www.jpnim.com Open Access eISSN: 2281-0692
Journal of Pediatric and Neonatal Individualized Medicine 2019;8(2):e080219
doi: 10.7363/080219
Received: 2019 Mar 24; revised: 2019 Jun 10; rerevised: 2019 Jun 22; accepted: 2019 Jun 25; published online: 2019 Oct 08

Original article

Congenital toxoplasmosis in a Portuguese tertiary hospital – report of 4 cases

Ana Luísa Pinhal[1], Marta Grilo[1,2], Marina Moucho[2], Rita Valente[2], Hercília Guimarães[1,2]

[1]Faculty of Medicine, University of Porto, Porto, Portugal
[2]Centro Hospitalar Universitário São João, Porto, Portugal

Abstract

Toxoplasma gondii is an intracellular parasite responsible for toxoplasmosis, a zoonosis with a worldwide distribution. Congenital toxoplasmosis occurs when a pregnant woman becomes infected during the gestation or when there is reactivation in an immunocompromised pregnant woman of a previous latent infection. Clinical manifestations of congenital infection can vary in severity, ranging from asymptomatic infection to abortion and still-birth. We are not aware of any published cases neither of confirmed congenital toxoplasmosis nor of any of its complications in Portugal. The incidence of congenital toxoplasmosis estimated in 2013 by the World Health Organization was of 5/10,000 live births for the region where Portugal is inserted (European region A).

In this study, we aimed to describe the cases of congenital toxoplasmosis in Centro Hospitalar Universitário de São João (CHUSJ) between January of 1999 and December of 2018. For that, we worked with the records of the Neonatology and Obstetrics Departments.

Records of 4 patients with confirmed congenital toxoplasmosis were found, 3 of which born in our hospital. The 4 cases are described in this paper. In 2 out of the 4 cases, infants developed complications secondary to congenital toxoplasmosis such as microphthalmia, chorioretinitis, congenital hydrocephalus, diabetes insipidus, seizures, intracranial calcifications, central apnea and disturbances of the thermal regulation.

The found cases reflect an incidence of 0.6/10,000 births. This low incidence can be explained by the precautions taken by pregnant women to avoid the infection, the early therapy administrated when seroconversion is detected and by the changes in food habits and improved hygiene practices that have taken place in Portugal in the last years.

Keywords

Congenital toxoplasmosis, *Toxoplasma gondii*, congenital infection, TORCH, newborn, intensive care.

Corresponding author

Ana Luísa Pinhal, Faculty of Medicine, University of Porto, Porto, Portugal; email: analuisapinhal@gmail.com.

How to cite

Pinhal AL, Grilo M, Moucho M, Valente R, Guimarães H. Congenital toxoplasmosis in a Portuguese tertiary hospital – report of 4 cases. J Pediatr Neonat Individual Med. 2019;8(2):e080219. doi: 10.7363/080219.

Introduction

Toxoplasma gondii is an intracellular parasite responsible for toxoplasmosis, a zoonosis with a worldwide distribution [1]. Infection is transmitted through 3 main routes: ingestion of raw or undercooked meat contaminated with bradyzoites, exposure to oocytes from feline feces, and vertical transmission [2-4].

Most of the infections on an immunocompetent patient are non-symptomatic. Latent infection, however, can persist for life and reactivate if the person becomes immunosuppressed later [2, 4]. Around 30% to 50% of the world population is estimated to be infected [5]. Toxoplasmosis may be responsible for severe symptoms in the immunocompromised population and even be lethal if not treated [6].

Congenital infection (transmission to the fetus) occurs when the pregnant woman becomes infected during the gestation or when there is reactivation on an immunocompromised pregnant woman of a previous latent infection [1]. Maternal infection may be symptomatic or not. The incidence of congenital toxoplasmosis in European region A, in which Portugal is included, is estimated to be 5/10,000 live births [7].

The incidence and severity of congenital toxoplasmosis vary according to the trimester during which the mother acquired the infection [6]. As gestational age increases, the risk of transplacental transmission rises but the risk of asymptomatic infection at birth decreases [6]. Infants born from mothers who acquired their infection in the 1st or 2nd trimester are at more risk of developing severe congenital toxoplasmosis [6]. In contrast, the majority (more than 80%) of the neonates born of women who acquire their infection during the 3rd trimester are asymptomatic [1]. Despite that, the infection must be treated even if it is non-symptomatic, since complications, such as chorioretinitis and neurologic deficits, might develop later in life in the asymptomatic newborns who were not appropriately treated [1, 8].

Clinical manifestations of congenital infection can vary. Most of them are nonspecific, and their severity is related to the trimester during which the infection was acquired as it was already mentioned. Signs include hydrocephalus, microcephaly, deafness, intracranial calcifications, chorioretinitis, strabismus, blindness, microphthalmia, optic neuritis, cataract, retinal necrosis, increased intraocular pressure, epilepsy, psychomotor or mental retardation, anaemia, jaundice, rash, petechiae due to thrombocytopenia, encephalitis, pneumonitis, diarrhea, splenomegaly, hepatomegaly, hypothermia, and nonspecific illness [6, 1]. Congenital infection can also be responsible for abortion and still-birth [1].

In Portugal, it is mandatory for pregnant women to be screened for toxoplasmosis. The goals of this universal screening are to avoid and treat the congenital infection. Each woman whose state of immunity is unknown must be tested for antibodies (IgM and IgG) against *Toxoplasma gondii* during the 1st trimester of pregnancy. In case of not being immune, the serological test must be repeated in the 2nd and 3rd trimester of pregnancy [9]. If seroconversion (detection of positive IgM antibodies) occurs in the pregnant woman, prophylactic therapy with spiramycin must be started, and fetal infection must be searched. Early treatment of the pregnant woman with spiramycin reduces the risk of vertical transmission. The earlier therapy is started, the more effective it is [10]. The most commonly used method for diagnosis of congenital toxoplasmosis in the fetus is the detection of *Toxoplasma gondii*'s DNA in the amniotic fluid by polymerase chain reaction (PCR) technique [11]. If there is no congenital infection detected, the treatment with spiramycin must be kept until the end of the pregnancy. If there is a congenital infection, the therapy must be changed, after the 18th week of pregnancy, to pyrimethamine and sulfadiazine and must be stopped at the 34th week of pregnancy [10].

The search for toxoplasmosis infection is done in an infant under 2 conditions: when the child is symptomatic or when the pregnant woman gets infected [10]. Congenital infection in the newborn can be diagnosed through detection of IgM and IgG antibodies, inoculation of fragments of the placenta in the mouse and detection of

Toxoplasma gondii's DNA in the blood by PCR technique [10].

Treatment of the newborn with confirmed infection, according to the Portuguese guidelines, must be made with sulfadiazine, pyrimethamine, and folinic acid and must be kept for a year (**Tab. 1**). Children of mothers infected during pregnancy should initiate the same treatment and maintain it until they get 2 negative serologic tests [10].

In children with suspected congenital toxoplasmosis, physical examination, transfontanellar ultrasound, ophthalmologic examination, and periodic hematologic evaluation should be done until it is certain that there is no infection. In children with confirmed infection, ophthalmological evaluations should be performed throughout adulthood due to the inherent risk of late chorioretinopathy [10].

The definitive diagnosis of congenital toxoplasmosis can only be established by 12 months of age [10]. The detection of *Toxoplasma* IgG antibodies by this age is considered the diagnostic gold standard [11].

Available data regarding the seroprevalence in Portugal are sparse. According to Gargaté et al., the seroprevalence of toxoplasmosis in Portugal in 2013 was 22% [12]. In another paper with information related to the period between 2009 and 2010, seroprevalence specifically in women of reproductive age of the north of Portugal was 24.4% [13], which means that more than 70% of women of childbearing age in Portugal were at risk of becoming infected with *Toxoplasma gondii* [14]. We are not aware of any cases of confirmed congenital toxoplasmosis or any of its complications to have been published in Portugal.

In this study, we aimed to describe the cases of congenital toxoplasmosis in Centro Hospitalar Universitário de São João (CHUSJ) between January of 1999 and December of 2018.

Methods

All the cases of congenital toxoplasmosis confirmed between January of 1999 and December of 2018 in the Neonatal Intensive Care Unit (NICU) of Centro Hospitalar Universitário de São João (CHUSJ) were included in this study. We considered confirmed cases of toxoplasmosis those with positive amniocentesis or positive IgM antibodies after birth for toxoplasmosis.

Maternal, pregnancy and children's clinical data were obtained from clinical records of the Neonatology Department and ObsCare® including: mother's age, date of birth, gestational age (weeks), birth weight (grams), serologies performed during pregnancy, surveillance during pregnancy, performance and results of amniocentesis, pregnancy complications, treatment implanted during pregnancy for the infection, signs or symptoms of toxoplasmosis infection during pregnancy, serologies of the newborn, treatment of the newborn, evaluations of the newborn and possible complications of the infection at birth and lifelong.

By the collected data, 4 confirmed cases of congenital toxoplasmosis are described in this paper.

Ethics committee approval, according to the requirements of our center, was obtained.

Results

Clinical characteristics and serologies of the 4 cases are shown in **Tab. 2** and **Tab. 3**.

Case 1

A female infant was born in March of 2000 in CHUSJ by cesarean section, induced due to fetal distress, at 38 weeks of gestation, with

Table 1. Therapy protocol for newborns of the Portuguese Society of Neonatology.

Symptomatic congenital toxoplasmosis	Subclinical congenital toxoplasmosis
Pyrimethamine (2 mg/kg per day for the first 2 days; then from day 3 to 6 months, 1 mg/kg per day and after that, 1 mg/kg per day, 3 times per week) *Plus* Sulfadiazine (100 mg/kg per day, divided twice per day, every 12 hours) *Plus* Folinic acid (10 mg, 3 times per week, until 1 week after the end of the treatment with sulfadiazine and pyrimethamine).	First 6 weeks: pyrimethamine plus sulfadiazine. After the first 6 weeks: • spiramycin (100 mg/kg per day, divided twice per day) for 6 weeks, • pyrimethamine plus sulfadiazine for 4 weeks. • The treatment should be alternated until 1 year of treatment is completed.
Add prednisone (1 mg/kg per day, divided twice per day, every 12 hours) to the treatment, if elevated CSF protein concentration > 1 g/dl or active chorioretinitis.	

Table 2. Clinical characteristics of the 4 cases.

	Case 1 (2000)	Case 2 (2002)	Case 3 (2009)	Case 4 (2010)
Birth place	Inborn	Outborn	Inborn	Inborn
Mother's age (years)	20	20	31	31
Trimester of seroconversion detection	2nd	1st	3rd	3rd
Performance of amniocentesis and confirmation of fetal infection	Yes	No	Yes	Yes
Pregnant woman's treatment	Sulfadiazine and pyrimethamine (between 32th week and 34th week)	No treatment	Spiramycin (since the time of seroconversion until confirmation of fetal infection). Pyrimethamine and sulfadiazine (since confirmation of the infection until the end of pregnancy)	Spiramycin, sulfadiazine and pyrimethamine
Gestational age (weeks)	38	35	38	39
Birthweight (grams)	3,070	2,377	3,102	3,995
Confirmed infection of the newborn	No	Yes	Yes	No
Newborn's treatment	Spiramycin	Sulfadiazine, pyrimethamine and folinic acid	Sulfadiazine, pyrimethamine and folinic acid	Sulfadiazine, pyrimethamine and folinic acid
Possible complications of congenital toxoplasmosis	No complications	Congenital hydrocephalus, seizures, intracranial calcifications, disturbances of the electrolyte (diabetes insipidus) and thermal regulation, bilateral microphthalmia, chorioretinitis, central apnea	Macular chorioretinitis, pyeloureteral junction syndrome, sub-ependymal hemorrhage	No complications

Table 3. Results of serologies.

		At birth	1-3 m	4-7 m	8-11 m	12-15 m	16-19 m	20-23 m
Case 1	**IgM**	-	-	-				
	IgG (UI/ml)	> 300	31	7				
Case 2	**IgM**	+						
	IgG (UI/ml)	631						
Case 3	**IgM**	+	-	-	-	-	-	
	IgG (UI/ml)	280	> 300	217.1	49.0	40.4	> 2,000	
Case 4	**IgM**	-	-	-	-	+	-	-
	IgG (UI/ml)	> 200	198.4	79	5.6	26.5	193.8	71.2

a birth weight of 3,070 g. The mother was 20 years old.

In the 2nd trimester of gestation, the mother was diagnosed with toxoplasmosis (positive IgM and IgG). The first ultrasound scan had been performed by the 20th week of pregnancy. Congenital infection was confirmed by amniocentesis. Treatment for toxoplasmosis (sulfadiazine and pyrimethamine) was initiated by the 32nd week of pregnancy and kept for 3 weeks.

Dubious Venereal Disease Research Laboratory (VDRL) test and positive Treponema Pal-

lidum Hemagglutination Assay (TPHA) test were detected in the 2nd trimester. Treatment for syphilis was performed during pregnancy with penicillin. Mother had had syphilis in 1998 but no further monitoring.

Anatomopathological study of the placenta was inconclusive for establishing toxoplasmosis infection.

After birth, the newborn displayed negative IgM antibodies for toxoplasmosis in the serum and IgG levels above 300 UI/ml. Cerebrospinal fluid (CSF) PCR for *Toxoplasma gondii* was negative.

The infant began treatment with spiramycin, and it was maintained for 4 months. It was suspended after 4 negative serologies.

Complete blood count, ophthalmologic examination, liver function, transfontanellar ultrasound, chest, and abdominal X-ray, abdominal ultrasound, and CSF analysis were all normal on the first days of life.

At the age of 2 years, she was diagnosed with pelvic rhabdomyosarcoma. She was treated with surgery, radiotherapy, and chemotherapy.

Subsequent ophthalmologic evaluations didn't show any findings related to toxoplasmosis.

The child had a normal development up to 2018.

Case 2

A female infant was born in August of 2002 in another hospital by elective cesarean section due to fetal hydrocephalus at 35 weeks of gestation. Her birth weight was 2,377 g. The mother was 20 years old. It was a high-risk pregnancy due to the fetal hydrocephalus diagnosed at 31 weeks of gestation. IgM and IgG antibodies for *Toxoplasma* in the 1st and in the 3rd trimester of gestation were positive (IgM was 0.25 UI/ml, and IgG was 15 UI/ml in the 1st trimester; IgM was 3.53 UI/ml, and IgG was 59,660 UI/ml in the 3rd trimester). Serology was not performed in the 2nd trimester. There is no information about the performance of amniocentesis or the treatment received during pregnancy.

On the 7th day of life, she showed positive IgM and IgG antibodies (**Tab. 3**). Treatment with sulfadiazine and pyrimethamine was started on day 10 and with folinic acid on day 15.

Transfontanellar ultrasound (day 4) was compatible with congenital hydrocephalus secondary to aqueductal stenosis and showed reduced brain parenchyma thickness. Cerebral CT (day 8) confirmed the ventricular dilatation observed and showed periventricular and basal ganglia calcifications. CSF examination (day 13) revealed high protein levels (3.44 g/l).

She was transferred to our hospital on the 8th day of life. A ventriculoperitoneal shunt with a low-pressure valve was placed on her on the 13th day of life. She started prednisolone because of chorioretinitis and an elevated concentration of proteins in the CSF. At a physical examination at admission, the newborn displayed macrocephaly (cephalic perimeter of 35 cm), narrow palpebral fissures, microphthalmia, enlarged and tense anterior fontanelle, pale and mottled skin, diminished reflexes. She showed a little reaction and weak crying to external stimuli, tremulous, and uncoordinated suction reflex. She had a normal blood count.

On the 17th day of life, she developed hypernatremia ($Na^+ = 154$), probably due to central diabetes insipidus. Water deprivation test was not performed because the patient was too young. She was treated with desmopressin for 2 days with clinical improvement.

Cerebral CT, on the 20th day of life, revealed diffuse enlargement of the brain CSF spaces and hypoplasia of the cerebellar hemispheres and brainstem. It also showed a sizeable intraventricular cyst on the left hemisphere. The parenchyma was thin, practically non-existent. The medial and anterior cerebral arteries showed parietal calcifications. There were also periventricular calcifications. Brain Magnetic Resonance imaging confirmed the lesions.

Electroencephalogram showed severe encephalopathy and paroxysmal activity.

Regarding the ophthalmologic examinations, she showed at birth: bilateral microphthalmia, a scar lesion in the macula of the right eye and active chorioretinitis in the left eye. She was treated with topical tropicamide, chloramphenicol, and prednisolone. Amaurosis was later diagnosed.

At 2 months of age, she presented with repeated episodes of clonic seizures. She was initiated on sodium valproate, vitamin D, and vitamin C. The cerebral CT showed severe hydrocephalus. It was performed surgery for revision of the ventriculoperitoneal valve and endoscopic fenestration of the intraventricular cyst.

At 5 months of age, the ventriculoperitoneal shunt was replaced by another with a 60 mmH_20 valve. During the hospital stay, the infant had episodes of seizures, hypothermia, and hypernatremia, in the context of diabetes insipidus. She also had episodes of apnea.

Cerebral CT at 6 months of age showed triventricular hydrocephalus.

The infant died at the age of 7 months. The autopsy was not performed due to parents' refuse.

Case 3

A male infant was born in April of 2009 in CHUSJ, by eutocic delivery, at 38 weeks of gestation, weighing 3,102 g. The mother was 31 years old. Pregnancy was kept under surveillance, and bilateral hydronephrosis was diagnosed at 21 weeks and 5 days of gestation. Positive anti-*Toxoplasma* IgM and IgG antibodies were detected in the 3rd trimester, and congenital infection was confirmed by amniocentesis. Serologies were negative in the first 2 trimesters. Ultrasounds performed at 33 weeks, 34 weeks, and 37 weeks of gestation didn't show any signs of toxoplasmosis infection. Mother was treated with spiramycin from the seroconversion until the performance of amniocentesis. After the amniocentesis test result come back positive, the treatment was changed to pyrimethamine and sulfadiazine. Therapy was maintained until the end of pregnancy. There were no other occurrences during pregnancy.

The newborn was started on sulfadiazine, pyrimethamine, and folinic acid on the 1st day of life and continued the treatment for a year.

On the first days of life (day 1 and day 12) serologies of the newborn for IgG and IgM antibodies were positive. PCR was negative for *Toxoplasma* DNA in both CSF and blood. Serology for IgM and IgG was positive in the CSF.

Blood count (day 1 and day 5) and hepatic function (day 7) were normal. Acoustic otoemissions were normal bilaterally. Acoustic evoked potentials were standard bilaterally.

Transfontanellar ultrasound (day 4) revealed right sub-ependymal hemorrhage and periventricular hyperechogenicity.

The newborn was diagnosed with left pyeloureteral junction syndrome with a diminished parenchymal thickness (demonstrated by ultrasound [day 4] and renogram [day 5]). His right kidney was normal. Pyeloplasty was performed at the age of 4 months with positive evolution. He was still showing a slight reduction of renal parenchyma thickness in subsequent examinations, without functional compromise, namely in the renogram. He didn't show any urologic symptoms.

Ophthalmologic examination (day 6) showed a macular scar lesion secondary to chorioretinitis in the left eye. The newborn was started on prednisolone on the 9th day of life, according to the protocol of the neonatology section of the Portuguese Society of Pediatrics.

Serologies were repeated periodically (**Tab. 3**). IgM antibodies turned negative 3 weeks after the introduction of the treatment. PCR for *Toxoplasma* DNA in the blood was also repeated periodically, and it was always negative.

Blood count evaluation was performed periodically, and it always displayed normal values until neutropenia was detected. The infant developed neutropenia as an adverse effect of the treatment with sulfadiazine and pyrimethamine. One month and 1 week after starting the therapy, he stopped it, when neutrophils count equaled 540/mm^3. He was directed to a hematology appointment and began treatment with granulocyte-colony stimulating factor (G-CSF). Three days after the G-CSF first dose, he restarted the treatment with sulfadiazine and pyrimethamine. He was neutropenic even with G-CSF treatment, but it was decided to stick with the toxoplasmosis' treatment because the infant didn't develop any infection during his neutropenic period.

When the neutrophil count was below 500/mm^3, prophylaxis with clindamycin was started.

The child was evaluated annually by ophthalmology. He keeps showing, since birth and in his last appointment (2018), a macular scar in the left eye with decreased visual acuity.

Case 4

A male infant was born in January of 2010 in CHUSJ, with 39 weeks of gestation, by eutocic delivery, weighing 3,995 g. In the 3rd trimester of gestation, seroconversion occurred with IgM and IgG antibodies being positive. There are no records on serologies being performed during the first 2 trimesters. The mother was 31 years old.

Fetal infection was confirmed by amniocentesis on the 31st week of gestation. Obstetric ultrasounds were normal. Treatment of the women was initiated 3 weeks after the confirmation of the infection, and it consisted of spiramycin, pyrimethamine, and sulfadiazine. There are no records regarding the time when the treatment was stopped.

By the time of birth, IgG antibodies for toxoplasmosis were positive, but IgM antibodies were negative. PCR was negative for toxoplasmosis in both CSF and blood (day 2). Hepatic function and blood count were normal. Acoustic otoemissions

were normal bilaterally (day 2). Acoustic evoked potentials were also normal bilaterally (day 2). Transfontanellar ultrasound was normal.

Treatment of the newborn consisted of pyrimethamine, sulfadiazine, and folinic acid. It was initiated on the 1st day of life, and it was continued for a year. When the child was 16 months old, the treatment was restarted. IgM antibodies had turned positive in 2 subsequent analyses, at 13 and 14 months old. The treatment was stopped at 24 months of age. Serologies were periodically repeated as we can see in **Tab. 3**. PCR for *Toxoplasma* DNA in the blood was also repeated periodically, and it was always negative.

There weren't any relevant findings in the examinations from ophthalmology and otorhinolaryngology. The child had normal development until 2017 (date of the last general medicine appointment).

Discussion

In the last 20 years in CHUSJ, 4 cases of congenital toxoplasmosis were observed. No cases were found between 2011 and 2018. Three out of these 4 were confirmed in the fetus by amniocentesis, and 2 were confirmed in the newborn. Three of these cases were born in CHUSJ, resulting in an incidence of 0.6/10,000 births.

In 2 out of the 4 cases, infants developed complications secondary to congenital toxoplasmosis. In both, case 2 and case 3, we observed ophthalmologic complications: bilateral microphthalmia, macular scar lesions secondary to chorioretinitis and active chorioretinitis.

Chorioretinitis is an inflammation of the retina and choroid, and it has been described as the most prevalent ophthalmologic complication of congenital toxoplasmosis [15]. In most cases, chorioretinitis causes little to no symptoms [16]. However, it may result in visual impairment if the macula is involved [15]. Microphthalmia is another described complication [15].

Case 2 presented with congenital toxoplasmosis with neurologic sequelae. The infant developed congenital hydrocephalus, seizures, intracranial calcifications, and disturbances of the electrolyte (diabetes insipidus) and thermal regulation. She also showed little reaction to stimuli and episodes of central apnea.

Congenital toxoplasmosis provokes an increase in the CSF protein levels, which leads to the obstruction of the aqueduct of Sylvius that results in a third ventricle dilation and hydrocephalus [15]. There are different mechanisms by which congenital toxoplasmosis can cause hydrocephalus: there can be an obstructive cause (e.g., obstruction of the aqueduct of Sylvius, obstruction of the foramina of Monro or mixed aqueductal and foraminal obstruction) or it can occur without obvious intraventricular obstruction (secondary to loss of brain parenchyma or due to poor reabsorption of CSF) [15, 17].

Congenital toxoplasmosis that affects the central nervous system (CNS) may target the hypothalamic-pituitary axis resulting in variable deficiencies of the pituitary hormones. Selective deficiency of one hormone like the one described in case 2 with the antidiuretic hormone is rare. There are only a few other cases like this described in the literature [18].

The episodes of apnea are likely to have a neurologic cause. Infection with the involvement of the CNS causes depression of the respiratory center. There is a cessation of output from the central respiratory center and, therefore, no respiratory effort [19].

Case 3 presented with pyeloureteral junction syndrome but, considering the absence of connection between the syndrome and congenital toxoplasmosis in the literature and given its prevalence in healthy children, we don't think it developed secondary to congenital infection [20]. This infant also showed sub-ependymal hemorrhage, which may, or may not, be related to the infection.

In case 3, the infant developed neutropenia secondary to toxoplasmosis treatment, and it was decided to suspend it. Pyrimethamine and sulfadiazine are known as medullar depressors [21, 22]. For that reason, it's advised for children who are going through this treatment to complement it with folinic acid and to perform periodic blood counts [10]. The infant didn't develop any infection despite his low neutrophil count.

One of the strengths of our study is that, as far as we are aware, it is the first paper in Portugal that describes cases of congenital toxoplasmosis and its complications. Furthermore, our results may contribute to future studies focusing on the incidence of congenital toxoplasmosis and its complications in Portugal.

The retrospective nature of this study resulted in some limitations: data was very difficult to collect, and some key information could not be obtained.

Conclusion

In 20 years of follow up, we only found 3 cases with congenital toxoplasmosis born in our hospital. This reflects an incidence of 0.6/10,000 births. The estimated incidence of congenital toxoplasmosis by the World Health Organization in 2013 was of 5/10,000 live births for the region where Portugal is inserted [7].

The low incidence observed in our hospital may be explained by the precautions taken by the nonimmunized pregnant women, detected through screening, to avoid possible sources of infection (e.g. avoiding changing cat litter, keeping cats indoors, not adopting or handling stray cats, especially kittens, avoiding drinking untreated water, cooking food to safe temperatures and peeling or washing fruits and vegetables thoroughly before eating [23]).

Another factor that may contribute to the small incidence is the early therapy with spiramycin administrated when seroconversion is detected, which may reduce the vertical transmission of the infection [10]. However, no randomized controlled trials have been performed to assess the effectiveness of the treatment with spiramycin [24].

At last, recent changes in alimentary habits and better hygiene practices in meat production may also have contributed to the reduction of exposure to *Toxoplasma gondii* [12] and therefore to our results.

In Portugal, universal screening is mandatory for all pregnant women. Further research is needed to evaluate the cost-effectiveness of such proceeding.

Declaration of interest

The Authors report no conflicts of interest. The Authors did not receive any funding for the present study.

References

1. Fallahi S, Rostami A, Nourollahpour Shiadeh M, Behniafar H, Paktinat S. An updated literature review on maternal-fetal and reproductive disorders of Toxoplasma gondii infection. J Gynecol Obstet Hum Reprod. 2018;47(3):133-40.
2. Benjamin IJ, Griggs RC, Wing EJ, Fitz G (Eds.). Andreoli and Carpenter's Cecil Essentials of Medicine, 9th ed. Philadelphia, PA: Elsevier-Sanders, 2016.
3. Paquet C, Yudin MH. No. 285 – Toxoplasmosis in Pregnancy: Prevention, Screening, and Treatment. J Obstet Gynaecol Can. 2018;40(8):e687-93.
4. https://www.cdc.gov/parasites/toxoplasmosis/epi.html#food, last access: February 18, 2018.
5. Flegr J, Prandota J, Sovičková M, Israili ZH. Toxoplasmosis – a global threat. Correlation of latent toxoplasmosis with specific disease burden in a set of 88 countries. PLoS One. 2014;9(3):e90203.
6. Mandell GL, Bennet JE, Dolin R (Eds.). Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, 7th ed. Philadelphia, PA: Elsevier/Churchill Livingstone, 2010.
7. Torgerson PR, Mastroiacovo P. The global burden of congenital toxoplasmosis: a systematic review. Bull World Health Organ. 2013;91(7):501-8.
8. Wilson CB, Remington JS, Stagno S, Reynolds DW. Development of adverse sequelae in children born with subclinical congenital Toxoplasma infection. Pediatrics. 1980;66(5):767-74.
9. Norma n° 037/2011 de 30/09/2011 atualizada a 20/12/2013.
10. Horta A, Leça A, Alexandrino AM, Ângelo H, Carapau J, Marques L, Varandas L, Areias MA, Carinhas MJ, Neto MT, Vasconcelos O, Ventura T. Protocolos de Diagnóstico e Terapêutica em Infecciologia Perinatal. Porto: Secção de Neonatologia da SPP, 2007.
11. Pomares C, Montoya JG. Laboratory Diagnosis of Congenital Toxoplasmosis. J Clin Microbiol. 2016;54(10):2448-54.
12. Gargaté MJ, Ferreira I, Vilares A, Martins S, Cardoso C, Silva S, Nunes B, Gomes JP. Toxoplasma gondii seroprevalence in the Portuguese population: comparison of three cross-sectional studies spanning three decades. BMJ Open. 2016;6(10): e011648.
13. Lopes AP, Dubey JP, Moutinho O, Gargaté MJ, Vilares A, Rodrigues M, Cardoso L. Seroepidemiology of Toxoplasma gondii infection in women from the North of Portugal in their childbearing years. Epidemiol Infect. 2012;140(5):872-7.
14. Lopes AP, Dubey JP, Dardé ML, Cardoso L. Epidemiological review of Toxoplasma gondii infection in humans and animals in Portugal. Parasitology. 2014;141(13):1699-708.
15. Khan K, Khan W. Congenital toxoplasmosis: An overview of the neurological and ocular manifestations. Parasitol Int. 2018;67(6): 715-21.
16. Wallon M, Garweg JG, Abrahamowicz M, Cornu C, Vinault S, Quantin C, Bonithon-Kopp C, Picot S, Peyron F, Binquet C. Ophthalmic outcomes of congenital toxoplasmosis followed until adolescence. Pediatrics. 2014;133(3):e601-8.
17. Hutson SL, Wheeler KM, McLone D, Frim D, Penn R, Swisher CN, Heydemann PT, Boyer KM, Noble AG, Rabiah P, Withers S, Montoya JG, Wroblewski K, Karrison T, Grigg ME, McLeod R. Patterns of Hydrocephalus Caused by Congenital Toxoplasma gondii Infection Associate with Parasite Genetics. Clin Infect Dis. 2015;61(12):1831-4.
18. Mohamed S, Osman A, Al Jurayyan NA, Al Nemri A, Salih MA. Congenital toxoplasmosis presenting as central diabetes insipidus in an infant: a case report. BMC Res Notes. 2014;7:184.
19. https://www.ncbi.nlm.nih.gov/books/NBK441969, last access: October 30, 2018.

20. Koff SA, Mutabagani KH. Anomalies of the kidney. In: Gillenwater JY, Grayhack JT, Howards SS, Mitchell ME (Eds.). Adult and Pediatric Urology, 4th ed. Philadelphia, PA: Lippincott Williams and Wilkins, 2002.
21. https://reference.medscape.com/drug/daraprim-pyrimethamine-342668#4, last access October 28, 2018.
22. https://reference.medscape.com/drug/sulfadiazine-342544#4, last access October 28, 2018.
23. https://www.cdc.gov/parasites/toxoplasmosis/prevent.html, last access: January 2, 2019.
24. Kravetz JD, Federman DG. Toxoplasmosis in pregnancy. Am J Med. 2005;118(3):212-6.