births and had no previous history of miscarriage, pre-eclampsia, ectopic pregnancy or pre-term delivery, we selected 224 controls subjects of the same ethnic distribution as that of RM subjects (Supplementary Table S1). The Supplementary Table (S1) reflects that there were no significant differences in terms of ethnicity among the patients and controls and that the differences seen in KIR frequencies are not due to non-ethnically matched controls as mentioned by Moffett and Hiby in their letter to the editor.

For the genotyping of KIR in our samples, we largely followed the method described by Vilches et al. (2007), with some modifications suited to our lab conditions. Vilches et al. (2007) primers amplify all the KIR alleles in the current Immuno-polymorphism Database (version 1.4.0, 4 June 2007). Individuals were determined to be negative for a KIR gene when a band of the expected size was absent in the presence of the control band. For easier size discrimination of KIR2DS4 full length and deletion variants, aliquots of PCR products of 2DS4 were run separately on the gel, and individuals were assigned positive when either or both the variants gave signals, whereas when both the variants were absent, the individual was labeled as 2DS4 negative. The data were verified and validated by Dr Raja Rajalingam from the University of California, Los Angeles (UCLA), CA, USA.

We used the working definition of assigning the KIR A and B haplotypes given by Rajalingam et al. (2008). Individuals who carried a fixed gene set of nine genes consisting of KIR3DL3–2DL3–2DL1–2DP1–3DP1–2DL4–3DL1–2DS4–3DL2, characteristic of Group A haplotypes, were considered as having two copies of Group A KIR haplotypes (AA genotypes). On the other hand, individuals lacking any of the four variable genes (KIR2DL1, 2DL3, 3DL1 and 2DS4) were regarded as carrying two copies of Group B haplotypes (BB genotypes). All the remaining combinations were regarded as heterozygotes carrying both the haplogroups, i.e. AB genotypes.

The RM control data reported by us varies from a previous report in North Indian population (Rajalingam et al., 2002) at several loci. To our understanding, this difference is because of the fact that our control data represent the healthy paous females of the eastern Uttar Pradesh Province of Northern India, and the absence of male individuals results in a bias as far as a representative population is concerned. Thus, we reckon our data cannot be considered as a representative of North Indian population because of the gender bias. Our data can very well be regarded as representative RM control data. Presently, we are working on the normal distribution of KIR genotypes among males and females from this part of the country which may provide a wider landscape of KIR distribution.

We agree with Moffett and Hiby that before publishing our control population data, we should confirm the accuracy and reliability of the KIR typing by using the DNA provided by the UCLA International KIR Exchange Program. However, the confusion about the role of KIR in RM is possible only through a multicentric study where samples of different ethnicities using the same selection criteria for the RM group are being used.

References


Rehan Mujeeb Faridi and Suraksha Agrawal1

1Department of Medical Genetics,
Sanjay Gandhi Post Graduate Institute of Medical Sciences,
Raebareli Road, Lucknow (U.P) 226014, India

1Correspondence address. Tel: 091-522-2668004-8 Ext. 2338, 2346, 2347, 2339; Fax: 091-522-26680973/26680017; Email: sur_ksha_agrawal@yahoo.co.in,
sur_ksha_agrawal@yahoo.co.in

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Re: Fertility preservation in adolescent males: experience over 22 years at Rouen University Hospital

Sir,

Menon et al. (2009) report the high success rate of cryopreservation of seminal fluid from adolescents with a malignancy who are planned to undergo chemotherapy. They also, however, report that 40% of the young patients in their series were unable to benefit from the cryopreservation programme because of masturbation-related problems. A significant proportion of these patients (21%) had testicular cancer and had undergone orchidectomy.

We recently described how it is possible to recover spermatozoa using a testicular sperm extraction technique on the malignant testicle.
at the time of orchidectomy (Carmignani et al., 2007). We used this technique in azoospermic patients. I believe that in the case of poor compliance by the patient or parental reluctance to masturbation, this method could be used to recover spermatozoa. With regard to concerns of transmission of the testicular cancer from father to son (Menon et al., 2009), there is currently no evidence that this occurs; furthermore, during cryopreservation it is not possible to prevent that some of the seminal fluid comes from the malignant testicle.

References
Luca Carmignani
Urology Unit, I.R.C.C.S. Policlinico San Donato, Via Morandi 30, 20097, San Donato Milanese, Milan, Italy
Correspondence address. Tel/Fax: +39-0252774329; E-mail: luca.carmignani@unimi.it
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Deeply infiltrating endometriosis and transvaginal ultrasonography

Sir,
I read with interest the article from Piketty et al. (2009). Regarding this article I would like to point out that:

First, I do not fully understand the performance of an analysis of sensitivity/specificity for transvaginal ultrasonography (TVUS) versus transrectal ultrasonography (TRUS), the first performed by a radiologist and the latter by a sonographer and both done for the diagnostic evaluation of the deeply infiltrating endometriosis, including the lesions located in uterosacral ligament (USL), vagina, bladder, intestine and ureter. I do think that the TVUS should be performed by the gynecologist who examines the patient and that the TVUS should be part of a systematically performed gynecological examination. In my opinion, a correct gynecological clinical evaluation should include: (1) Appropriate history or questioning, which for suspected endometriosis should include a visual-analogic scale. (2) Speculum examination, observing possible lesions in the vagina or exocervix, or endometriotic nodules in the posterior vaginal pouch. (3) Bimanual pelvic examination via the vagina (and if it is not possible, transrectally). In patients with endometriosis, the vaginal and especially the transrectal exam will let us detect those hard and painful endometriotic nodules located in USL, pouch of Douglas and recto-vaginal septum with a better precision that any other imaging technique. (4) TVUS performed routinely and systematically as a part of the gynecological examination. Such TVUS should be done in the normal outpatient surgery and on the same gynecological examination table in the normal gynecological position. If the TVUS is not possible (girl, virgin, etc.), the same gynecologist can perform a TRUS to provide us with similar information and it does not require sedation nor any other special conditions.

Second, the TVUS and the TRUS are extremely helpful in the diagnosis of endometriomas and are also really useful (I think as much as MRI) in all endometriosis patients including those with lesions located in USL-pouch of Douglas–intestine–rectum–vaginal septum. Naturally, those techniques will help little in the case of bladder lesions, for example. But as pointed out above, the best diagnostic method in the case of lesions located in vagina, exocervix, posterior vaginal pouch or rectovaginal septum is simply the vaginal and rectal exam and the speculum examination which may let us see the lesions and take a biopsy.

Third, I think that endometriosis is much more of a systemic disease (probably related to immunotolerance) than just being able to count and resect a number of implants; and that the disease is not cured (although the pain or the deep dyspareunia can be temporarily improved) by the resection of all the visible implants nor by the performance of a ‘bowel segmental resection’. Therefore, except in very special cases with big nodules and severe symptoms, I think that a surgical operation with ‘a real risk of complications’ is not justified. In the meta-analysis by Vercellini et al. (2009) on surgery for rectovaginal lesions they conclude that excision of rectovaginal lesions is of doubtful value and associated with severe morbidity; and also, that excision of rectovaginal plaques does not improve the likelihood of pregnancy nor reduces the time-to-conception in women with endometriosis-associated infertility. Likewise, we point out that the possibility of treating peritoneal and ovarian endometriomas only without exciting rectovaginal plaques should be considered especially in women with limited pain. Certainly, we also think that very rarely can surgery involving or forcing a bowel resection be justified. In many cases with rectovaginal septum involvement nothing can be done, or women do well simply with the pill (low dose) or antiprostaglandins (and/or possibly aromatase inhibitors in the future). If there is recurrent endometriosis and great pelvic blockade and hysterectomy and double adnexectomy are necessary, we consider that the affected intestine can be left untouched (including nodules that apparently occlude its light partially). Evenmore, I consider that in these cases you can give replacement hormonal therapy with low doses without any problem.

References

Pedro Acien
Service of Obstetrics and Gynecology, San Juan University Hospital and Department and Division of Gynecology, School of Medicine, Miguel Hernández University, Campus of San Juan, 03550 Alicante, Spain
Correspondence address. E-mail: acien@umh.es
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