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Detrimental role of GATA transcription factors on Gn rh receptor gene expression is counterbalanced by LIM homeodomain proteins through a bi-functional response element
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GATA2 transcription factor and LIM homeodomain proteins LHX3 and ISL1 play leading roles in the determination and differentiation of endocrine cell lineages in the developing pituitary. They are thought to be involved in gonadotrope cell fate and maintenance and, thus, implicated in the expression of marker genes of this lineage. One of this gene, the GnRH receptor gene (Gnrhr), crucial for gonadotrope function, is expressed in the developing pituitary gland from embryonic day 13 onward, thus well before the LH and FSH beta subunits. This expression pattern suggests the implication of early transcription factors in Gnrhr promoter activation and inspection of promoter sequences indeed revealed the presence of several WGA/TAR and TAAT motifs that may confer GATA and LHX3/ISL1 responsiveness, respectively. In this study, using a well-characterized transgenic mouse model, GATA2, LHX3 and ISL1 were co-localized with Gnrhr promoter activity in the pituitary. Transient transfection of Gnrhr promoter luciferase fusion constructs together with either GATA2 expression vectors or Small interfering RNA in gonadotrope cell lines indicated that GATA2, which typically acts as a trans-activator, unexpectedly repressed Gnrhr promoter activity. We demonstrated using DNA chromatography affinity and EMSA that GATA2 operates via a response element containing a WGA/TAR motif and two TAAT motifs that bound LHX3 and ISL1. Despite the inhibitory action of GATA2, this element nevertheless displayed a clear-cut enhancer activity, even if placed upstream of a minimal promoter. ChIP assays indicated that GATA2, LHX3 and ISL1 interact with Gnrhr promoter fragment encompassing this element in gonadotrope cell lines. Altogether these data strongly suggest that the trans-repressive action of GATA2 on Gnrhr promoter activity is balanced or even hindered by trans-activating effects of LIM homeodomain proteins via this novel bi-functional LIM/GATA response element. This hierarchical interplay may contribute to gonadotrope cell fate and maintenance.
Hormonal results showed increased prolactin (9000 ng/mL), with associated panhypopituitarism.
Intravenous antibiotics and hydrocortisone replacement therapy lead to a favourable clinical outcome. An endoscopic transphenoidal debulking procedure was performed. At surgical exploration, a breach in the inferior part of the sphenoid sinus was detected, occluded by a massive tumour protrusion. Histological evaluation confirmed the diagnosis of pituitary adenoma.
Meningitis is an unusual complication of pituitary macroadenomas. A missed or delayed diagnosis could have a major impact on morbidity and mortality. Disrupted bony skull may induce CSF rhinorrhea and promote infection of cerebrospinal fluid causing acute meningitis.
CSF rhinorrhea is a well known complication of transphenoidal surgery and radiotherapy. Less commonly, it is reported as a complication of medical treatment of prolactinomas by dopamine agonists. Spontaneous CSF rhinorrhea is a far less frequent complication of invasive macroadenoma, being reported only in isolated cases.
Acute bacterial meningitis not preceded by CSF rhinorrhea in patients with an untreated pituitary macroadenoma represents an exceptional event. Only three cases have been reported in literature.
Bacterial meningitis complicating an invasive macroadenoma may clinically mimic pituitary tumour apoplexy. Differentiating the two entities in an emergency setting may be challenging.
In our patient CSF analysis was the clue in the differential diagnosis between meningitis and pituitary apoplexy.
Our case shows that in case of detection of a macroadenoma in a patient with headache and high body temperature, lumbar puncture should be considered to rule out bacterial meningitis, even if a clinical history of rhinorrhea is absent.

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Macroprolactinoma and meningitis: An atypical presentation
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We report the case of a 31-year-old man presenting a six days history of severe headache and vomiting. A body temperature of 38.5°C was measured. Neuroimaging showed an invasive pituitary lesion, extending to both the cavernous sinuses and the sphenoid sinus, involving the third ventricle and compressing the optic chiasm. No cerebrospinal fluid leakage was detected by imaging.
At lumbar puncture, a purulent cerebrospinal fluid (CSF) was observed, containing 11,900 white blood cells/µL, 6.3 g/L proteins; 39 mg/dL glucose; 81 mg/dL lactate.

Hormonal results showed increased prolactin (9000 ng/mL), with associated panhypopituitarism.
Intravenous antibiotics and hydrocortisone replacement therapy lead to a favourable clinical outcome. An endoscopic transphenoidal debulking procedure was performed. At surgical exploration, a breach in the inferior part of the sphenoid sinus was detected, occluded by a massive tumour protrusion. Histological evaluation confirmed the diagnosis of pituitary adenoma.
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