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Pituitary adenoma in monozygotic twins with Cri du Chat syndrome: a rare case report

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Abstract: Pituitary adenomas are rare tumours of pediatric population. In etiology, genetic factors are more common than they are in adults. Because of the rarity of the cases, there are only a few large case studies in the literature. Pituitary tumours in children are often related with syndromes like MEN type 1, Carney Complex and McCune Albright, but there is no case in the literature associated with Cri Du Chat syndrome. Statistically, it has been reported that, pediatric tumours occur more often in twins, in the pediatric population. Main treatment for prolactinomas is medical intervention with dopamine agonists, as in adults. Surgery is preferred when the tumour is resistant to medical treatment or shows mass effects around sellae. In that situation, as in adults, both transcranial and transsphenoidal approach is possible.

Key words: pituitary, Cri du Chat, twins, adenoma

Introduction

Pituitary adenomas are rare tumours in children and adolescents. They comprise approximately 3% of all suprasellar pediatric tumors and 2-6% of them can be surgically treated (3, 13). Pituitary tumours in children are rarely malignant and secretory. ACTH secretory adenomas occur more frequent in early childhood but the most common secretory adenomas in elder children are prolactinomas (5, 9, 17). Although etiology is uncertain, concordance with genetic syndromes, oral contraceptive use in

pregnancy, twinning and some malignancies are reported (4). The best known genetic syndromes accompanying pituitary adenomas are multiple endocrine neoplasia type 1 (MEN 1), Carney complex, familial isolated pituitary adenoma (FIPA) and McCune Albright syndromes.

Case presentation

14 years old monozygotic twin sisters, who had been diagnosed with Cri Du Chat syndrome, were admitted to hospital with premenarcheal galactorrhea complaint.

Pituitary magnetic resonance imaging (MRI) was performed. Both sisters presented with a pituitary lesion of 5.8mm x 3.3mm and a 3.4mm x 2.6mm, respectively, with low contrast enhancement, which was compatible with pituitary microadenoma (figures 1, 2).

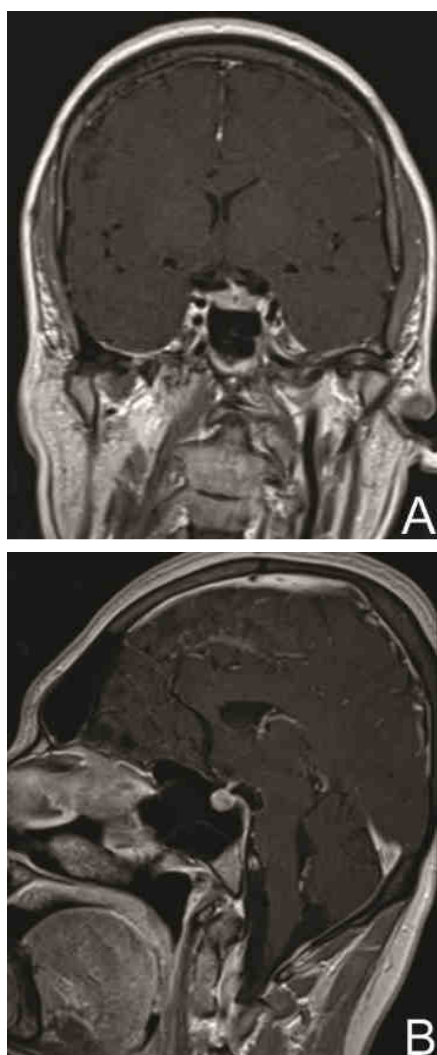


Figure 1 - MRI study showing a 5.8mm x 3.3mm solid lesion with low contrast enhancement in the right portion of the pituitary gland, suggestive for a microadenoma. A. Coronal view. B. Sagittal view

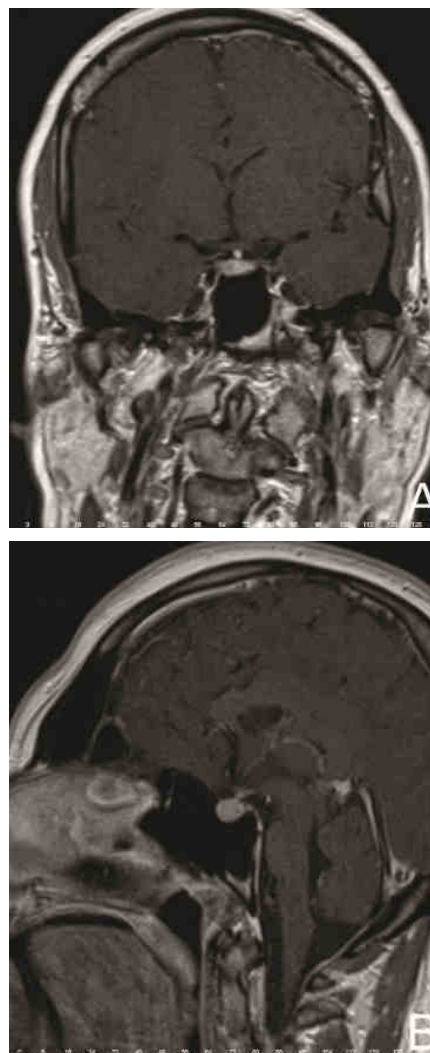


Figure 2 - MRI study showing a 3.4mm x 2.6mm sized cystic lesion with low, peripheral contrast enhancement in the right side of the pituitary gland. A. Coronal view. B. Sagittal view

Prolactin levels were respectively 120 $\mu\text{g/L}$ and 70 $\mu\text{g/L}$ (normal range 3.3-26.7 $\mu\text{g/L}$). Laboratory studies revealed no renal dysfunction or hypothyroidism. Visual examination appeared suboptimal, although the exam was scarcely reliable because of the

patient mental retardation. Surgical intervention was suggested for both patients, but family refused the surgery. Patients were directed to the endocrinology department for medical treatment and follow-up.

Discussion

Cri Du Chat syndrome is a hereditary congenital syndrome, caused by a deletion on short arm of 5th chromosome (7). Incidence is 1/20.000-50.000 birth (11). Microcephaly, round face shape, hypertelorism, micrognathia, low ear line, hypotonia and various psychomotor symptoms and mental retardation are common findings. The main clinical feature is, a high-pitched monochromatic cry, that gives the name to the syndrome (7, 12). 'Some studies demonstrated the association between deletions on 5q and neoplasia like acute myeloid leukemia, myelodysplastic syndrome and Crohn disease (14). Morphological anomalies of the clivus and sella turcica, but not any pituitary disorders nor increase in the risk of neoplasia has been reported in Cri du Chat syndrome (6).

Some studies have reported an increased prevalence of some tumors, i.e. testicular and non-thyroid endocrine cancers - in twins. On the other hand, colorectal cancer and leukemia appear to be less frequent in twins. In a study including 3,200 twin cancer patients, the reported frequency of pituitary tumours was two-fold higher than in the general population, but the etiopathological mechanisms remain to be defined (4).

Pediatric pituitary adenomas are extraordinarily rare tumours in early childhood. Frequency is a little bit higher in

adolescents but still very rare relative to adults (9). These tumours in pediatric population are frequently part of a genetic condition. Pituitary tumors often present in the context of MEN type 1, Carney complex, FIPA and McCune Albright syndromes. Mutations to oncogenes and tumour suppressor genes, like GNAS, PTTG, HMGA2, and FGFR-64, have been also identified in sporadic cases of pituitary adenoma (2, 15). In early childhood, ACTH secretor tumours are the most common functional adenomas although they are very rare. They usually occur as a part of MEN type 1(8). During adolescent period, rate of prolactinomas and growth hormone secretory tumours evaluated relatively higher (1). Beside genetic factors, oral contraceptive use, high parity count and twinning also considered among potential risk factors (4). Some authors suggest that pituitary adenomas in children are more aggressive than in adults, although this matter is still largely debated' and add references.

50% of all pituitary tumors are prolactinomas. They occur more often in late childhood and girls (9). Two main complaints are headache and visual deficits, due to mass effect, but delayed puberty, amenorrhea and galactorrhea are more characterised complaints in girls.

"The first line treatment for prolactinomas in both children and adults is dopamine agonists. Main purpose is to reduce both prolactin levels and tumour size (10). Conditions like acute visual deficit, hydrocephaly, CSF leakage require emergency surgery. Elective surgery should be reserved to cases of resistance to medical treatment (16).

Conclusion

Pediatric pituitary adenomas are extremely rare tumors which relationship with genetic syndromes have been revealed. Beside known syndromes, their concomitance with different syndromes in some cases, shows the importance of genetic studies. Further investigations are necessary to enlight the possible genetic etiology.

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