

Scientific letter

Miliary Tuberculosis during Pregnancy After In Vitro Fertilization



Tuberculosis miliar durante el embarazo tras fecundación in vitro

Dear Editor,

Tuberculosis (TB) during pregnancy is a cause of maternal morbidity and mortality, and is associated with an increased risk of miscarriage, intrauterine growth retardation, prematurity, fetal death and congenital TB.¹

Miliary tuberculosis (MTB) is a rare but particularly serious presentation resulting from massive hematogenous dissemination of *Mycobacterium tuberculosis*. MTB cases have been reported in pregnant women after *in vitro* fertilization (IVF) techniques.

We describe the case of a 41-year-old autochthonous female patient with infertility secondary to Fallopian tube obstruction demonstrated by hysterosalpingography and pregnant by IVF. At 23 weeks of gestation (WG), she was admitted for threatened preterm labor and was treated with atosiban and corticotherapy, being discharged and readmitted at 33 WG for the same reason. Since 18 WG the patient had presented a dry cough, initially attributed to residual post-SARS-CoV-2 infection, but later, it was

diagnosed as gastro-esophageal reflux. Despite the administration of symptomatic treatment, the cough persisted. At 34 WG, a chest X-ray with abdominal protection was performed, which revealed a bilateral micronodular pattern. A diagnosis of MTB was confirmed by molecular techniques (GeneXpert MTB/RIF positive) in gastric aspirate. Cesarean delivery at 34 WG was performed on obstetric indication. The patient received conventional tuberculostatic treatment for 6 months, presenting a satisfactory clinical and radiological evolution. Chest high-resolution tomography (HRCT) demonstrated the resolution of the bilateral nodular pattern at the end of treatment (Fig. 1).

The newborn, premature and of low weight, received isoniazid chemoprophylaxis and did not present congenital or postnatal TB at follow-up up to 12 months of age.

In recent years, several case series of MTB in pregnant women after IVF have been published, mostly in countries with a high TB burden; the report of cases in Western European countries is exceptional.²⁻⁵

During pregnancy, hormonal and immunological changes have an inhibitory effect on T lymphocytes, increasing susceptibility to infection and reactivation of TB. The levels of progesterone and corticosteroids in IVF pregnant women are much higher than the requirements of natural pregnancy, thus increasing the risk of TB. Furthermore, the increased microvascular permeability during

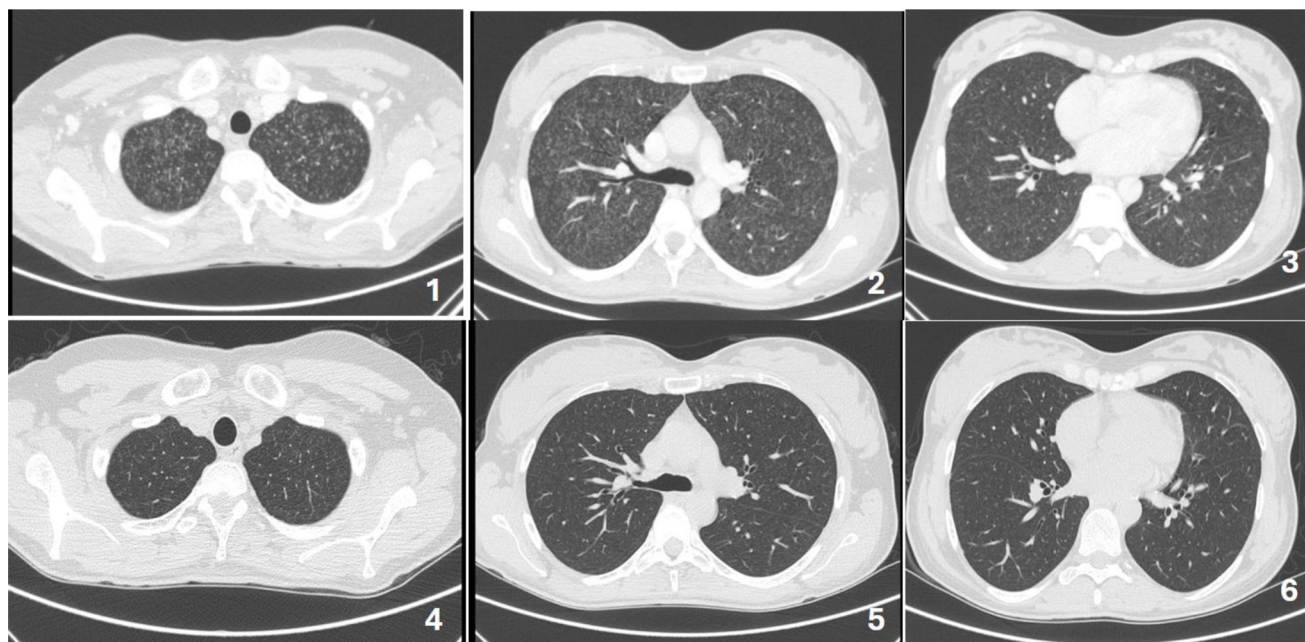


Fig. 1. Chest high-resolution computed tomography (HRCT) images of a case of miliary tuberculosis showing diffuse distribution of multiple miliary nodular lesions in both lungs (1–3). Chest HRCT after 6 months of treatment showed absorption of miliary nodular lesions in both lungs (4–6).

pregnancy favors hematogenous dissemination and the development of MTB.

Latent tuberculosis infection, previous TB, and especially genital tuberculosis are frequent causes of female infertility that, in many cases, are not correctly diagnosed or treated prior to the start of IVF techniques, posing a risk of reactivation and progression during pregnancy.

In the case discussed, tubal obstruction, probably secondary to genital tuberculosis, was not studied and specific treatment was not prescribed prior to IVF. The diagnostic delay was also considerable due to several factors: non-specific respiratory symptoms, delay in radiological examinations, and lack of clinical suspicion.

In conclusion, MTB can appear during pregnancy, especially after IVF, and is associated with poor maternal and fetal prognosis. TB screening prior to assisted reproduction techniques should be systematized, especially in patients with evidence of tubal involvement and in those from areas with a high burden of disease.

Informed consent

The authors obtained informed consent from the patients.

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Authors' contributions

All authors have contributed intellectually, comply with the conditions of authorship and have approved the final version of the case.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Declaration of artificial intelligence

The submitted manuscript has not been produced in whole or in part with the help of generative artificial intelligence software or tools.

References

1. Barquero-Artigao F, Mellado Peña MJ, del Rosal Rabes T, Noguera Julian A, Gonze Mellgren A, de la Calle Fernandez-Miranda M, et al. Guia de la Sociedad Española de Infectología Pediátrica sobre tuberculosis en la embarazada y en el recién nacido (I): Epidemiología y diagnóstico. *Tuberculosis congénita. An Pediatr (Bar)*. 2015;83. <http://dx.doi.org/10.1016/j.anpede.2015.08.009>, 285.e1–285.e8.
2. Wang K, Ren D, Qiu Z, Li W. Clinical analysis of pregnancy complicated with miliary tuberculosis. *Ann Med*. 2022;54:71–9. <http://dx.doi.org/10.1080/07853890.2021.2018485>.
3. Dong S, Zhou R, Peng E, He R. Analysis of clinical features and risk factors in pregnant women with miliary pulmonary tuberculosis after in vitro fertilization embryo transfer. *Front Cell Infect Microbiol*. 2022;12:885865. <http://dx.doi.org/10.3389/fcimb.2022.885865>.
4. Xia L, Mijiti P, Liu XH, Hu ZD, Fan XY, Lu SH. Association of in vitro fertilization with maternal and perinatal outcomes among pregnant women with active tuberculosis: a retrospective hospital-based cohort study. *Front Public Health*. 2022;10:1021998. <http://dx.doi.org/10.3389/fpubh.2022.1021998>.
5. Gai X, Chi H, Cao W, Zeng L, Chen L, Zhang W, et al. Acute miliary tuberculosis in pregnancy after in vitro fertilization and embryo transfer: a report of seven cases. *BMC Infect Dis*. 2021;21:913. <http://dx.doi.org/10.1186/s12879-021-06564-z>.

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