Title Laboratory diagnosis of acquired toxoplasmosis in immunocompetent subjects (including pregnant woman), congenital toxoplasmosis (pre- and postnatal diagnosis) and ocular toxoplasmosis

Agency HAS (French National Authority for Health - Haute Autorité de Santé)
5 avenue du Stade de France – F 93218 La Plaine Cedex, France
Tel.: +33 (0)1 55 93 70 00 – Fax: +33 (0)1 55 93 74 35, contact.seap@has-santé.fr, www.has-sante.fr

Reference ISBN number: 978-2-11-151461-4, link to full report in French: http://www.has-sante.fr/portail/jcms/c_2653655/fr/diagnostic-biologique-de-la-toxoplasmose-acquise-du-sujet-immunocompetent-dont-la-femme-enceinte-la-toxoplasmose-congenitale-diagnostic-pre-et-postnatal-et-la-toxoplasmose-oculaire

Aim

This assessment is in response to a request from the Caisse nationale d'assurance maladie des travailleurs salariés (CNAMTS [National Health Insurance fund for salaried workers]) to update the Nomenclature of Procedures in Laboratory Medicine (NABM) in relation to procedures for laboratory diagnosis of toxoplasmosis. This assessment focuses on diagnostic tests for toxoplasmosis in the following contexts: acquired toxoplasmosis in immunocompetent subjects (including pregnant woman), congenital toxoplasmosis (pre- and postnatal diagnosis) and ocular toxoplasmosis.

Conclusions and results

Diagnosis of toxoplasmosis in immunocompetent subjects, including pregnant women

The indications for laboratory diagnosis of toxoplasmosis in immunocompetent subjects are as follows: pregnant women (routine screening), subjects suspected to have ocular toxoplasmosis and patients with non-specific symptoms, especially if they are severe.

In these indications, laboratory diagnosis of toxoplasmosis consists of:

- testing for anti-Toxoplasma IgG and IgM serum antibodies, usually performed using an immunoassay technique (immunoenzymatic, chemiluminescence, etc.);
- repeating this first test in the following situations and according to the following methods:
  - presence of IgM and/or doubtful results for IgG, which requires confirmation using a different technique (dye test, IIF, immunoblot, or ISAGA) by an expert laboratory for diagnosing toxoplasmosis,
  - a suspected acute toxoplasmosis infection, which requires IgG kinetic testing with the initial test repeated once or twice at a two- or three-week interval; subsequent samples should be titrated in the same series, with the same immunoassay technique,
  - extension of the monthly follow-up by an IgG and IgM test two to four weeks after delivery, which is to be performed in seronegative mothers throughout pregnancy;
- IgG avidity testing for Toxoplasma to date the infection in the presence of a suspected recent infection (presence of IgM, confirmed by a second technique, and anti-Toxoplasma IgG). In pregnant women and symptomatic subjects, this test only makes it possible to rule out a recent infection in the presence of a high avidity.

In this context of diagnosis of toxoplasmosis in immunocompetent subjects, testing for anti-Toxoplasma IgA and IgE serum antibodies is not relevant.

Pre- and postnatal diagnosis of congenital toxoplasmosis

This diagnosis consists of:

- Toxoplasma DNA testing by gene amplification (PCR) on amniotic fluid, specifying the following elements:
  - amniocentesis for this purpose should only be performed after at least 16-18 weeks of pregnancy, and not less than four weeks since the onset of suspected acute maternal infection,
  - the results are qualitative and a negative prenatal diagnosis result does not totally rule out the possibility of congenital toxoplasmosis;
- Toxoplasma DNA testing by gene amplification (PCR) in cord blood, newborn peripheral blood, amniotic fluid and placenta, specifying that a positive result in the placenta should be confirmed by the positive result of another postnatal diagnostic test to make the diagnosis of congenital toxoplasmosis;
- testing for anti-Toxoplasma serum antibodies in newborns and children under 1 year of age, as follows:
  - specific IgM and/or IgA testing on cord blood or peripheral blood between D0 and D3 after birth, using an immunoassay technique, re-tested after 10-15 days of life in case of a positive result with the first test,
  - testing for neosynthesised IgG and/or IgM in cord blood or peripheral blood of the child by comparison of the mother-child profiles in immunoblot or ELIFA, between D0 and D3 to D15 and D30 (then M2 +/- M3 if the diagnosis remains undetermined at D30),
  - monitoring of the specific IgG serum levels of the child, measured between D0 and D3, at D15 and D30 then monthly until disappearance of the antibodies to confirm the absence of congenital infection.

Given the complexity of interpretation of some tests, and to ensure a continuity between the pre- and postnatal diagnosis, the tests for pre- and postnatal laboratory diagnosis of congenital toxoplasmosis should be performed by expert laboratories for diagnosing toxoplasmosis, working together and in collaboration with clinicians.

Diagnosis of ocular toxoplasmosis

The indications for laboratory diagnosis of ocular toxoplasmosis are as follows: subjects seropositive for toxoplasmosis with atypical ocular lesions, fulminant expression of the disease, uncertain differential diagnosis with other causes of retinochoroiditis and delayed response to anti-toxoplasmosis empirical treatment.

This diagnosis involves the following tests, the implementation and interpretation of which are the responsibility of expert laboratories :

- Toxoplasma DNA screening by gene amplification (PCR) in ocular fluids;
- screening for local production of IgG by comparison of immune loads of paired serum-ocular fluid samples;
- screening for local production of IgG and/or IgA by comparison of immunological profiles via immunoblotting of paired serum-ocular fluid samples.

For all clinical contexts of toxoplasmosis (within the scope of this assessment):

- the mouse inoculation technique is beneficial only in the case of symptomatic patients for whom a hypervirulent strain is suspected, for the purposes of typing and adapting treatment;
- cell culture of Toxoplasma is no longer beneficial.

As regards where they are performed, diagnostic testing for toxoplasmosis should be done at either “polyvalent” or “first-line” laboratories or at toxoplasmosis “expert” laboratories. This distinction is based on the specific technical aspects of the tests used and/or on the complexity of the clinical situation. An expert laboratory is primarily defined by its ability to perform less widely used techniques or manual techniques, its capacity to handle complex cases, and its inclusion in a think-tank and collaboration with different clinicians and other specialist laboratories.

Methods

The method selected is based on a critical analysis of the literature (systematic reviews, meta-analyses, good practice guidelines, technological assessment reports, general reviews), identified by a systematic literature search, together with a request for information from the National Reference Centre for Toxoplasmosis.

Written by

Carole Giraud, HAS (French National Authority for Health - Haute Autorité de Santé), France.