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Difficulties in the diagnosis of toxoplasmosis in pregnancy

Partnership for a better future

HEALTH-PREGN RO-HU

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Case presentation

- 37-year old pregnant woman
- Anti-*Toxoplasma* screening: IgA: POSITIVE (index: 3.279); IgM: POSITIVE; IgG: 1669 UI/ml
- Pregnancy without any (other) difficulties

Evaluation of serology

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REVIEW
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Congenital Toxoplasmosis: The State of the Art

Lina Bollani[1], Cinzia Auriti[2], Cristian Achille[1], Francesca Garofoli[1], Domenico Umberto De Rose[2], Valeria Meroni[3], Guglielmo Salvatori[2] and Chryssoula Tzialla[1]*

[1] Neonatal Intensive Care Unit, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy, [2] Neonatal Intensive Care Unit, Medical and Surgical Department of Fetus – Newborn – Infant, "Bambino Gesù" Children's Hospital, IRCCS, Rome, Italy, [3] Department of Molecular Medicine, University of Pavia, Pavia, Italy

TABLE 2 | Results of serological tests during pregnancy and their interpretation.

Scenario	IgG antibodies	IgM antibodies	Interpretation	Comment
1	Negative	Negative	Absence of immunity	Monthly serologic follow-up and 1 month after delivery
2	Positive	Negative	Infection acquired before pregnancy	- Repeat tests after 1 month to confirm previous infection - Stop follow-up if only IgG antibodies are positive
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4	Positive	Positive	Acute infection or Persistence of IgM	- Date infection - Second level tests - Eventual prenatal diagnosis - Neonatal follow-up

Case presentation: *T. gondii* serology (Mother)

IgA: POS. (i.: 3.279)
IgM: POSITIVE
IgG: 1669 UI/ml
IgG avidity: High

20. 07. 2021.

IgA: POS. (i.: 1.94)
IgM: POSITIVE
IgG: 1721 UI/ml
IgG avidity: High

14. 09. 2021.

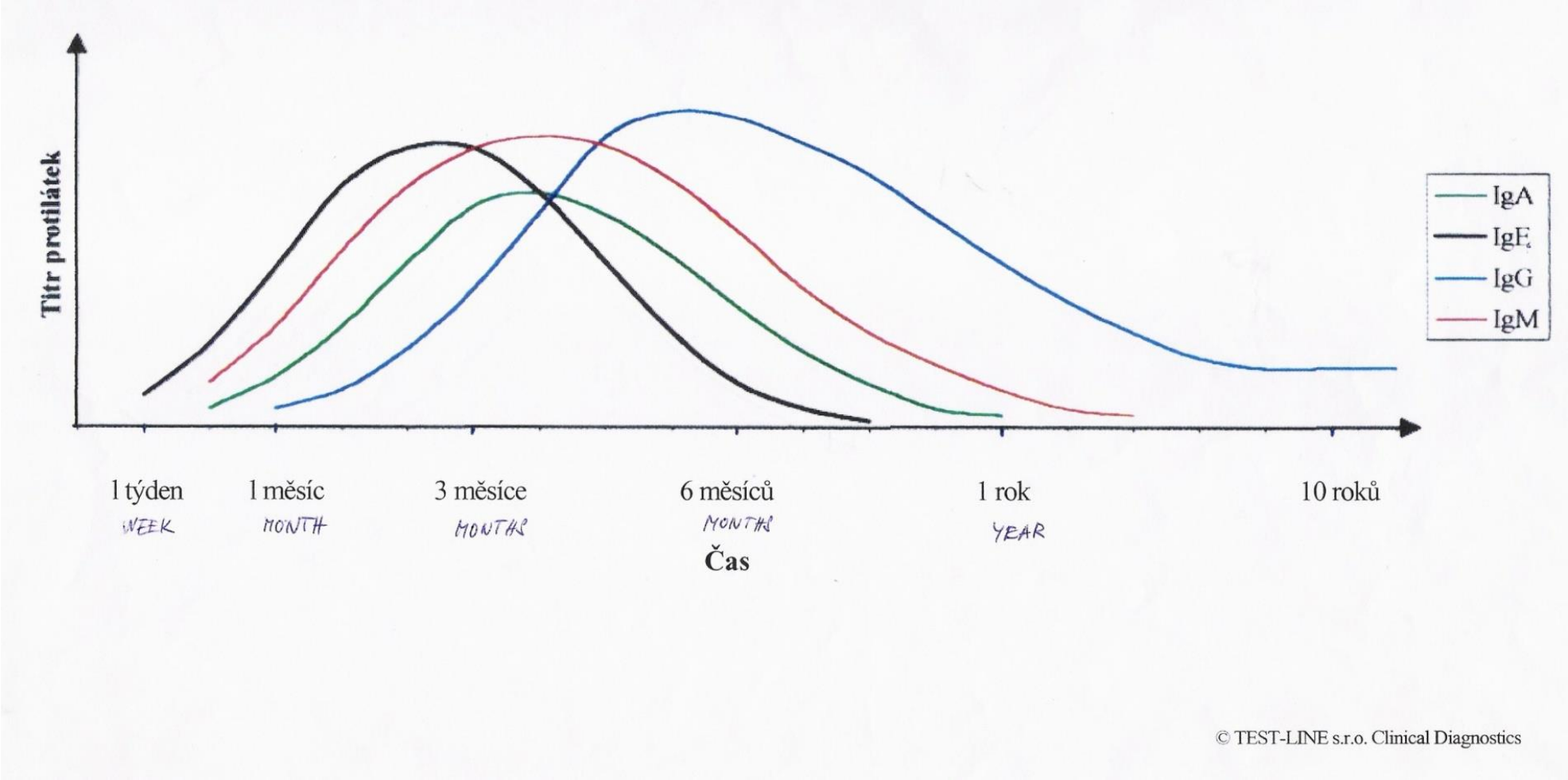
IgA: POS. (i.: 1.93)
IgM: POSITIVE
IgG: 1898 UI/ml
IgG avidity: High

10. 12. 2021.

IgA: POS. (i.: 2.334)
IgM: POSITIVE
IgG: 1068 UI/ml
IgG avidity: High

22. 03. 2022.

Serodiagnosis of toxoplasmosis



Questions, edifications (Mother): Date of infection

- Extremly high AND increasing (high-level avidity) IgG-titer, positivie IgM (fluctuant IgA-titer)

- Latent reactivation → acute infection?

- If YES, has she got any (unknown) underlying disease?

- Are these serological markers enough for the exact determination of the date of infection?

Questions, edifications (Mother): Date of infection

- What are the possible causes of **IgM-positivity**?
  - Is it an **acute infection**?
  - Is it **long-persisting IgM**?
  - Is it **aspecific reaction** (originated from natural antibodies)?

Questions, edifications (Mother): Date of infection

- What does **high** AND **elevating level IgG-positivity** mean?
  - Is it originating from an **acute infection**?
  - A significant (at least 2-fold in a no-treatment context) increase is a marker of acute infection.
    (Villard *et al*., 2016)
  - Is our **kit suitable** for the **detection of this increase** at very high titers?

Case presentation: Questions, edifications (Mother)

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Second level test: IgG avidity (Mother)

- High IgG avidity index suggests acute infection acquired at least 16 weeks before.

- (Specific therapy reduce avidity maturation.)

- (Some individuals have persistent low IgG avidity for months after infection.)

→ (Low/intermediate IgG avidity DOES NOT necessarily mean recent/acute infection.)

Questions, edifications (Mother): Second level test

- **Why has the IgG avidity been HIGH-level throughout the pregnancy? (Good serological marker???)**

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Parasitology

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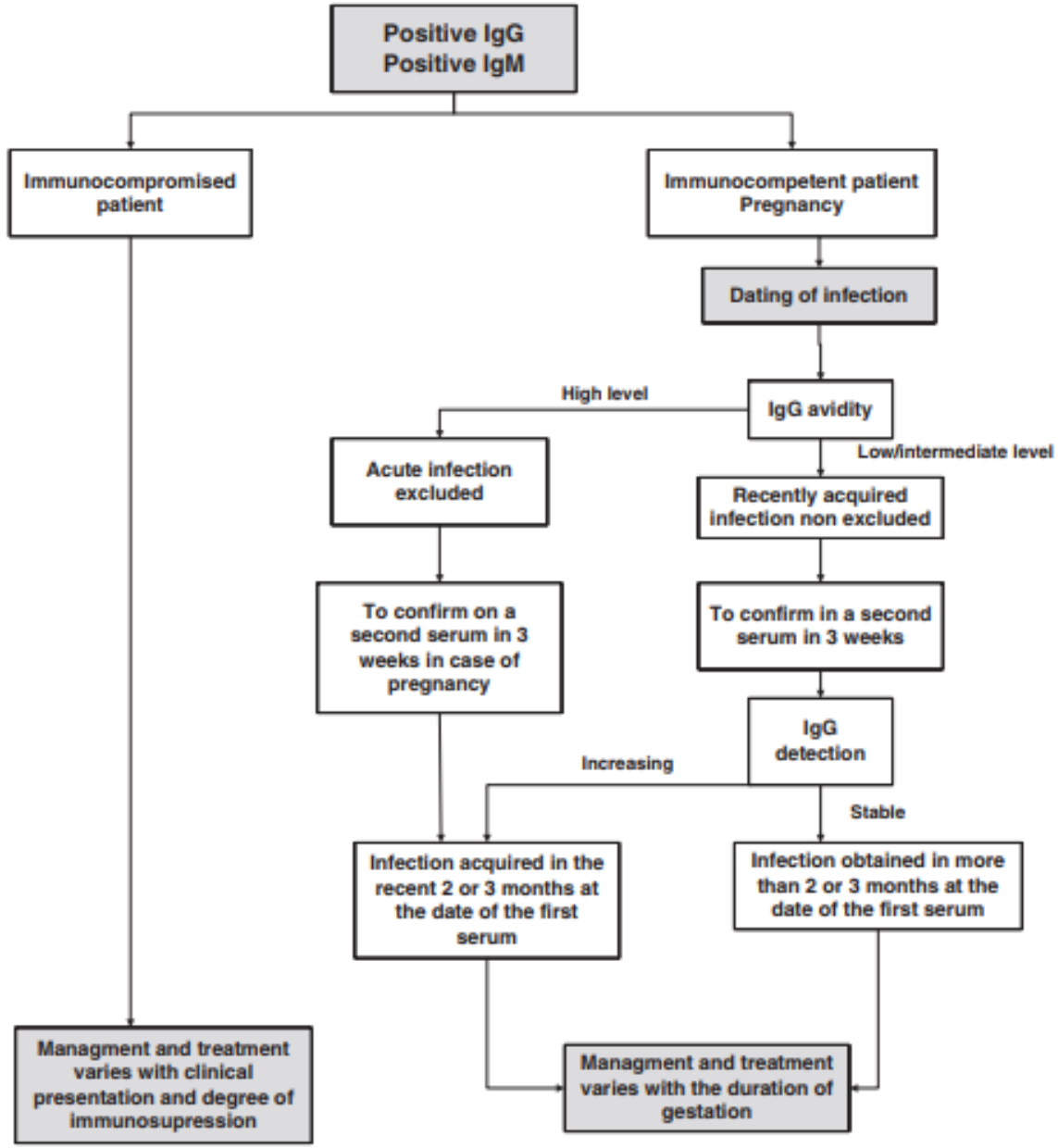


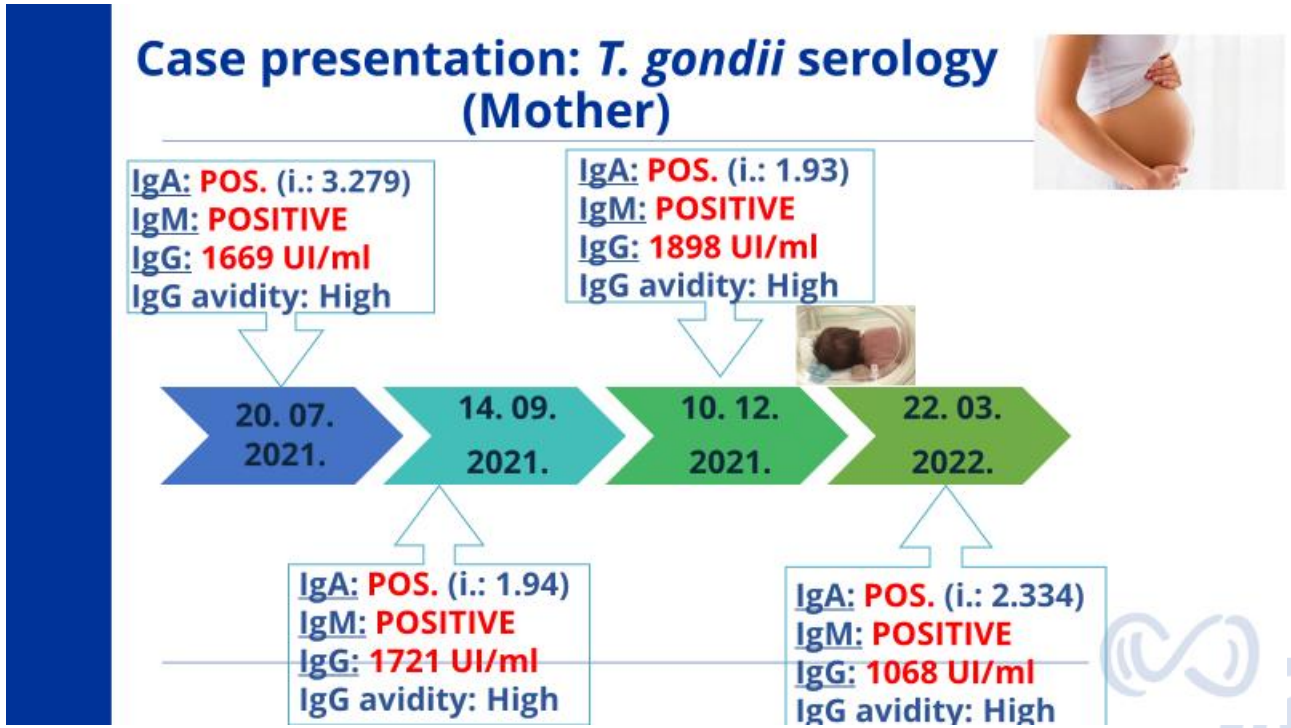
Fig. 4. Serological monitoring for toxoplasma serology with positive IgG and IgM. Adapted from Villard et al., 2011.

Second level test: Immunoblot (Mother)

- **More specific** and **more sensitive**, than other serologic methods.
- Detection of specific **IgG and IgM**
- Can be used for the follow-up of the infant's anti-*Toxoplasma* serostatus.

Questions, edifications (Mother): Date of infection

- **Sample collection time is essential:** compliance with the submission time of controll sera.



Case presentation: Questions, edifications (Mother)

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Questions, edifications (Mother and fetus): Eventual prenatal diagnosis

- Are serological methods sufficient to establish a correct diagnosis in such case? Other options?
  - Molecular (PCR–based) method

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PCR-based methods (Mother and fetus)

- These methods developed (not only) for **prenatal diagnosis** of **congenital toxoplasmosis**.
  - Amniocentesis:
    - Performed after 18th week of pregnancy
    - Trasmission rate ↑, morbidity of fetus↓ in paralel with the age of pregnancy in case of acute infection
    - Risk of procedure–related fetal loss <0.1%.

PCR-based methods (Mother and fetus)

- Positive predictive value: 100%
- Negative predictive value: 98.1%
  - Very low density of parasites in the amniotic fluid
  - Delayed transplacental transmission

Case presentation

- Rovamycin therapy during the pregnancy
- Delivery: 25.12.2021
- **Newborn's status:** microcephal, dysphagia → dystrophy
- What was the possible **cause of the morbidity**? Infection or developmental disorder?

Case presentation: Questions, edifications (Newborn/infant)

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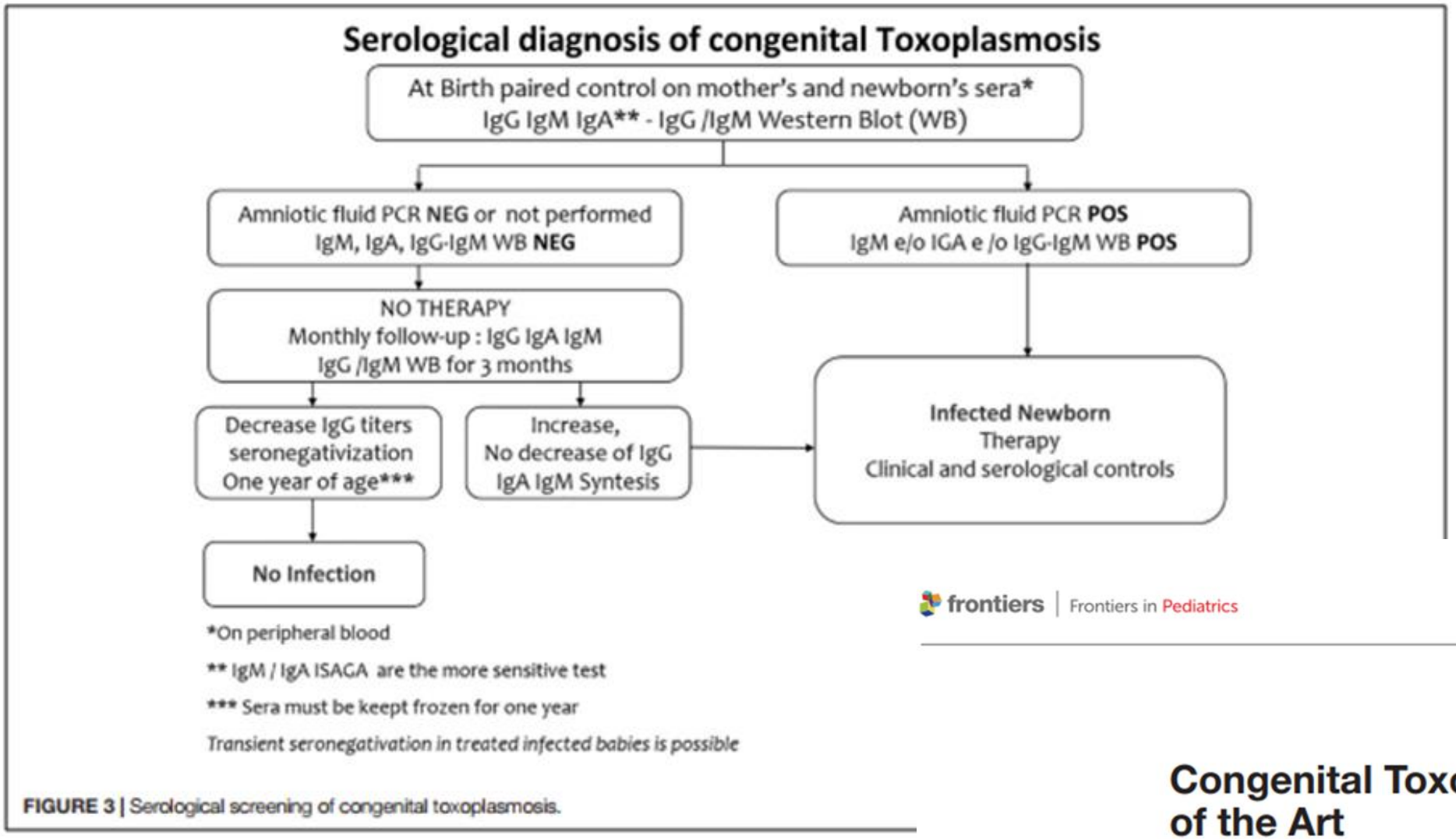

FIGURE 3 | Serological screening of congenital toxoplasmosis.

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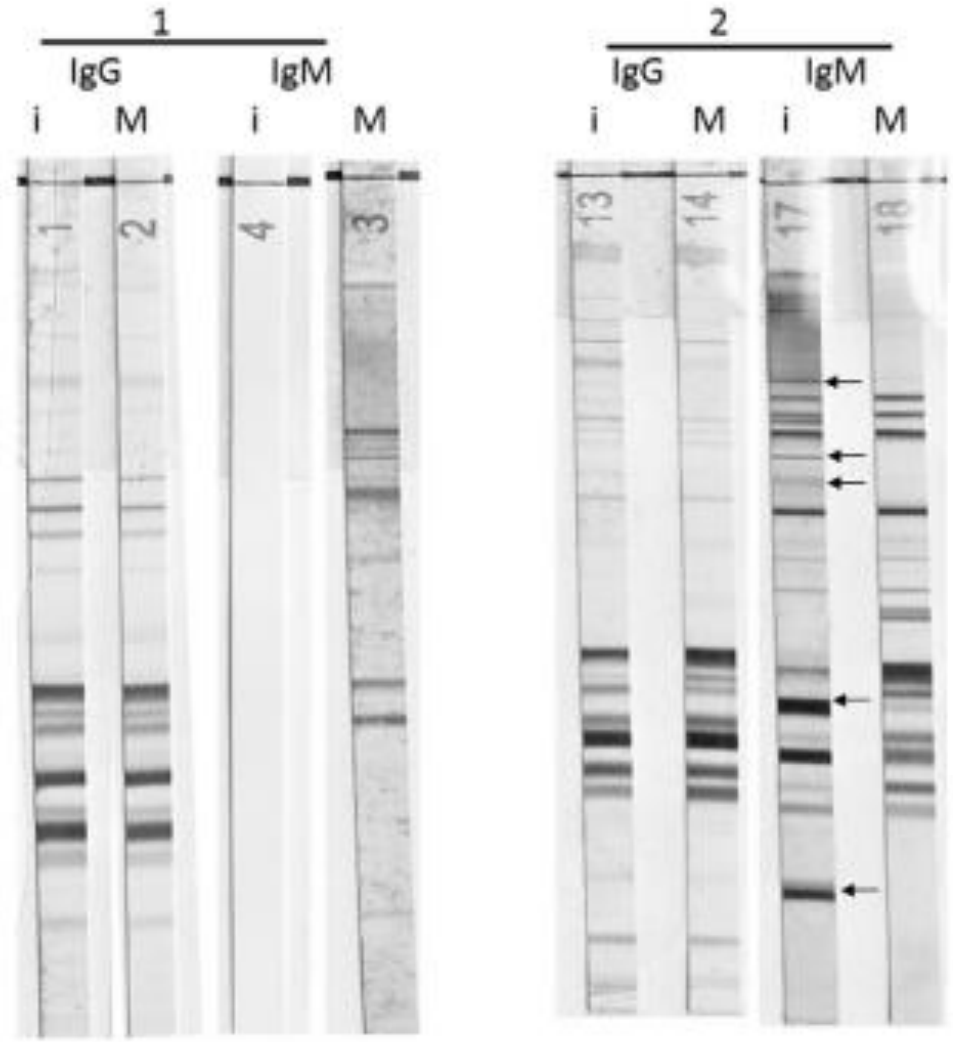

Fig. 8. Comparison of immunoblot IgG and IgM with paired mother (M) and infant (i) at birth.
1. Absence of IgM and same profile of IgG in favor of passive transmission of maternal IgG.
2. Same profile for IgG and different profile IgM (arrows) confirming congenital toxoplasmosis.

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Questions, edifications (Newborn/infant): Neonatal follow-up

- In the first month of life IgA and IgM may not be produced in congenitally infected infant.
- Maternal infection in late pregnancy → false negative serology at birth.
- Maternal IgG decline to disappear within 6-12 months.

Questions, edifications (Newborn/infant): Neonatal follow-up

- Persistence IgG up to 1 year OR increase in the first months → possible congenital toxoplasmosis.

- Transient seronegativity can be occurred in treated infected infants.

- Seronegativity in untreated babies at one year → congenital toxoplasmosis can be excluded.

Case presentation: *T. gondii* serology (Newborn/infant)

IgA: Negative
IgM: Negative
IgG: 913 UI/ml

28.12.
2021.

IgA: Negative
IgM: Negative
IgG: 407 UI/ml

17.01.
2022.

IgA: Negative
IgM: Negative
IgG: 117 UI/ml

22.03.
2022.

Case presentation: Neonatal follow-up

- **Decreasing IgG-titers WITHOUT any other, acute-phase antibodies (IgA and/or IgM)**

↓

- **Congenital toxoplasmosis can be excluded.**

Thank you for your attention!

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