary
Ulcerated hemangiomas → overlying skin breaks down and an open wound results

- In most, bleeding can be stopped with pressure
- treated with an antibiotic ointment
- if bleeding prevails → requires sustained pressure, combined with suture placement or urgent surgical intervention
Diagnosis

- Medical history: enlarging red/purple bump that began shortly after birth
- Physical examination: appearance of a strawberry-colored patch of skin
- Problematic cases → ultrasound or MRI scan is usually the preferred diagnostic test
Treatment 1

- Conservative observation
- Most shrink on their own → no treatment necessary
Treatment 2

- Laser treatment → multiple
- Selectively injure the blood vessels of a hemangioma
Treatment 3

- Medical treatment: steroids (e.g. Orapred) or interferon
- Suppresses growth and accelerates regression
Treatment 4

- Surgical intervention
- Remove/reduce a hemangioma
- Needs to be carefully planned
Thank you!

That's all Folks!
Exam Questions

1) In which area(s) does hemangioma most commonly occur? (HEAD/NECK AREA)
2) What is the physical appearance of hemangioma? (BRIGHT RED MARK)
3) What gender is more prone to developing hemangiomas? (FEMALE)
4) At what age do hemangiomas usually appear? (INFANCY)
5) Name one type of treatment for hemangioma (LASER)