Klinik Olgular 12

Is "Meow" the diagnostic criteria, indication of verdict of Cri dé Chat, Cat Cry Syndrome? A consideration of Disabilities by a case report*

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Mainly from the perspective of PossumWeb and OMIM
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Meowing is really for diagnostic criteria or the interesting findings for this patients? Odd looking infants are so close, therefore some form required that they can be easily discriminate. Cat Cry, "Meow" is one of the aspects. The case has to be considered human and humanity act must be learned or adapted, Disabilities must be considered and innovation mostly required.

Meow is specific criteria for Cat Cry Disease. We can have encountered at special cases as hypocalcemia or even hypoglycemia such kind of meow, but they are limited. After the given the substrates, all are dismissed or nearly gone. In some defective, handicapped infants, such kind of crying can be notices. They are high pitched but not really as meow. Thus, the typical meow, cat-cry noticed but not any dysmorphic and severe developmental features of the syndrome has been found in

individuals with a deletion confined to 5p15.3. 62-year woman diagnoses as cat cry syndrome and had a soft, high-pitched, cat-like voice is also recorded.

Therefore, here we are indicating the diagnosis is not confirmed by cat crying, but only be suspicious aspect for evaluation.

The best for all odd looking infants is genetic approach and routine investigation at the pregnancy period. For all, not only for Trizomi 21 or not for 18 and 15, but all other congenital malformations, have to be in check list of the ultrasound evaluation.

To be a member of the community, all the disable infants must be educated and be ready for the community life.

Özet

AMAÇ: Kedi Miyavlamasının tanı için yeterli olamayacağı belirgindir ama şüphe çekecek bir bulgu olacağı vurgulanmaktadır.

Dayanaklar/Kaynaklar (Materyal ve Metot): Bir olgu nedeniyle Kedi Miyavlamasının bir bulgu olarak ele alınabileceği POSSUM ve OMIM kaynakları temelinde incelenmektedir.

Kedi Miyavlaması Sendromu olan bir olgu nedeniyle, hastalığın genetik tanımlaması, kliniği ve ayırıcı tanısı sunulmaktadır.

Bunun ötesinde miyavlamanın oluşumu, miyavlamanın tipi ve boyutları üzerine değinilmektedir.

Bu olgu nedeniyle özürlülük durumları ve bunların izlenmesi konusu ele alınmaktadır. Bozukluk, yapamamazlık ve özürlük konusunda Gerçek tanı, Aktif yaşamsal durum, Eğitilebilir düzeyi, olup olmaması ve Zaman süreci (GAYE), (RAID=Rapid, Advancing, Improving, Daily) boyutu gündeme getirilmiştir.

1-Gerçek; Medikal Realite: Tanı Kedi Miyavlaması olması yeterli olmayıp, burada olgunun özürlerinin aktif yaşamına göre değerlendirilmelidir.

2-Aktif Yaşamsal boyut: Miyop olması değil, görme kusurunda gözlük kullanabilmesi önemlidir. Okumayı çözmesi ve okuyup değerlendirmesi, işlevsel olmalıdır.

3-Yaşamsal Boyut: Eğitilebilir, beceri kazandırılabilir ve insanlık boyutu önemlidir.

4-Eğitim Durumu, Süreç, Zaman: Birey özellikle çocuklar büyüyecek, gelişecek ve yaşlarına göre farklı konum ve boyutlarda olacaklardır. Bu açıdan da zaman içindeki gelişim dikkate alınmalıdır.

Anahtar Kelimeler: Aklı kullanma

Outline

Aim: Cat Crying is not a diagnostic criterion, but be a suspected aspect.

Grounding Aspects: The basic aspects on Chromosome 5, partial del 5p Disease are considered by POSSUM and OMIM perspectives.

The Syndrome of Cat Cry is evaluated by a case report. The clinical findings, the genetics and differential diagnosis also evaluated.

The king of meow is considered.

The impairment, Disability and Handicap is also discussed.

There are four dimensions of the perspectives to handicaps and stages are as followed.

RAID=Rapid Applications Induced for the Disease.

1-R. Rapid evaluation the Reality: Evaluation of the impairments and disabilities and handicaps
2-A. Advancing status, Application aspects due to the Educational condition: Restrictions of the functioning for daily life
3-I. Improving: Functional refining, inducing the training of daily acts as human necessities: Participation to be active living Word, but for an individual rights and as equal rights at the Human Rights, with humanity aspects.
4-D. Daily assessment to Disease, problems; Time concept, improving or steady state, or declination condition

Key Words: Cat Cry Disease, Chromosome 5, partial del 5p

A perspective to Cri du chat, Chromosome 5, partial del 5p, Cat Cry «Meow» disease

From POSSUM and OMIM

Cri du chat

- Syndrome Id: 3073
- OMIM Link: 123450
- Gene Location: 5p15
- Alternate Names: Chromosome 5, partial del 5p Cri-du-Chat Syndrome Cri du Chat Syndrome Chromosome 5, del 5p15.1-15.3
- **Updated:** 12/11/2013 - Catherine Rose

Description

Clinical

- Cri du chat syndrome. Named for the characteristic mewing cry in infancy. This cry disappears as the child's larynx grows, but altered voice and cry may persist.
- Moderate to severe mental retardation, mild dysmorphic features (round face, hypertelorism, micrognathia).
- In the adult features include microcephaly and mild facial coarseness, loss of hypertelorism, long face with prominent nasal bridge, prognathism and macrostoma.
- Report (Martinez 1993) of mother and daughter with del(5)(p14p15.3); and report (Cornish, JMG 1999) of a father and three children with deletion 5(p15.3-pter), with minimal intellectual impairment.
- Reduced cranial base angle was reported in cases with terminal deletions (Kjaer 1999).
- Case reported (Stathopulu 2003) with terminal deletion of chromosome 5p and phenotypical features of Lujan-Fryns syndrome (3705).
- A study of 50 cases (Marinescu 1999) demonstrated that there was no correlation between the size of the deletion and the level of developmental delay, and that

patients with cri-du-chat syndrome show high variability in the level of developmental achievement.

- Case report (Tsao 2006) with a complex karyotype, infantile spasms, hypsarrhythmia, nonketotic hyperglycinemia, and heterotopia.
- Three generation family reported (Fang 2008) with terminal 5p deletion (5p15.2-pter); the affected family members apparently share deletions of the same size, with variable mental symptoms within this family. Two affected females presented with moderate mental retardation and psychotic symptoms including delusions of persecution, auditory hallucinations, self-talking, and self-laughing, which are rare in cri-du-chat syndrome. In contrast, the other three affected males had mild-to-moderate mental retardation without psychotic symptoms.

Genetics

- In 85% of cases the deletion is de novo.
- Deletion of 5p15.3 associated with the cat-like cry and with speech delay; deletion of 5p15.2 results in the presentation of the other major clinical features of the syndrome.
- See also Chromosome 5, interstitial del 5p (5362).

Traits list

Stature (Also see Limbs)/Short stature - postnatal
Syndrome Aetiology/Chromosomal abnormality on karyotype
Chromosomal Site/Chromosome 5
Chromosomal Site/Arm p
Build/Small for gestational age (IUGR)
Build/Wasted, very thin build, FTT
Hair - Pigmentary Changes/Premature greying of hair
Skull and Scalp (See Radiology - Skull)/Microcephaly
Face - General Impression/Facies significantly abnormal
Face - General Impression/Expressionless, hypotonic, myopathic face
Face - Shape of Face/Round face
Face - Shape of Face/Long face
Face - Shape of Face/Broad cheeks
Face - Shape of Face/Structural asymmetry of face
Face - Orbital Region/Hypertelorism - Eyes widely spaced
Face - Orbital Region/Down-slanting palpebral fissures
Face - Orbital Region/Prominent supraorbital ridges
Face - Orbital Region/Deep set eyes, eye deeply set
Face - Lower Jaw/Micrognathia; agnathia; retrognathia
Ocular Region - Lids and Lashes/Lateral placement of inner canthi, telecanthus
Ocular Region - Lids and Lashes/Epicanthic folds, epicanthus
Eyes - Eye Movement Disorders/Paresis of ocular muscles, squint
Nose/Broad nasal bridge (see telecanthus)
Nose/Depressed nasal bridge
Lips and Mouth/Midline cleft lip
Oral Cavity - Palate and Alveolus (Also see Facial Clefts)/Cleft hard palate
Oral Cavity - Palate and Alveolus (Also see Facial Clefts)/High vaulted and narrow palate
Oral Cavity - Teeth/Abnormal tooth position, malocclusion, open bite
Ears - Location and Orientation/Low set ears
Ears - Location and Orientation/Posterior angulation of ears
Ears - Shape and Structure/Anotia, microtia
Ears - Shape and Structure/Preauricular tags, ear pits, ear sinuses
Ears - Hearing Loss/Hearing abnormal congenital or acquired
Abdominal Wall including Hernias/Inguinal hernia
Spine - Curvatures/Scoliosis
Upper Limbs - Hand and Wrist (see Radiology - Phalanges)/Small hand

Upper Limbs - Hand and Wrist (see Radiology - Phalanges)/Brachydactyly
Upper Limbs - Hand and Wrist (see Radiology - Phalanges)/Irregularities of length or shape of fingers
Upper Limbs - Hand and Wrist (see Radiology - Phalanges)/Syndactyly of fingers
Upper Limbs - Hand and Wrist (see Radiology - Phalanges)/Clinodactyly of 5th finger
Upper Limbs - Hand and Wrist (see Radiology - Phalanges)/Single transverse palmar crease, simian crease
Upper Limbs - Hand and Wrist (see Radiology - Phalanges)/Abnormal palmar dermatoglyphics, abnormal skin creases
Foot and Ankle/Talipes
Foot and Ankle/Syndactyly (other than minimal 2nd and 3rd toes)
Neurological - Structural Abnormalities/Holoprosencephaly, arhinencephaly
Neurological - Functional Abnormalities/Mental retardation - moderate to severe
Neurological - Functional Abnormalities/Hypotonia
Neurological - Functional Abnormalities/Muscular hypertonia, spasticity, rigidity, brisk reflexes
Neurological - Functional Abnormalities/Abnormal cry or voice
Respiratory, including Diaphragm/Laryngeal abnormality
Cardiovascular/Abnormal cardiovascular structure or function
Gastrointestine/Abnormal oesophagus including tracheo-oesophageal fistula
Gastrointestine/Dysphagia or feeding difficulty
Gastrointestine/Malplaced anus
Genitalia/Hypospadias, epispadias
Genitalia/Undescended or ectopic testes
Immune and Haematological system, Spleen/Thymic aplasia or hypoplasia
Radiology - Skull/Abnormal or J-shaped sella turcica
Radiology - Hands and Feet - Proximal Parts/Some metacarpals short and deformed

OMIM: CRI-DU-CHAT SYNDROME

CHROMOSOME 5p DELETION SYNDROME

NB: I hereby considered the OMIM report as contrubuted above, for full considerations.

Text

A number sign (#) is used with this entry because cri-du-chat syndrome is a well-described partial aneusomy resulting from deletion of the short arm of chromosome 5. There is a high probability that deletion of multiple genes is responsible for the phenotype as well as evidence that deletion of the telomerase reverse transcriptase gene (TERT; 187270) is specifically involved in the phenotypic changes of cri-du-chat syndrome.

Description

Cri-du-chat syndrome was first described by Lejeune et al. (1963) as a hereditary congenital syndrome associated with deletion of part of the short arm of chromosome 5. The deletions can vary in size from extremely small and involving only band 5p15.2 to the entire short arm. Although the majority of deletions arise as new mutations, approximately 12% result from unbalanced segregation of translocations or recombination involving a pericentric inversion in one of the parents.

Clinical Features

Cri-du-chat syndrome is characterized in young children by microcephaly, round face, hypertelorism, micrognathia, epicanthal folds, low-set ears, hypotonia, and severe psychomotor and mental retardation. One of the most characteristic features in newborns is a high-pitched cat-like cry that is usually considered diagnostic for the syndrome (see Overhauser et al., 1994); however, the characteristic cat-like cry without the typical dysmorphic and severe developmental features of the syndrome has been

found in individuals with a deletion confined to 5p15.3 (see Overhauser et al., 1994 and Gersh et al., 1995).

Kjaer and Niebuhr (1999) studied profile radiographs of the cranial face in 23 patients with cri-du-chat syndrome collected in Denmark in the 1970s. Twenty-two patients had terminal deletions of chromosome 5, and 1 patient had an interstitial deletion. The cranial base angle was in most cases reduced and in no cases increased compared to age-related standards for normal individuals. Malformations in the bony contours of the sella turcica and the clivus occurred in cri-du-chat patients with terminal deletions. They pointed out that this specific cranial base region develops around the notochord at the location from where the rhombencephalic-derived brainstem, pons, and cerebellum develop dorsally, and from where the neurons to the larynx migrate ventrally. They suggested that a cranial developmental field, originating from the notochordal location, is involved in the manifestations of cri-du-chat syndrome.

Van Buggenhout et al. (2000) pointed out that with advancing age the clinical picture of the cri-du-chat syndrome becomes less striking. They presented 7 patients with 5p deletion syndrome, with ages ranging from 16 to 47 years. Some of the clinical characteristics, such as long face, macrostomia, and scoliosis, became more evident. All patients were severely or profoundly mentally retarded except for one who was mildly retarded. Diagnosis was difficult to make in some of the patients who were first seen at an older age. In some of them, the craniofacial appearance resembled that of Angelman syndrome (105830). Most patients had periods of destructive behavior, self mutilation, and aggression.

Fang et al. (2008) reported a 3-generation Chinese Han family in which 5 members had cri-du-chat syndrome. The proband was a 62-year-old woman who presented to a psychiatric ward with temper tantrums, self-injuries, aggressive behavior, and psychotic symptoms, including delusions of persecution, auditory hallucinations, self-talking, and self-laughing. She had a soft, high-pitched, cat-like voice. Her 41-year-old daughter had mental retardation and similar psychotic features, which are rare in cri-du-chat syndrome. She did not have a high-pitched voice. In contrast, the other 3 affected males had mild to moderate mental retardation without psychotic symptoms. All affected individuals were found to have a 10.5-Mb terminal deletion at chromosome 5p15.2, which was confirmed and characterized by karyotyping, FISH, array CGH, and quantitative PCR analyses. The ROPN1L gene (611756) was found to be disrupted by the breakpoint. Although the affected family members apparently shared deletions of the same size, the variation in mental symptoms within this family suggested that other factors besides the size and location of 5p deletions may modify the mental presentation of patients with cri-du-chat syndrome. Fang et al. (2008) noted that familial occurrence of this disorder is rare.

Clinical Variability

Ladekarl (1968) reported a patient with features of cri-du-chat syndrome and Goldenhar syndrome (164210) associated with a 5q deletion. Choong et al. (2003) reported a male infant, born of nonconsanguineous parents, who had clinical features of cri-du-chat syndrome and Goldenhar syndrome. At birth, he was noted to have dysmorphic facial features, including bilateral preauricular tags, rotated ears, epicanthal folds, a left epibulbar lipodermoid, and an accessory left nipple. He also had hearing loss and feeding difficulties due to esophageal atresia with tracheoesophageal fistula, and horseshoe

kidney. In addition, he had a high-pitched, cat-like cry, characteristic of cri-du-chat syndrome. Cytogenetic analysis detected a terminal deletion of chromosome 5p14, consistent with the cri-du-chat locus. The association of Goldenhar syndrome and cri-du-chat syndrome in this patient suggested that the chromosome 5p14 locus may harbor a gene implicated with Goldenhar syndrome.

Population Genetics

The cri-du-chat syndrome appears to be one of the most common human deletion syndromes, with an incidence varying between 1 in 20,000 to 1 in 50,000 births (Niebuhr, 1978). The frequency in populations of profoundly retarded patients (IQ less than 20) is approximately 1% (Niebuhr, 1978).

Molecular Genetics

Overhauser et al. (1994) analyzed the 5p deletion breakpoints in 49 individuals using somatic cell hybrids. They used 5p-specific DNA probes to unambiguously order most of the chromosomal breakpoints present by hybridization to somatic cell hybrid DNA. Comparisons between the deletions present in the patients and their clinical features identified several chromosomal regions that were involved in specific clinical features. A critical chromosomal region involved in the high-pitched cry mapped to proximal 5p15.3 (probe D5S727), while the chromosomal region involved in the remaining features of the syndrome mapped to a small region within central 5p15.2 (probe D5S721). This latter region was estimated to be about 2 Mb in size. Deletions that did not include these 2 chromosomal regions presented varying clinical phenotypes from severe mental retardation and microcephaly to a clinically normal phenotype.

Gersh et al. (1995) studied 4 families in which patients with 5p deletions had only the characteristic cat-like cry, with normal to mildly delayed development. The precise location of the deletion in each family was determined by fluorescence in situ hybridization using lambda phage and cosmid clones. All of the deletion breakpoints mapped distal to a chromosomal region implicated with the facial features and severe mental and developmental delay in the cri-du-chat syndrome. The breakpoints were located distal to the 5p15.2 region and indicated to Gersh et al. (1995) that another genetic component of this contiguous gene syndrome is located in that area.

Simmons et al. (1997) isolated cDNAs from the cri-du-chat critical region by direct sequencing of a chromosome 5-specific cDNA library. A thrombospondin-like gene and 3 other cDNAs were considered candidate genes for the cri-du-chat contiguous gene deletion syndrome.

Cerruti Mainardi et al. (2001) studied 80 patients with cri-du-chat syndrome. Sixty-two had a 5p terminal deletion with breakpoints ranging from p13 to p15.2. Seven patients had a 5p interstitial deletion; 4 had a de novo translocation, and 3 had a familial translocation. Three had a de novo 5p anomaly involving 2 rearranged cell lines, and 1 had a 5p deletion arising from a paternal inversion. Cerruti Mainardi et al. (2001) identified a critical region at p15.2 for dysmorphism and mental retardation and a separate region at p15.3 for the cat-like cry, this region being bounded by the markers at D5S13 and D5S731. They also suggested a separate region at p15.3 for speech delay. The 62 patients were subdivided into 4 groups according to deletion size and a significant trend was identified, with increased severity of dysmorphism and developmental delay corresponding to increased size of deletion.

Medina et al. (2000) determined that the CTNND2 gene (604275) maps to a specific region in chromosome 5p15.2 implicated in the mental retardation phenotype of cri-du-chat syndrome. They characterized the breakpoints in patients with 5p terminal deletions with respect to the severity of mental retardation and the physical location of the CTNND2 gene and found a strong correlation between hemizygous loss of CTNND2 and severe mental retardation. Medina et al. (2000) concluded that these findings, and the properties of CTNND2 as a neuronal-specific protein, expressed early in development and involved in cell motility, supported its role in the mental retardation of cri-du-chat syndrome when present in only 1 copy.

The TERT gene is localized to the distal portion of chromosome 5p (viz., 5p15.33) and is the rate-limiting component for telomerase activity, which is essential for telomere length maintenance and sustained cell proliferation. Zhang et al. (2003) showed that a deletion of the TERT allele had occurred in all 10 patients with cri-du-chat syndrome whom they examined. Induction of TERT mRNA in proliferating lymphocytes derived from 5 of 7 patients was lower than that in unaffected control individuals. The patient lymphocytes exhibited shorter telomeres than age-matched unaffected individuals (P less than 0.0001). A reduction in replicative life span and a high rate of chromosome fusions were observed in cultured patient fibroblasts. Reconstitution of telomerase activity by ectopic expression of TERT extended the telomere length, increased the population doublings, and prevented the end-to-end fusion of chromosomes. Zhang et al. (2003) suggested that haploinsufficiency for telomere maintenance in vivo may be one genetic element contributing to the phenotypic changes in cri-du-chat syndrome.

Perfumo et al. (2000) reported 3 children with mosaic 5p rearrangements, 2 with a partial monosomic cell line and a partial monosomic/trisomic cell line and 1 with 2 different partial monosomic cell lines.

Zhang et al. (2005) used array comparative genomic hybridization to map DNA copy number changes in 94 patients with cri-du-chat syndrome who had been carefully evaluated for the presence of the characteristic cry, speech delay, facial dysmorphology, and level of mental retardation. Most subjects had simple deletions involving 5p; the deletion was terminal in 67 and interstitial in 12. Genotype-phenotype correlations localized the region associated with the cry to 1.5 Mb in distal 5p15.31, between BACs containing markers D5S2054 and D5S676; speech delay to 3.2 Mb in 5p15.33-p15.32, between BACs containing D5S417 and D5S635; and the region associated with facial dysmorphology to 2.4 Mb in 5p15.31-p15.2, between BACs containing D5S208 and D5S2887. Mental retardation depended approximately on the 5p deletion size and location, but there were many cases in which the retardation was disproportionately severe, given the 5p deletion. All 15 of these cases, approximately two-thirds of the severely retarded patients, were found to have copy number aberrations in addition to the 5p deletion. Restriction of consideration to patients with only 5p deletions clarified the effect of such deletions and suggested the presence of 3 regions, referred as MR-I, MR-II, and MR-III, with differing effect on retardation. Deletions including MR-I, a 1.2-Mb region overlapping the previously defined cri-du-chat critical region but not including MR-II and MR-III, produced a moderate level of retardation. Deletions restricted to MR-II, located just proximal to MR-I, produced a milder level of retardation, whereas deletions restricted to the still more proximal MR-III produced no discernible phenotype. However,

mental retardation increased as deletions that included MR-I extended progressively into MR-II and MR-III, and mental retardation became profound when all 3 regions were deleted.

South et al. (2006) reported a child with cri-du-chat syndrome and a terminal deletion 5p14.3 which microsatellite analysis confirmed was inherited from the mother. FISH analysis identified a paracentric inversion, inv(5)(p13.3p15.3), in the mother. South et al. (2006) noted that this was an unusual case because paracentric inversion carriers usually do not have liveborn children since recombination is predicted to result in unstable chromosomes that are embryonic lethal. South et al. (2006) proposed a mechanism involving dicentric chromosome formation with subsequent breakage and telomere healing during meiosis to explain the findings in this case.

Differential Diagnosis, Other Similar Syndromes

1) Lujan-Fryns syndrome

- Syndrome Id: 3705
- OMIM Link: 309520
- Gene Location: Xq13.1, Xq24
- Alternate Names: Lujan-Fryns syndrome X-linked mental retardation, Marfanoid build X-linked M.R., Marfanoid build
- **Updated:** 03/05/2016 - Catherine Rose

Clinical

- X-linked mental retardation syndrome with marfanoid build, lax joints, macrocephaly, absent corpus callosum, double row of teeth, micrognathia, long/narrow face, high arched palate, macrotestes, cardiac defects and normal karyotype.
- Behavioural disorders including autistic-like behaviour reported.
- Some cases have borderline or normal IQ.
- Reported in sister of an affected male (Gurrieri 1991).
- Report (Donders 2002) of a case with partial preservation of neurobehavioural abilities.
- Report (Alonso 2006) of a male case with a severe eating disorder.

Differential Diagnosis

- Different facial appearance from Marfanoid M.R. syndrome, Fragoso-Cantu type (3698), a recessively inherited Marfanoid mental retardation syndrome.
- Compare other X-linked mental retardation syndromes eg FG syndrome (3566); X-linked mental retardation, MED12 mutation, Lesca type (6981); X-linked M.R., Snyder-Robinson type (6201) also with marfanoid build; X-linked mental retardation, Tarpey type (6506).
- See also X-linked mental retardation, marfanoid habitus, mutations in the ZDHHC9 gene (6751).

Genetics

- X-linked dominant with higher penetrance and greater expressivity in males suggested (Gurrieri 1991).
- Caused by mutations in **MED12** (OMIM 300188) on chromosome Xq13.

- Mutations in MED12 also found in FG syndrome (3566); Blepharophimosis-mental retardation syndrome, Maat-Kievit-Brunner type (X-linked Ohdo syndrome) (6468); and X-linked mental retardation, MED12 mutation, Lesca type (6981).
- For a comparison of features of syndromes with MED12 mutations, see (**Graham & Schwartz 2013**).
- Mutations in **UPF3B** (OMIM 300298) on Xq24 reported (Tarpey 2007) in 2 families with Lujan-Fryns (6506), and one family with FG syndrome (3566)
- Case reported (Stathopulu 2003) with terminal deletion 5p, and additional features of hypotonia, scoliosis, kyphosis, asymmetric IUGR.

2) Chromosome 5, interstitial del 5p

- Syndrome Id: 5362
- OMIM Link:
- Gene Location:
- Alternate Names: Chromosome 5, interstitial del 5p Chromosome 5, terminal del 5p
- **Updated:** 23/05/2012 - Catherine Rose, **Reviewed:** 05/03/2015 - Catherine Rose

Clinical

- Report (Keppen 1992) of a 3 generation family with an interstitial deletion of the short arm of chromosome 5, with variable features including microcephaly, mental retardation, hypertonia and micrognathia. [Karyotype del 5(pter->14.3::p13.3->qter)]. These features appear specific to del 5p13.
- Report (Johnson 2000) of a father and son with interstitial del 5p14; the father was considered to be phenotypically normal, the son has microcephaly, seizures, and global developmental delay.
- Report (Hulinsky 2005) of a fetus with interstitial del 5p(p13.1p14.2) diagnosed postnatally with Cornelia de Lange syndrome (3183).
- Cases reported (Descartes 2006, Josifova 2004) with Oculoauriculovertebral spectrum (3339) with 5p15.33-pter deletion.
- Case reported (Bayrakli 2010) with a heterozygous 5p13.3-13.2 deletion with type I Chiari malformation and bilateral Duane retraction syndrome.
- Report (Barber 2011) of a family in which a transmitted interstitial deletion of 5p13.3 to 5p14.3 co-segregated with learning and/or behavioural difficulties in six family members. Facial dysmorphism was not a feature but a father and daughter both had lacrimal fistulae.

Chromosome 5, terminal del 5p: Three generation family reported (Fang 2008) with terminal 5p deletion (5p15.2-pter); the affected family members apparently share deletions of the same size, with variable mental symptoms within this family. Two affected females presented with moderate mental retardation and psychotic symptoms including delusions of persecution, auditory hallucinations, self-talking, and self-laughing, which are rare in cri-du-chat syndrome. In contrast, the other three affected males had mild-to-moderate mental retardation without psychotic symptoms.

3) Chromosome 5, interstitial del 5q

- Syndrome Id: 4825
- OMIM Link:

- Gene Location:
- Alternate Names: Chromosome 5, interstitial del 5q
- **Updated:** 21/08/2015 - Catherine Rose

Description

Clinical

- Phenotype varies with size of deletion.

Del 5q12:

- Cases reported with psychomotor retardation, coarse facies and ocular anomalies (6888).

Del 5q13.1q15:

- Interstitial del 5q13.1q15 reported (Krishna 1997) with growth hormone deficiency.
- Del 5q14.3-q15 (6697) with MEF2C deletion, variable phenotype including periventricular heterotopia, severe mental retardation, stereotypic movements, and epilepsy; or with NR2F1 deletion.
- Del 5q13 specific to Werdnig-Hoffman/SMA1 (Burlet 1996).
- Report of microdeletion 5q13.2 and Oculo-auriculo-vertebral syndrome (3339) (Huang 2010).

Del 5q15q21.3:

- Interstitial deletion 5q15q21.3 reported (Malan 2006) with renal anomalies, facial dysmorphism with high forehead, downslanting palpebral fissures, and ear anomales; and talipes and flexion of fingers.
- Case reported (Ofner 2006) with 5q21.1-q23.1; features include bilateral epicanthal folds, low-set dysplastic ears, short nose with anteverted nostrils, conically shaped fingers, generalised increase of subcutaneous fat, multiple fine venous telangiectasia on back, mild pectus carinatum, and a general muscular hypotonia.
- See also Chromosome 5, interstitial deletion 5q14.3-q21 (6639).

Del 5q15q34:

- Interstitial deletion 5q15-q31.1 with features of congenital contractural arachnodactyly (3027) (Courtens 1998); and with microcephaly and dysmorphic facies (De Michelina 1990).
- Interstitial del 5q31q33 (Kramer 1999) with multiple congenital anomalies.
- Report of childhood myelodysplasia with del 5q21-q34 (Shikano 1992).
- Interstitial microdeletion 5q31.1q31.2 reported (Mosca 2007) in a girl presenting with abnormal cry (cri-du-chat like), upslanting palpebral fissures, hypertelorism, anteverted nostrils, microretrognathia, growth retardation, and an adenoid cyst at the base of the tongue.
- See also Chromosome 5, microdeletion 5q31.3 (6861).
- Note possible schizophrenia susceptibility at 5q21-q23.1 (Bennett 1997).

Del 5q22-5q31:

- Report (Ansari 2014) of cases with deletions in 5q22-5q31 with Pierre Robin sequence, talipes equinovarus, finger contractures and crumpled ear helices.

- Report (Tecos 2015) of a case with deletion in 5q23, cleft palate, bilateral club feet, high grade myopia, possible mild hearing loss, dysphagia, hypotonia, and developmental delay.

Del 5q33q35:

- Interstitial del 5q33-q35 with hypertonicity, microcephaly, short neck, apparently low-set ears, micrognathia, camptodactyly, mild rocker bottom feet, large VSD, PDA, pulmonary hypertension, hypoplastic right ventricle and death at age 3 months (Gibbons 1999).
- Interstitial del 5q33.3-q35.1 (Spranger 2000) with mild psychomotor delay, seizures, minor facial anomalies including small, deep set eyes with apparent hypertelorism, thin upper lip, thick everted lower lip, bulbous nose, congenital hypotonia, and dystonic movements of arms.
- Interstitial del 5q33.1q35.1 (Northup 2008) with primary amenorrhoea, seizures, and severe beavioural and developmental deficiencies.
- Refractory macrocytic anemia is associated with del 5q31.1 (OMIM 153550).
- See also terminal deletion 5q (5344).

4) Mental retardation, short stature, DeLozier-Blanchet type

- Syndrome Id: 4613
- OMIM Link:
- Gene Location:
- Alternate Names: Mental retardation, short stature, DeLozier-Blanchet type M.R., S.S., DeLozier-Blanchet type

Description

Clinical

Single case report of severe growth and mental retardation, hyperextensible joints, triangular face and multilobulated ear tags.

This girl has a 5p15 microdeletion.

Differential Diagnosis

See Chromosome 5, partial del 5p (3073) (Cri-du-Chat syndrome).

5) M.R., microcephaly, unusual facies

- Syndrome Id: 4033
- OMIM Link:
- Gene Location:

Description

Clinical

Single case report (Theile) of a mentally retarded boy with distinctive facies and scoliosis. Features include microcephaly, hypertelorism, epicanthic folds, narrow palpebral fissures, broad nasal bridge, small nose with anteverted nares, high arched palate and crowded teeth, low-set ears and undescended testes.

Differential Diagnosis

These are fairly non-specific features.

Compare Chromosome 5, partial del 5p (3073) (Cri-du-Chat syndrome)

Genetics
Uncertain.

The types of meowing

For the cat owner, ask me how is the meow form? I have a patient diagnosed as cat cry disease, therefore ı said I can answer to you. First I must indicate that, please, not yell at the cat, for meowing. It is the only communication with the people and cat. Please try to understand what the cat wants to say.

Types of meowing (http://www.petful.com/behaviors/cat-meows-constantly/);
They are;

- For attention; please look at me, listen me
- Meaning of sickness; so, pitched cry, astonishing you and you feel restless
- Hunger; you are not giving my food; I am hungry
- Stress; even animals are under stress, mostly because of human, by not considered them. Annoying to you also an indication of the meow. Afraid of, fearing and frightening is nearly same meow.
- Old age problems and confusions; if you want to estimate the real age of the cats and be comparable to human, you must multiply by 7-8. 10 years old cats are near 80 years old. So, the problem of getting older as seen same as cats and human.
- The cat is in heat; Because of the fur, the hot seasons are so anxious for them, they need cooling places.
- The cat just wants to say hello; want to communicate
- Sexually to find a partner; March meow of the cats.

At the cat cry disease, I have noticed the meow as indicated above; as if it wants to say hello.

For cultural evidences, there are 3 kind of acts to the cats/pets and cats to human beings; a) Friendly and want to be petting, b). anxious and only for demanding of food, but keep a distance with the people, c) run away as soon as possible, when noticed a human.

Case Description

Case Report

33 gestational week preterm girl is delivered because of PPROM and two twisted chord by Cesarean/Section. The third children of 28 years old women, with two normal kids, with 1905 grams' (50^{th} percentile) birth weight, 32 cm (90^{th} percentile) Head Circumference, Thorax is 30.5 cm, length is 43 cm (50^{th} percentile) in circumference.
There is no obvious finding at the 33 Gestational Week old preterm. Slight blond hair, as usual finding for an indication of genetic evaluation. The crying is so obvious and like the cat cry. This is also mentioned by the nurses and all the Intensive Care medical staff. Anatomic and other functional examination is performed with the professions of Ear,

Nose, Throat and Neurology. Not obvious mental retardation, may be because of the age or clinically normal phenotype.
After informative consent, the blood is taken for the genetic evaluation.

History

The Baby was born, at 18th January 2016, delivered by C/S, 1905 grams; and discharged at 10th February 2016, at 1985 grams, to bring after a week for controlling and genetically evaluation.

All this duration she was followed at Neonatology Intensive Care Unit. Clinically, Respiratory Distress Syndrome (required ventilation and Continuous Positive Airway Pressure/CPAP), Patent Foramen Ovale (PFO), septic attacks, indirect hyperbilirubinemia, anemia, hypoglycemia, feeding problems (Total Parenteral Nutrition and Peripherical Partial Nutrition is given).

Genetic Evaluation

After indicating the family for notice the concept of meowing, the informative consent is taken. At the Periferal blood/lymphocytes/cell cultures the diagnosis is confirmed.
29 metaphase plate and 100 interphase core/nuclei is evaluated. The FISH analysis demonstrates 5p.15.2 (D5S721, D5S23) region, deletion at the mono allele, indicating positive for Cat Cry Disease/Syndrome.
More detailed information is given to the family and amniocentesis and chorion villus biopsy is advice for early detection for the other probable pregnancies.
After the discharge, general Survey for the estimated problems/finding is mentioned to the family.
NB: Overhauser et al. (1994) analyzed the 5p deletion breakpoints in 49 individuals using somatic cell hybrids. A critical chromosomal region involved in the high-pitched cry mapped to proximal 5p15.3 (probe D5S727), while the chromosomal region involved in the remaining features of the syndrome mapped to a small region within central 5p15.2 (probe D5S721). This latter region was estimated to be about 2 Mb in size. Deletions that did not include these 2 chromosomal regions presented varying clinical phenotypes from severe mental retardation and microcephaly to a **clinically normal phenotype**.

Genetic Counselling

a) Medical Reality, true diagnosis

For discussion Trisomy 21 may be taken in notice.
Diagnosis of 21 Trisomy is not real medical confirmation. Each person is unique and not be classified, the concept of case as unique as yes, not as diagnosis of a disease. Impairments, disabilities and handicaps in order the other congenital malformations and for the evaluation as an individual one, the only person, as sole; so on at Human Rights. Therefore, there are at least three basic legs, for stabilization of the diagnosis; 1)

Geneticist perspective, 2) Clinical concepts, 3) Perinatologist, pregnancy. For follow up; a) Pediatric Genetics, b) Developmental Pediatrics, c) Pediatric Neurologist, d) Pediatric Psychiatry, e) other medical sciences concerning the malformations and problems.

b) Family History

De novo or other considerations mostly be noticed by family history. The evaluation of genetic aspects of the family; mother and father may be a good contributor for the diagnosis.

c) Risk Evaluation

What will be, and what will be other perspectives? The only way is to follow up medically and education must be performed by special teacher, professional activity on the problems, conditions.

d) Medical Precautions

The medical aim for each individual, is early diagnosis, check-up procedures, carefully evaluated and required to follow up and be concerned the impairments, not to be handicaps, confirmed them.

e) Medical Counselling

Medical counselling is not only informed the disease, the condition. This is a collaboration of these 5 aspects all together, with special team as consultation concepts.

Discussion

From; a) http://www.aihw.gov.au/WorkArea/DownloadAsset.aspx?id=6442455478, b) Wikipedia

The 1980 ICIDH provides a conceptual framework for disability which is described in three dimensions. We can have classified the problems at 3 concepts (ICIDH=International Classification of Impairments, Disabilities and Handicaps):

a) Impairment

In the context of health experience an impairment is any loss or abnormality of psychological, physiological or anatomical structure or function.
This can be notices, single tissue, organ, system or multisystem dysfunction Slight, moderate or severe is the conditional state. They must be objective evidences.

b) Disability

In the context of health experience, a disability is any restriction or lack (resulting from an impairment) of ability to perform an activity in the manner or within the range considered normal for a human being.
Disability is concerned with functional performance or activity, and limitations therein, affecting the tissue, organ or system but influenced to whole person. The daily life is directly concerned about the disabilities.

c) Handicap

In the context of health experience, a handicap is a disadvantage for a given individual, resulting from an impairment or a disability, that limits or prevents the fulfilment of a role that is normal (depending on age, sex, and social and cultural factors) for that individual. (WHO 1980)

Handicaps must be objective and grounding on the evidence. Evidence based classification have to be encountered.

Handicap focuses on the person as a social being and reflects the interaction with and adaptation to the person's surroundings. The negative concepts are indicated.

The differences are can be considered as;

1) Myopia. Mostly the common reflection problem of the eye is myopia. This can be corrected by the lens. The disabilities are corrected. But it not, the sight is blurring and cannot see the foresight and like a blind condition. This unresolved conditions are handicaps. This one is objective physical condition.
2) Mental conditions can be corrected by special medical approach, medical education for the impairments and also medical drug therapy adjustments. Drugs have to be balanced due to the condition of a person. If any brain damage, it is disabilities and later on handicapped person. Physiological aspects are also considered as IDH facets.
3) Cultural conditions. People want to be slave and like and admired to be slave. If you are considering even to teach or put in an environment of liberties, they strictly turned back to be a slave. This is a protection, sheltering and obeying to be a good person, by easiest way not any responsibility. The other side, you cannot make slave to a born free person even an animal. They are died in the cages.

We have to consider the third dimensions as stated 1980 ICIDH and 1997 ICIDH-2.

Table 1: Third dimensions of the 1980 Handicap roles and 1997 ICIDH-2 Participation of other concepts

1980 Handicap—six survival roles	**1997 ICIDH-2 Participation—seven domains of Participation**
✓ Orientation handicap	✓ Physical independence handicap
✓ Physical independence handicap	✓ Mobility handicap
✓ Mobility handicap	✓ Occupation handicap
✓ Occupation handicap	✓ Social integration handicap
✓ Social integration handicap	✓ Economic self-sufficiency handicap
✓ Economic self-sufficiency handicap	✓ Another handicap
✓ Another handicap	✓ Participation in personal maintenance
	✓ Participation in mobility
	✓ Participation in exchange of information
	✓ Participation in social relationships
	✓ Participation in the areas of education work, leisure and spirituality
	✓ Participation in economic life
	✓ Participation in civic and community life

Note

This patient has to be on the follow-up procedures, considering with a team; specialist on the problems, physiotherapist, pediatric physiatrist, psychology, developing pediatrics, neurologist etc. This team will be also being in a close contact and be evaluated by council formation, continuously. Sharing the responsibilities in a same way, in a same line, in front.

This will be done, have to done, for all the human, who needs special care.

Last Words

Congenital conditions that causing of the IDH points, for functionally there is still something we have done. This perspective can be noticeable for four dimensions as RAID=Rapid Applications Induced for the Disease.

Fourth dimensions of the disabilities before considering the handicaps:

1-R. Rapid evaluation the Reality: Evaluation of the impairments and disabilities and handicaps

2-A. Advancing status, Application aspects due to the Educational condition: Restrictions of the functioning for daily life

3-I. Improving: Functional refining, inducing the training of daily acts as human necessities: Participation to be active living Word, but for an individual rights and as equal rights at the Human Rights, with humanity aspects.

4-D. Daily assessment to Disease, problems; Time concept, improving or steady state, or declination condition

This is basically considering for the Cat Cry disease patient.