CASE REPORT --- Cornelia de Lange Syndrome

Cornelia de Lange Syndrome: A rare disorder with Ophthalmologic findings
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Abstract: An 8 year old male pediatric patient presented with Cornelia De Lange syndrome, a rare disorder associated with significant ocular findings. Blepharitis, microcornea, synophrys, long lashes, hypertichosis of the brows, and myopia were also present.

1. Case History:
   a. Demographics: 8 year old Caucasian male
   b. Chief Complaint: itchy red eyes, decreased since last visit.
   c. Reason for visit: blepharitis follow up
   d. History:
      i. Ocular: bilateral microcornea (photo), bilateral chronic blepharitis (photo), intermittent alternating exotropia, latent nystagmus, superficial punctuate keratitis
      ii. Medical: Cornelia De Lange Syndrome, gastroesophogeal reflux disease (GERD), bilateral complete phacomelia of upper limb (photo), mental retardation
   e. Medications:
      i. Zegrid 20 mg pack, Prevacid (GERD)
      ii. Multivitamins
      iii. Artificial tears QID, Ocusoft lid scrubs, Refresh 1% solution, Refresh .5% solution (Blepharitis)

2. Pertinent Physical findings: Wheel chair bound, bilateral phacomelia, patient unable to communicate verbally or with sign language

3. Pertinent Ophthalmic findings:
   a. Bilateral chronic blepharitis
   b. Bilateral microcornea
      i. OD: 8-9 mm OS: 8-9 mm first measured 12/2005
      ii. Last IOP: 3/2010 16/12 pulsair
      iv. Gonio deferred secondary to normal IOP range, small cup to disc ratio, negative corneal straie OU.
   c. Optic Nerve Head
      i. C/D: 0.3 OD, 0.4 OS
      ii. Disc: pink round choroidal crescent 360 OU
   d. Bilateral synophrys (photo), bilateral long lashes (photo), bilateral hypertichosis of the brows (photo), bilateral mild myopia, moderate astigmatism OU
      i. Rx:
         • OD: -2.00 -2.50 X 180 2 BU ADD +1.00
         • OS: Plano -2.50 X 180 2 BU ADD +1.00

4. Differential Diagnosis:
   a. Primary leading diagnosis: Microcornea
      i. Differential Dx:

ii. Treatment:
- Treatment of glaucoma (most often surgical), prosthesis, low vision aids.

b. Secondary leading diagnosis: blepharitis
i. Differential Dx: Pediculosis
ii. Treatment:
- Warm compresses, artificial tears, erythromycin or bacitracin ung, restasis, oral tetracycline or doxycyclin

5. Diagnosis and discussion:
   a. Condition:
      i. Cornelia De Lange Syndrome (CdLS) has an incidence of approximately 1 in 10,000 births in USA, 1 in 50,000 in Denmark with no sex predominance. (i) Studies have established an autosomal dominant inheritance pattern arising from spontaneous mutations. (ii) More recently it has been noted that 65% of patients with CdLS have genetic mutations. Both Krantz et. al. and Tonkin et. al. noted mutations in \textit{NIPBL} on chromosome 5p13, where as Musio A and Deardorf MA noted mutations in \textit{SMC1A} on chromosome Xp11, and \textit{SMC3} on chromosome 10q25 (iii). These genes are all associated with the cohesion complex which is responsible for the control of sister chromatid segregation during mitosis and meiosis. (iii)
      ii. Unique ocular symptoms:
         - Patients affected with CdLS have been known to have: synophrys (99%), long lashes (99%), hypertrichosis of the brows (96%), peripapillary pigment (83%), myopia (58-60%), ptosis (44-45%), nystagmus (37%), blepharitis (25%), epiphora (22%), microcornea (21%), and nasolacrimal duct obstruction (16%), some of which were observed by Sommer A and Jackson L during their research as cited by Barakat et. al. (vi) (vii). Two cases of CdLS patients with coats disease have been reported. (v) (vi)
            o Over the course of his care at our institution our patient exhibited the classic CdLS signs of microcornea, blepharitis, synophrys, long lashes, hypertichosis of the brows, peripapillary pigment, myopia, and nystagmus.
      iii. Unique Systemic features:
         - The diagnosis of CdLS is done entirely on phenotypic findings. Ranzini et. al. found that the presence of long eyelashes in conjunction with unusually long hair on the fetal back being pathognomonic to this syndrome (i).
         - CdLS is a multisystem disorder in which Brachmann W, and De Lange C. characterized by pre and post-natal growth delay, mental retardation, microbrachycephaly, hirsuitism, visceral and limb anomalies and a characteristic face including synophrys, long eye lashes, antverted nostrils, a long philtrum, thin lips, downturned corners of the mouth, micrognathia, a low-pitched growling voice, flexion contractures, and micromelia (i). Schwartz et. al. found that patients with CdLS are more likely to have endocrinopathies such as hyperthyroidism,
panhypopituitarism, and/or deficient growth hormone secretion. (i).
Other systemic abnormalities reported by Sommer A and Jackson L
include: severe hearing loss (52%), gastrointestinal reflux (48%),
seizures (23%), ureteral reflux (12%), cryptorchidism, repeated upper
respiratory infections and pneumonia (25%) (i), and congenital heart
disease (29% with the most frequent finding of ventricular septal defect)
(iv)
- Beck B reported that CdLS has a 5-20% mortality rate especially in boys
age 0-4, often caused due to cardiac or gastrointestinal complications (i).
  - Of these features, our patient exhibited growth delay, mental
retardation, limb anomalies including bilateral phacomelia, and
gastroesophageal reflux disease. No information regarding other
systemic features of CdLS were noted in his chart.

6. Treatment, management:
   a. Treatment and response to treatment:
      i. Bifocals were prescribed for full time wear to correct his myopic/astigmatic
correction, accommodative spasm, as well as BU yolked prism to help the child
focus his attention on near activities. Chronic blepharitis was treated with lid
scrubs and warm compresses daily. Also he has been given artificial tears to be
used qid, and gel tears qhs. Due to the complexity of this syndrome, those
affected require care from multiple practitioners such as optometrist, cardiologist,
endocrinologist, gastroenterologist, and various occupational/physical therapist.

7. Conclusion:
   When evaluating patients with CdLS, the most common clinical features to look for are:
synophrys, long lashes, myopia, peripapillary pigment, and hypertrichosis of the brows.
These patients have also been noted to having ptosis, epiphora, nasolacrimal duct obstruction,
and microcornea. The knowledge of the key findings associated with CdLS combined with
proper follow up can minimize complications and improve the quality of life of these
patients.

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