CENTRIOLE DYSFUNCTIONS AND MICROCEPHALY

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Microcephaly is a neurological developmental disorder that leads to an extreme reduction in brain size associated with a reduced pool of neural precursors (NPCs). This is often due to defects in centrosome biogenesis that impairs symmetric divisions during early brain development and leads the premature differentiation of these cells.

A mutation in the centrosomal protein CPAP causes Seckel syndrome, characterized by microcephaly and reduced body size. Ultrastructural analysis of Seckel cells shows cilia longer than normal, due to a delay in their disassembly. Consequentely NPCs do not re-entry into the cell cycle leading to their premature differentiation. Therefore, the primary cilium plays a key role in NPCs maintenance and the timely cilium disassembly mediated by CPAP is very important in neurogenesis and brain size control.

Microcephaly could be also due to viral infections. It has been reported that the Zika virus (ZIKV) is associated with microcephaly in newborns. Human brain organoids derived from induced-Pluripotent Stem Cells (iPSCs), infected by an Asian strain of ZIKV, were analyzed ultrastructurally by TEM. ZIKV infection perturbs the centrosomal structures and affects the orientation of the mitotic spindle of the apical neural progenitor cells. This results in the premature differentiation of NPCs and leads to progenitor depletion and impairment of neurogenesis.

Keywords: Microcephaly, Zika virus, Centrioles.

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OSTEOPOROSIS: NOT JUST A DISEASE OF WOMEN

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Osteoporosis is a systemic skeletal disease characterized by a reduction in bone mass and qualitative skeletal changes (macro- and microarchitecture, material properties, geometry, and micro-damage) that cause an increase in bone fragility and higher fracture risk. There are two forms of the disease: (a) primary osteoporosis, which includes juvenile, postmenopausal, and male and senile osteoporosis; and (b) secondary osteoporosis, which is caused by a large number of diseases and medications. Fragility fractures may occur in almost all skeletal segments, but the preferential locations are the vertebral column, the proximal femur and humerus, and the distal radius (Colles fracture). In 2017, only in Italy, there were about 560,000 fragility fractures with a cost for the National Health System of 9.4 billion euros; these are important numbers destined to grow. In fact, in the coming decades the many Italians born in the 50s (the so-called Baby Boomers) will arrive at the critical age for fragility fractures, it is therefore estimated that in 2030 the incidence of bone fragility will increase by 22.4% to reach 690,000 with an increase in direct costs of 26.2%, equal to 11.9 billion euros, thus clearly exceeding the costs associated with ischemic stroke and chronic obstructive pulmonary disease.

Many people think that osteoporosis is a problem that only affects women. It is not so! Although the disease certainly affects women the most, it has an impact that is far from negligible even in men, in which it can have more serious and devastating consequences. It is estimated that around the world about one man in five above the 50 years will undergo sooner or later a fracture due to osteoporosis and in most cases, in men, the disease is not diagnosed and treated, even after the fracture event. As for women, the mortality rate after a femur fracture increases with age and is greatest in the 12 months after the event. However, in males the mortality rates following a fracture are higher and men are more likely to have serious consequences after the event.

Male osteoporosis is frequently secondary (about two thirds in males against one / third in women) and therefore pathological conditions associated with osteoporosis should always be excluded. As in other primitive osteoporosis, the pathogenesis of male osteoporosis is multifactorial with the sharing of genetic, nutritional and hormonal factors and risk factors for osteoporosis for males are largely the same as those of women, but two more may be added to these: testosterone deficiency (primary or secondary hypogonadism) and the possible use of androgen deprivation therapy (ADT), a treatment commonly used in prostate cancer. In the presence of these risk factors, a man between 50 and 69 years should undergo a dual-energy X-ray absorptiometry (DXA), to assess whether he has osteoporosis; the examination to assess bone density should be performed in any case at the age of 70 years and in particular in men who have already suffered a fracture following a fall after the age of 50 years, in those being treated with steroids or ADT or have low testosterone levels.

Keywords: Osteoporosis, Fragility Fracture, Male Osteoporosis, Androgen Deprivation Therapy.

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