Trisomy 4p and ocular defects

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Trisomy of the short arm of chromosome 4 is a relatively well studied pathology. At least 85 cases have been reported,4-12 74 of them were reviewed by Kleczkowska et al.13 Despite the fact that most patients with trisomy 4p have no serious eye defects, some recent data suggest that some forms of ocular pathology may be relatively common for this condition.

Case report
A girl was born at term after the first pregnancy of healthy 22-year-old unrelated parents. Her birth weight was 3200 g and length was 52 cm. Severe microphthalmos on the right and uveal tract coloboma on the left were mentioned in the delivery room. Further ophthalmic examination revealed coloboma of the iris, choroid, and retina. The right eye was encleated and replaced by a prosthesis.

Examination at the age of 4 years and 4 months showed a relatively short girl (97 cm, just below the 5th percentile) with normal weight (17.2 kg, above 50th percentile) and head circumference. Her fine motor development and speech were delayed. She had brachycephaly, a large nose

lateral part of the globe and angulation was seen during adduction. Histological examination showed fibrosis and minimal atrophy of the medial rectus.

Comment
Hugonnier and Magnard1 claimed that the aetiology of MM is myositis. Our patient showed limited abduction and positive forced duction test as in Hugonnier and Magnard's cases, but in addition there was atrophy and fibrosis of medial rectus muscle fibres by histological examination. Knapp2 also reported the same ocular motility abnormalities in patients with high myopia without histological abnormalities. Zolog3 found disappearance of muscular fibres of lateral recti in two similar patients.

Bagolini and coworkers claimed that pressure of the large globe on the lateral rectus results in paralysis of the muscle with subsequent esotropia in six patients with MM. They stated that in addition to paralysis of the lateral rectus, direct pressure on the muscle or capillary bed may play an important role in the aetiology. Instead of a marked forced duction test at adduction, they found only a slightly increased cytoplasmic component of muscle fibres and moderate hypertrophy on histological examination of the medial rectus; but we found substantially increased connective tissues and diminished dimension of myofibres.

Demer and Von Noorden4 reported a high myope patient with restrictive motility disturbance owing to the contact between the elongated globe and the medial wall of the orbit. But orbital CTs and MRIs of our patient demonstrated enough space at maximum abduction between the medial rectus and the globe. Ruttum et al5 demonstrated flattening of the posterosomal wall of the globe against the medial orbital wall at abduction in a patient with MM. We have seen flattening of the posterolateral wall of the globe at adduction but not at abduction, so we do not think that the limitation of abduction is caused by contact between the globe and medial wall of the orbit.

In patients with myopia, the globe continues to enlarge during adulthood while the orbit ceases to grow. When the eye continues to grow, it begins to compress on the lateral rectus. As a result of this compression, lateral rectus becomes atrophic and esotropia occurs. Long standing esotropia may cause medial rectus fibrosis, in turn further increasing esotropia. In the later decades, atrophy of the soft orbital tissues may contribute to lateral rectus dysfunction by decreasing the protective effect of the muscle.

with bulbous tip, short philtrum, chubby cheeks, and massive chin. Her hair was thick and coarse. The asymmetric convexity of the left half of thorax, simian crease on the right palm, brachydactyly of thumbs, partial syndactyly of 2-4 toes on the right and 2-3 toes on the left were also mentioned. Second toes were placed above third ones.

A cytogenetic study showed partial trisomy 4p: 46,XX,der(15)(4;15)(p14;p11). Her mother was a balanced carrier of a t(4;15)(p14;p11). The mother’s second pregnancy resulted in a spontaneous abortion at 9-10 weeks.

Comment
Some ophthalmic abnormalities (epicanthus, strabismus, ptosis, mongoloid, or antimongoloid slanting of the eyes, etc) are relatively common for many syndromes of autosomal imbalance, including trisomy 4p. The structural eye defects (micro/anophthalmos, colobomata) are less common but much more specific.

Including our case, microphthalmos has been found in at least 10 patients with trisomy 4p. In six patients it was an isolated structural eye pathology, in two patients (Wiegand; our case) it was associated with colobomata, and in one patient with microcornea. In the case of Schinzel and D’Apuzzo right sided microphthalmos was associated with left sided anophthalmos. Anophthalmos was described twice: in the patient of Herva and von Wendt where a large segment of chromosome 4 was duplicated [dup(4)(pter-q21)], and in the patient of Schinzel and D’Apuzzo with a duplication of the most distal segment of 4p (pter-p15.2). We are not inclined to oppose anophthalmos and microphthalmos because these defects may be only different steps of the same morphogenic disturbance. Therefore it is obvious that duplication of the chromosomal material from the ‘tip’ of 4p may be responsible for anophthalmos (and microphthalmos) in this condition.

Coloboma of the uveal tract was detected in our patient and in three more patients with trisomy 4p. In two of these cases colobomata were the only structural defects of the eyes and in two other patients there were associations of colobomata and microphthalmos. In all four patients colobomatous defects involved iris, choroid, and retina. The optic disc was involved in two patients. The minimal size of duplication in patients with coloboma is 4pter-p14 (our case).

Colobomata and microphthalmos/anophthalmos were found in patients with varying forms of trisomy 4p. Both sporadic and familial 4p rearrangements were found. In the latter group there were patients with recombinant forms of pericentric inversion of chromosome 4p. 4p malsegregation of different reciprocal translocations or more complex rearrangement. These data suggest that trisomy for the short arm of chromosome 4 leads to serious ocular defects (microphthalmos or anophthalmos, colobomata of the uveal tract) in at least 15% of patients. The coexistence of coloboma and microphthalmos in some patients with trisomy 4p and in some other conditions allows us to anticipate a common mechanism for the origin of these defects.

Only three syndromes of chromosomal imbalance are characterised by higher frequency of micro/anophthalmos and coloboma (trisomy 13, distal monosomy 13q, triploidy). In this connection trisomy 4p should be regarded as a condition with a relatively high probability of serious ocular defects.

Coloboma of the iris is typical also for patients with Wolf-Hirschhorn syndrome, where a distal part of the short arm on one chromosome 4 is lost. Mild microphthalmos and microcornea have been also described in some patients. Severe psychomotor and growth delay, cleft lip and/or palate, and various visceral abnormalities are the typical non-ophthalmic findings in this syndrome. Although most cases of the Wolf-Hirschhorn syndrome are sporadic, sometimes genetically opposite syndromes – partial trisomy 4p and partial monosomy 4p (Wolf-Hirschhorn syndrome) have been described in different persons from the same families with translocations or pericentric inversions. Coloboma is also characteristic of the so-called ‘cat eye’ syndrome.

Because colobomata, microphthalmos, and other ocular defects may be results of different chromosomal rearrangements, cytogenetic examination of every patient with eye abnormalities and developmental delay (or mental retardation) should be recommended.

Meningitis as a complication of dacyrocystorhinostomy

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A blocked lacrimal drainage system may cause much inconvenience because of epiphora and recurrent infections. Lacrimal block can give way to serious complications such as recurrent dacryocystitis (acute or chronic) and orbital cellulitis, which is a potentially life threatening condition. The ultimate solution for a blocked drainage system is surgical opening. Dacyrocystorhinostomy is a commonly used procedure for relieving lacrimal drainage obstruction. Among the possible complications of this operation are inadequate drainage because of intra-nasal pathology, contracted sac, or postoperative closure and intraoperative bleeding either as a result of incision of the nasal mucosa or, in more severe bleeding, because of laceration of the anterior ethmoidal artery in anteriorly placed ethmoidal air cells. No mention of postoperative infectious complications in remote organs has been made in English language reports. We feel it is of interest, therefore, to report a case in which bacterial meningitis developed in an otherwise healthy girl 1 day after dacyrocystorhinostomy.

Case report
A 9-year-old girl was admitted to our department for dacyrocystorhinostomy because of right nasolacrimal obstruction. She had a history of recurrent dacryocystitis and epiphora since birth and had not been relieved by two attempts at tubing and probing. On admission, no history of upper respiratory tract infection in the child or in her close neighbourhood was reported, nor was any other complaint reported. On physical examination, the child looked healthy; body temperature was 36.7°C, and no pathology was revealed except epiphora. The lacrimal sac was neither enlarged nor tender and showed no signs of acute infection.

The following day the girl underwent a dacyrocystorhinostomy. Surgical incision was made about 8 mm medial to the medial commissure, beginning at the level of the medial canthal tendon and extending downward some 15 mm. The skin incision and angular vein were put on haemostatic suture. The ipsilateral nostril was packed with an ENT tampon saturated with 1% cocaine and 1:1000 adrenaline solution in the region of the attachment of the anterior end of the middle turbinate.

The subcutaneous tissue was separated with Freer elevators down to the bone, and the peristeum was elevated. The medial canthal tendon was put on suture and cut down to the bone. The peristeum was elevated on both sides of the incision and over the anterior lacrimal crest downward into the nasolacrimal canal and backward to the posterior lacrimal crest. The bone of the anterior lacrimal crest and wall of the lacrimal fossa were removed with a small trephine and the nasal mucosa carefully separated from the bony margins. The opening was enlarged with a flat nosed Kerrison punch. The bony medial half of the nasolacrimal canal was removed. The nasal mucoperiosteum was elevated from the canal down to the inferior turbinate. The sac was opened by a pointed Bard-Parker blade through both the peristeal and mucosal walls, and a similar incision was made in the nasal mucoperiosteum adjacent and parallel to the one in the tear sac.

Flaps were sutured using 6/0 plain gut after washing out the anastomosis with an antibiotic solution (amoxicillin). The periosteum was closed with a running 6/0 plain gut suture, and the subcutaneous tissue with a similar one. The skin was closed with a running mattress 6/0 nylon suture. Nasal packing was changed with a sterile piece of gauze.

During the operation body temperature was