Immunohistochemically, the endometrial glands were CK20 negative and CK7 positive, while the endometrial stroma was CD10 positive. Similarly the colon mucosa stained positive for CK20 and negative for CK7.

From her medical history, we learnt that in 2003, at 19 years of age, she had presented with galactorrhea and abdominal pain to an obstetrics and gynecology clinic. With the discovery of hyperprolactinemia [49 ng/ml (6–30)] a hypointense mid-adenohypophyseal lesion of 4 × 2 mm in size was detected on MRI. She was prescribed on a slow-release formulation of bromocriptine at a dose of 2.5 mg/day. By May 2005, she was switched to 0.25 mg cabergoline, twice a week. Follow-up prolactin levels are depicted in Fig. 1. A hypophyseal MRI in April 2007 did not reveal any lesion prompting discontinuation of treatment. However, despite normal findings on a repeat MRI in March 2009, her symptom of galactorrhea recurred.

Endometriosis is a rare cause of gastrointestinal bleeding that may be undetectable on endoscopic biopsy (Miller et al., 1994; Yantiss et al., 2001). The submucosal localization of the endometriosis in this case may have contributed to the negative histopathological findings on repeat biopsies. For colorectal endometriosis, MRI and rectal endoscopic sonography are both diagnostic modalities with comparable accuracy (Bazot et al., 2007). Surgical extirpation is recommended for advanced endometriosis (Bailey et al., 1994).

The recurrence of galactorrhea followed by rectal bleeding between April 2007 and March 2009, during which period the patient was not on Cab2 treatment seems to support the ideas proposed by Novella-Maestre et al. Apparently the patient had neglected her follow-up visits for her prolactinoma after receiving a premature diagnosis of rectal cancer.

**References**


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**Reply: Rectal endometriosis and prolactinoma**

We thank Dr Kurt and co-workers for providing a clinical example showing a possible link between hyperprolactinaemia and endometriosis, and the potential beneficial effect of dopamine agonists (DA) in the treatment of the disease.

Several previous reports have focused on the association between hyperprolactinaemia and endometriosis (Gregoriou et al., 1999; Cunha-Filho et al., 2002). It has been postulated that the hyperprolactinaemic state could explain infertility related to mild and moderate endometriosis, but perhaps this misses the main point: hyperprolactinaemia may increase angiogenesis and induce/maintain endometriotic lesions. Their letter describes a patient with rectosigmoid endometriosis and simultaneous galactorrhea and hyperprolactinaemia. She had recurrent rectal bleeding but, during the period of time that she was under DA treatment, bleeding stopped and appeared again when the medication was discontinued.

We know that active angiogenesis is a requisite for the endometriotic implants in order to be established and grow (Nisolle et al., 1993; Maas et al., 2001; Lasche and Menge, 2007). We employed DA to target angiogenesis and endometriosis experimental lesions for several reasons: (i) the demonstrated effect of DA as angiogenic in experimental oncologic models (Basu et al., 2001); (ii) Our own experience in ovarian hyperstimulation syndrome, both in animals (Gomez et al., 2006) and humans (Alvarez et al., 2007); and (iii) the safety of these drugs even in pregnant patients (Robert et al., 1996; Ricci et al., 2002). With this background we anticipated that DA can be an ideal drug to treat a chronic disease such as endometriosis. Our published work shows the effect of cabergoline on experimental endometriosis lesions through an inhibition of angiogenic process (Novella-Maestre et al., 2009). Moreover, we have finished a pilot study in humans that basically confirms the findings in rodents.

We have only focused so far in peritoneal endometriosis because we believe it is the first step of the disease and because it is easier to design studies with lesions in this stage. The case reported by Kurt et al. suggests that DA may be also useful to treat deep endometriosis, the most severe presentation of the disease. Several hormonal treatments have been shown to provide pain relief (Vercellini et al., 2009), but if the description of Kurt et al. is confirmed, we may have found a drug able to target more complicated symptoms, such as rectosigmoid bleeding. This would represent an important advancement in the treatment of the disease and deserves to be further explored.

**References**


Birth of a second healthy girl more than 3 years after cryopreserved ovarian graft

Sir,

Since the first pregnancy reported after transplantation of ovarian tissue in 2004 (Donnez et al., 2004), cryopreservation of ovarian tissue became a valid procedure to preserve fertility of patients with high risk of premature ovarian failure. Despite the publication of eight births following this first report, the procedure is still experimental as many issues can be addressed concerning its risk and its success rate (Demeestere et al., 2009). The success of the procedure is often limited by the lifespan of the graft. Ovarian function restoration usually occurs around 4–5 months after the graft and most pregnancies were obtained within the first year. Ernst et al. (2010) reported a second birth from a woman who conceived 2 years after ovarian tissue graft. We also recently obtained a second birth resulting of a transplantation procedure more than 3 years before. At age 24, the patient affected by Hodgkin lymphoma underwent a unilateral oophorectomy for ovarian tissue cryopreservation before conditioning treatment for bone marrow transplantation. Four years after the remission of the oncological disease, a first ovarian tissue orthotopic and heterotopic (sub-cutaneous) transplantation procedure resulted in the restoration of ovarian function and in a first spontaneous pregnancy. Unfortunately, the patient had a miscarriage at 7 weeks gestation (Demeestere et al., 2006). As the hormonal FSH levels progressively returned to menopausal status, a second orthotopic and heterotopic graft was performed in May 2006, leading to the birth of a first healthy girl in June 2007 (Demeestere et al., 2007). Menstruations were still regularly observed during the first year after the delivery, with a basal FSH level fluctuating between 3 and 26 mIU/ml. The FSH levels then started to increase and reached 45 mIU/ml in November 2008. However, the patient reported menstruation in January 2009 and growing follicles were observed in the transplanted ovary. Spontaneous ovulation was confirmed and the patient became pregnant the following cycle leading to the birth of a second healthy girl in November 2009. Despite follicular growth and embryo transferred following IVF of collected oocytes at the heterotopic transplantation sites, the pregnancies were obtained spontaneously, confirming that orthotopic site may be more efficient (Demeestere et al., 2009). These two cases of a second birth 2–3 years after cryopreserved ovarian tissue transplantation confirm that long-term fertility restoration could be achieved after this procedure. These reports offer new data to validate the cryopreservation of ovarian tissue procedure for young women with high risk of premature ovarian failure.

References

