Commentary

Pituitary abnormalities in midline brain defects

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Pituitary is centrally located in the middle of the brain and embryologically originates from two different groups of cells, the first deriving from an upward protrusion of ectodermal cells from the pharynx (anterior pituitary), the second from a downward evagination of diencephalic neuroectodermal cells (posterior pituitary). Several genes are implicated in such a complex development (HESX1, OTX2, PROP1, POU1F1, LHX3, LHX4, SOX2/SOX3, and others) [1,2] and their mutations often cause congenital hypopituitarism, with possible deficiency of one or more hormones produced by the gland. Since the eye and the forebrain share a common embryological origin with the pituitary gland (mutations in the genes HESX1, SOX2/SOX3 and OTX2 has been found to affect both the embryonic development of the eyes, optic nerves and pituitary gland) [3], the association between pituitary and ocular defects are not rare. Among these, septo-optic dysplasia (SOD), firstly described in 1956 by the French-Swiss neurologist de Morsier [4], is the most known. Typically, SOD is characterized by optic nerve hypoplasia, agenesis of septum pellucidum and/or corpus callosum and finally by various degrees of pituitary hypoplasia. Its prevalence in Europe has recently been calculated between 1.9 and 2.5 per 100,000 births [5], therefore can be classified as rare disease (OMIM 182230). Phenotype is highly variable with only 30% presenting the classic triad: for the diagnosis of SOD, in fact, two out of the three above-mentioned signs are sufficient. If the pituitary is involved, growth hormone deficiency is the most frequent defect, followed by thyroid-stimulating hormone defect, adrenocorticotropic hormone, gonadotropins and less frequently arginine vasopressin with diabetes insipidus. As a whole, the clinical picture is characterized by optic nerve hypoplasia, agenesis of septum pellucidum and/or corpus callosum and

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study was led, has presumably an efficient National Health System, with specialists able to treat properly all patients with pituitary hormonal deficiencies.

As a whole, pituitary involvement in midline brain defect is common and multiple pituitary deficiencies are almost inevitable in case of pituitary stalk interruption and ectopic posterior pituitary, regardless the presence of optic nerve abnormalities. SOD is a complex syndrome with sometimes unpredictable endocrine outcome: only centres having an expert team made of pediatric endocrinologist, ophthalmologist, neurologist, cardiologist and others will be able to follow these complex patients and avoid sometimes life-threatening complications.

The findings obtained by Cerbone et al. thanks to the unique case series described, gives an extensive overview on the possible endocrine involvement in patients with SOD, optic nerve hypoplasia and multiple pituitary hormone deficiency, making every reader more expert in this difficult topic.

Declaration of Competing Interest

None.

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