Toxoplasmosis in immunocompetent and immunocompromised population of Constanța, Romania

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Background

- Toxoplasmosis is a parasitic disease caused by the protozoan *Toxoplasma gondii*.

- The parasite infects most animals, including humans, but the primary host is the felid (cat) family.

- Toxoplasma may be transmitted via mouth-to-hand contact from improper handling or ingestion of raw meat or undercooked meat containing cyst from cat feces.
Geographical spread

• Up to a third of the world's human population is estimated to carry a *Toxoplasma* infection.

• Some studies show that in the world is very different seroprevalence
  – USA: 22.5%
  – Latin America: 50–80%
  – Eastern and Central Europe: 20–60%
  – Middle East: 30-50%
  – Southeast Asia: 20–60%
  – Africa: 20–55%
HIV population

- Findings on the association of HIV and toxoplasmosis seroprevalence are varied in different parts of the world.
  - some authors found higher prevalence of T. gondii specific IgG in HIV-infected patients (>70%) compared to non-infected individuals
  - others did not find any differences between the two groups

Seroprevalence of toxoplasmosis in HIV-infected patients.
Light red equals prevalence above 60%, brown equals 40-60%, blue 20-40%, yellow 10-20% green equals prevalence <10%, white equals absence of data.

Acute toxoplasmosis

- Immunocompetent persons with primary infection are usually asymptomatic (90%), but latent infection can persist for the rest of the host's life.

- The most common signs in acute infection are:
  - influenza-like symptoms
  - enlarged lymph nodes, especially around the neck in adults, but in children multiple sites may be more common
Latent toxoplasmosis

– Recent research has also linked toxoplasmosis with attention deficit hyperactivity disorder, obsessive compulsive disorder, and schizophrenia.

– Numerous studies found a positive correlation between latent toxoplasmosis and suicidal behavior in humans.

– “Crazy cat lady syndrome' is a term coined by news organizations to describe scientific findings that link the parasite Toxoplasma gondii to several mental disorders and behavioral problems.

– Jaroslav Flegr (biologist) is a proponent of the theory that toxoplasmosis affects human behavior.

• Toxoplasma gondii can sometimes cause or contribute to **Chronic Fatigue Syndrome**
  – is a neurological condition characterized by cognitive dysfunction, mood disorders, fatigue
Immunosuppressed persons

- More serious disease can develop due to *Toxoplasma* reactivation in AIDS, especially when the lymphocyte CD4 cell count drops below 100 cells / mm3
  - cerebral toxoplasmosis (Fig.1)
  - chorioretinitis (Fig.2)

- Toxoplasmosis is the most common parasitic CNS opportunistic infection in AIDS patients

- The HLA-DQ3 antigen is associated with susceptibility to toxoplasmic encephalitis in HIV-infected patients

Fig. 1. Cerebral toxoplasmosis
Multiple ring enhancing lesions are present throughout both cerebral hemispheres, with associated marked edema.

Fig. 2. Toxo chorioretinitis
Cutaneous toxoplasmosis

- **Skin lesions** may occur in the acquired form of the disease, including:
  - roseola
  - erythema multiforme-like eruptions,
  - prurigo-like nodules,
  - urticaria, and
  - maculopapular lesions.

Fig. After bone Marrow transplant
• Chemotherapy patients can develop eye, heart (myocarditis), lung or brain involvement when parasites become reactivated.

• In transplant patients, Toxoplasmosis
  – may result from reactivation of latent infection or from primary infection and
  – involve febrile myocarditis, encephalitis or pneumonitis.
• The aim of the study was to evaluate:
  
  – prevalence of toxoplasmosis
  
  – clinical manifestations in immunocompetent and immunocompromised persons.
  
  – risk factors for toxoplasma infection
Material and methods

- Were analyzed a total of 386 adult patients diagnosed with toxoplasmosis in the Clinical Infectious Diseases Hospital Constanta in the last 5 years.

- The reported acute toxoplasmosis cases were considered when serologic assays indicated an acute infection in accordance with clinical manifestation:
  - IgM Toxo – positive
  - Low IgG Toxo avidity
Results

- Of these 386 adult patients
  - 173 were diagnosed with acute infection based on laboratory protocol (44.8%).
  - most of them were female, majority aged between 30-49 years, 85% from urban area
  - 3% were diagnosed with HIV infection (12 patients),
    • in 3 patients, toxoplasmosis was the primary clinical manifestation.

<p>| | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Gender F/B (pts)</td>
<td>297 / 89</td>
</tr>
<tr>
<td>Age (median) (years)</td>
<td>32</td>
</tr>
<tr>
<td>Urban/rural area (pts)</td>
<td>328 / 58</td>
</tr>
<tr>
<td>Immunocompetent pts (No)</td>
<td>374</td>
</tr>
<tr>
<td>HIV infected pts (No)</td>
<td>12</td>
</tr>
<tr>
<td>Pregnant female (No)</td>
<td>56</td>
</tr>
<tr>
<td>Toxocara positive (pts)</td>
<td>43</td>
</tr>
</tbody>
</table>
• The most common clinical manifestation in non-HIV infected patients was **painless cervical adenopathy**

• **Cerebral toxoplasmosis** (mass lesions) only in a female with chronic hepatitis B and non-Hodgkin lymphoma, after chemotherapy

• **Pulmonary involvement** – after chemotherapy or renal transplantation (1 patient) - PCR assay for T. gondii

<table>
<thead>
<tr>
<th>Clinical Manifestation</th>
<th>Number of Patients</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>Cervical adenopathy</td>
<td>102 pts</td>
<td>27.3%</td>
</tr>
<tr>
<td>Flulike symptoms and generalized lymphadenopathy</td>
<td>36 pts</td>
<td>9.6%</td>
</tr>
<tr>
<td>Retroperitoneal and mesenteric lymphadenopathy</td>
<td>30 pts</td>
<td>8.1%</td>
</tr>
<tr>
<td>Seizures, persistent headache</td>
<td>62 pts</td>
<td>16.6%</td>
</tr>
<tr>
<td>Retinochoroiditis</td>
<td>42 pts</td>
<td>11.2%</td>
</tr>
<tr>
<td>Pulmonary involvement</td>
<td>4 pts</td>
<td>1.1%</td>
</tr>
<tr>
<td>Cerebral toxoplasmosis</td>
<td>1 pt</td>
<td>0.3%</td>
</tr>
<tr>
<td>Skin itching and rash</td>
<td>43 pts</td>
<td>11.5%</td>
</tr>
<tr>
<td><strong>(Toxocara canis positive)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pregnant women (acute/chronic)</td>
<td>56 pts (5/51)</td>
<td>14.9%</td>
</tr>
</tbody>
</table>

Total =374 non-HIV infected patients
Acute toxoplasmosis

- 173 were diagnosed with acute infection (44.8%)
  - **Cervical adenopathy** – 102 pts
  - Flulike symptoms and generalized lymphadenopathy – 36 pts
  - Retroperitoneal and mesenteric lymphadenopathy – 30 pts
  - **Pregnant women with** Flulike symptoms – 5 pts

*Note - other possible etiologies were excluded by pathological examination of the lymph nodes (67 pts)*

A microscopic examination of the specimens of cervical and axillary lymph node shows marked follicular hyperplasia with proeminent small granulomas composed almost entirely of epithelioid cells.
• In HIV infected patients prevailed cerebral toxoplasmosis
  – toxoplasmic encephalitis, +/- focal CNS lesions

<table>
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<tr>
<th>Cerebral toxoplasmosis</th>
<th>11 pts</th>
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<tbody>
<tr>
<td>Generalized lymphadenopathy and pulmonary involvement</td>
<td>1pt</td>
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</table>

Fig. 5.6 Cerebral toxoplasmosis
Multiple ring enhancing lesions are present throughout both cerebral hemispheres, with associated marked edema.

Fig. 7. Toxoplasmic encephalitis

Fig. 8. Toxo pneumonia
TOXO Seroprevalence in HIV infected patients

• 1024 patients under the supervision of the HIV/AIDS Regional Center Constanta,

  We tested for Toxo all patients

• 798 (78%) have positive Toxo IgG (latent toxoplasmosis)

  12 patients with AIDS (CD4 = 2 - 62 cel/mm3) were developed symptomatic toxoplasmosis in the last 5 years
Risk factors

- in all 386 patients we applied a standardized questionnaire on risk factors for infection with toxoplasma and compared the responses of these patients with another 200 noninfected patients.

<table>
<thead>
<tr>
<th>Risk factor (Yes/No)</th>
<th>Toxoplasma positive pts</th>
<th>Toxoplasma negative pts</th>
<th>95 % CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contact with cat</td>
<td>95/291</td>
<td>49/151</td>
<td>0.6765 - 1.4961</td>
<td>0.9763</td>
</tr>
<tr>
<td>Living on farm, working with animals</td>
<td>58/308</td>
<td>33/167</td>
<td>0.5974 to 1.5202</td>
<td>0.8398</td>
</tr>
<tr>
<td>Contact with soil</td>
<td>64/312</td>
<td>41/184</td>
<td>0.5974 to 1.4185</td>
<td>0.7075</td>
</tr>
<tr>
<td>Raw/undercooked meet (pork, lamb, sheep)</td>
<td>102/284</td>
<td>22/178</td>
<td>1.7671 to 4.7785</td>
<td>0.0001</td>
</tr>
<tr>
<td>Taste meat cooking</td>
<td>153/233</td>
<td>48/152</td>
<td>1.4174 to 3.0507</td>
<td>0.0002</td>
</tr>
<tr>
<td>Unpasteurised milk</td>
<td>24/362</td>
<td>12/188</td>
<td>1.0390 to 2.9101</td>
<td>0.5382</td>
</tr>
<tr>
<td>Untreated water</td>
<td>14/372</td>
<td>9/191</td>
<td>0.6412 to 2.0875</td>
<td>0.5944</td>
</tr>
<tr>
<td>Travel outside Europe</td>
<td>22/364</td>
<td>10/190</td>
<td>0.5329 to 2.4748</td>
<td>0.7240</td>
</tr>
</tbody>
</table>

Risk factors for infection with Toxoplasma in our county were: Raw / undercooked meat, taste meat cooking
Conclusion

• Reporting the number of cases of toxoplasma infection in Constanța population (254,693 inhabitants), we obtained a prevalence of **151.5 cases/100,000 inhabitants = patients with symptomatic toxoplasmosis**

• Most patients were female and their supervision is required for possible implications in pregnancy.

• Risk factors for infection with Toxoplasma in our county were:
  – raw/ undercooked meat,
  – taste meat cooking
Conclusions

• Because in the general population 90% of people infected with Toxoplasma are asymptomatic and TOXO Seroprevalence in HIV infected patients is 78% – we believe that Toxoplasma infection is underdiagnosed in our county.

• It requires a screening study – to establish real seroprevalence – to prevent developing complications
Last case (11.09.2014)

- male, 25 years old
- admitted to hospital with
  - seizures, persistent headache
  - severe labial herpes simplex
  - oftalmic herpez zoster
  - wasting syndrome
- HIV positive
- Cerebral Toxoplasmosis
Cerebral Toxoplasmosis

Associated marked edema

Ring enhancing lesion
Constanta
The best in communicable disease surveillance programs

Thank you for your attention!