Down syndrome

Down syndrome is a multiple malformation syndrome due to the trisomy of chromosome 21.

Complications

In Down syndrome children, functional constipation and lower urinary tract infections have been described, together with higher risk for incontinence and delayed sphincter control. At present, no clear association between Down syndrome, Bladder Bowel Dysfunction and neural tube defects has been previously described.

Case presentation: We describe two female patients with Down syndrome presenting Bladder Bowel Dysfunction in association with neural tube defects, who both underwent personalized multidisciplinary intervention and pelvic floor rehabilitation, with good clinical outcomes.

Conclusion: At present, no screening program has been established in order to rule out neural tube defects or neurogenic urinary anomalies in Down syndrome patients presenting bowel and/or bladder dysfunction. In our opinion, presence of spinal abnormalities, despite rare, may be contribute to urinary symptoms and should be ruled out in patients presenting progressive or persistent Bladder Bowel Dysfunction. Early diagnosis and management of spinal cord defects associated with neurogenic urinary dysfunction may allow to prevent possible complications [1)]

Down syndrome may be associated with various neurologic complications such as moyamoya disease, cervical spinal cord compression due to atlanto-axial subluxation, and basal ganglia damage, as well as epileptic seizures and stroke [2)].

Down syndrome is associated with ligamentous laxity of the spine. This has implications whenever a fusion is contemplated, as adjacent segment failure with kyphosis is very common. Ligamentous laxity may also result in atlanto-axial subluxation (AAS).

Atlanto-axial subluxation in Down syndrome

Atlanto-axial subluxation in Down syndrome

Neurological complications

(Cerebral) amyloid angiopathy may be more prevalent in patients with Down syndrome.

Many cases of Down syndrome accompanied by isolated neurologic manifestations have been

reported in children; however, Down syndrome with multiple neurologic conditions is rare [3].

There is epidemiological evidence that individuals with Down syndrome are at decreased risk for solid tumors including brain tumors. It has been suggested that some genes expressed on the extra copy of chromosome 21 act as tumor suppressor genes and contribute to the protection against tumorigenesis.

Yolk sac tumor [4]

Yamamoto et al. report the first Down syndrome patient, an 8-year-old boy, with a meningioma in the posterior fossa. The diagnosis was based on histological study of the surgically resected tumor. Postoperatively his neurological status improved and there was no tumor regrowth in the next 2 years. Fluorescence in situ hybridization (FISH) for chromosome 22 confirmed high allele loss involving the NF2 gene locus, a finding typical in meningiomas. FISH also revealed chromosome 21 heterogeneity in tumor cells; not only cells with trisomy 21 but also cells with disomy and monosomy 21 were present. All blood cells from the patient manifested trisomy 21.

This finding suggests that deletion of the chromosome 21 allele may be associated with the tumorigenesis of meningioma in Down syndrome. It supports the hypothesis that some genes whose expression is increased on the extra copy of chromosome 21 function as tumor suppressor genes and that they contribute to the reduced tumor incidence in individuals with Down syndrome [5].

Down syndrome (DS) patients with early-onset dementia share similar neurodegenerative features with Alzheimer disease (AD) [6].

Individuals with Down syndrome (DS) are at increased risk of developing AD in adulthood as a result of chromosome 21 trisomy and triplication of the amyloid precursor protein (APP) gene. In both conditions, the central nervous system (CNS) basal forebrain cholinergic system progressively degenerates, and such changes contribute to the manifestation of cognitive decline and dementia. Given the strong dependency of these neurons on nerve growth factor (NGF), it was hypothesized that their atrophy was caused by NGF deficits. However, in AD, the synthesis of NGF is not affected at the transcript level and there is a marked increase in its precursor, proNGF. This apparent paradox remained elusive for many years [7].

Down syndrome results in neuromotor impairment that affects selective motor control, compromising the acquisition of motor skills and functional independence.

A study received approval from the Institutional Review Board of Universidade Nove de Julho (Sao Paulo,Brazil) under process number 1.540.113 and is registered with the Brazilian Registry of Clinical Trials (N° RBR3PHPXB). The participating institutions have presented a declaration of participation. The volunteers will be permitted to drop out of the study at any time with no negative repercussions. The results will be published and will contribute evidence regarding the use of this type of intervention on children [8].

Cervical spine pathologies

Cervical spine pathologies are common in Down syndrome (DS) patients. Cervical pathologies may cause cord compression and neurologic deterioration if left untreated. Complication rates of 73-100% have been reported in DS patients after cervical spine surgery in historical studies.

Current techniques may improve pseudarthrosis ($p = 0.009$), LOR ($p = 0.043$), and first attempt ($p = 0.038$) and overall fusion rates ($p = 0.018$) compared with historical studies. Complications continue to challenge most patients (82.4%). A total of 16 of 17 patients (94.1%) demonstrated stabilization or improvement in neurologic status. Apparent successful outcome in the majority appears to warrant the high complication risk associated with cervical spine surgery in DS patients. The anterior approach resulted in a higher risk of complications than posterior ($p = 0.032$). Siemionow et al report a higher than expected incidence of pseudarthrosis in DS patients receiving rhBMP-2, putting its benefit in DS patients into question [9].

Mouse model of Down syndrome

see Ts65Dn.

Case reports

A 7-year-old boy with Down syndrome and atlanto-axial subluxation. The patient presented with an ischemic stroke in the left hemisphere and cervical cord compression with increased cord edema. Diagnostic digital subtraction angiography revealed unique patterns of vascular involvement, with retrograde flow through the anterior spinal artery, ascending cervical artery, occipital artery, and multiple leptomeningeal arteries compensating for bilateral vertebral artery occlusion. This case underscores the underreported phenomenon of upward retrograde flow through the anterior spinal artery in bilateral vertebral artery occlusion. They address the rare manifestation of posterior circulation involvement in moyamoya syndrome, highlighting the importance of considering atlantoaxial instability as a contributing factor, as the absence of atlantoaxial stability is a risk factor for vertebral artery dissection. This study contributes valuable insights into the intricate relationship of moyamoya syndrome, Down syndrome, and atlantoaxial instability, urging clinicians to consider multifaceted approaches in diagnosis and treatment. It also emphasizes the potential significance of the anterior spinal artery as a compensatory pathway in complex vascular scenarios [10]

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