

Acute liver failure: a rare clinical presentation of visceral leishmaniasis

Caterina Sagnelli¹, Francesca Di Martino², Nicola Coppola³, Antonello Crisci², Evangelista Sagnelli³

¹Department of Clinical and Experimental Medicine and Surgery "F. Magrassi e A. Lanzara, Second University of Naples, Italy;

²Department of Public Medicine, Law Medicine, Second University of Naples, Italy

³Department of Public Medicine, Section of Infectious Diseases, Second University of Naples, Italy

SUMMARY

We recently re-examined a case of Visceral Leishmaniasis, in a 36-year-old caucasian immune-competent men with an unusual clinical presentation. Together with symptoms and signs of a severe acute liver involvement, he presented weight loss, huge spleen enlargement, pancytopenia and increased γ -globulin serum level with a high polyclonal peak. He had no fever, but over-abundant night sweats were frequent. The patient was considered to have liver cirrhosis, and the diagnosis of visceral leishmaniasis was made with a year's delay. From this case report we may learn that, despite an unusual clinical presentation, the diagnosis of visceral leishmaniasis should not be excluded when other characteristic signs and symptoms and laboratory abnormalities are present.

KEY WORDS: Visceral leishmaniasis, Acute hepatitis

Received June 23, 2011

Accepted October 12, 2011

INTRODUCTION

Few cases of visceral leishmaniasis mimicking an acute hepatitis have been described in adults. This clinical presentation is infrequent also in infants and children, in these cases raising a difficult differential diagnosis with cholestatic syndromes in infancy (Pahwa R *et al.*, 2004; Moragas A, *et al.*, 1986; Giannitrapani L, *et al.*, 2009; Singh NP, *et al.*, 2006).

The most frequent and prominent clinical symptoms and signs in visceral leishmaniasis are recurring fever, weight loss, weakness, profuse night sweats, enlargement of liver, spleen and lymphoid organs, anemia, neutropenia and thrombocytopenia. Patients with symptomatic visceral leishmaniasis may show all or some of these symptoms and signs, some factors such malnutrition or immune suppression, including HIV coinfection,

increasing the likelihood of a more severe or prolonged clinical course.

Visceral leishmaniasis is usually fatal if not treated both in adults and children. Some authors recently investigated the risk factors for death associated with visceral leishmaniasis in children and found a case-fatality rate of 10%, the independent predictors of risk of dying from visceral leishmaniasis being mucosal bleeding, jaundice, dyspnea, suspected or confirmed bacterial infections, neutrophil count $<500/\text{mm}^3$ and platelet count $<50,000/\text{mm}^3$ (Sampaio M J, *et al.*, 2010).

CASE REPORT

In August 1999 a 36-year-old Italian men had fever for 15 consecutive days, spontaneously remitting in the absence of other signs or symptoms. Two months later the patient was hospitalized in a local hospital because of jaundice, asthenia, anorexia and over-abundant night sweats. Liver and spleen were enlarged, and the following abnormalities were recorded: AST 1339 IU/mL, ALT 951 IU/mL; total bilirubin 8.6 mg/dL (conjugated 6.3 mg/dL), serum albumin 3.3 g/dL, serum γ -globulin 4.4 g/dL with a polyclonal peak,

Corresponding author

Evangelista Sagnelli

Department of Public Medicine

Section of Infectious Diseases

Second University of Naples

Via L. Armanni, 3 - 80135 Naples, Italy

E-mail: evangelista.sagnelli@unina2.it

protrombin activity 51%. Other abnormalities were high IgG (4.260 mg/dL) and IgM (537 mg/dL) serum values, and pancytopenia. HAV-Ab IgM, anti-HCV and HBsAg were negative and HAV-Ab IgG and IgM anti-HBc positive. Physical examination revealed an enlarged liver and an enlarged spleen with the inferior margin 6 cm below the costal arch, there was night sweat but no fever. During the hospitalization a reduction in AST to 152 IU/mL, ALT to 123 IU/mL and bilirubin (total to 2.15 mg/dL and conjugated to 0.75 mg/dL) was observed. Prothrombin activity remained low (53%), pancytopenia persisted, albumin lowered to 2.8 g/dL and γ -globulin increased to 5.6 g/dL with a characteristic polyclonal peak; no monoclonal component was found. The patient was discharged and the diagnosis was "acute hepatitis B".

One month later the patient was admitted to another local hospital for reactivation of liver disease, AST 864 IU/mL, ALT 584 IU/mL, total bilirubin 2.9 mg/dL (conjugated 2.5 mg/dL), protrombin activity 39%, serum albumin 2.5 g/dL; γ -globulin remained unchanged. HBsAg, total and IgM anti-HBc were negative raising doubts over the previous positive results. The volume of liver and spleen remained unchanged. A US examination described an enlarged liver with coarse echopattern, irregular surface and irregular inferior margin, signs of portal hypertension and a normal spleen volume, but serious doubts remain on the truthfulness of this US report particularly in the light of subsequent US and CT and of the clinical course of the illness. Fever was absent and overabundant night sweats present during hospitalization. Aminotransferases and bilirubin consistently decreased during hospitalization and the patient was discharged the 15th December with the diagnosis of "liver cirrhosis and polyclonal gammopathy". A few days later the patient was admitted again to the same hospital with AST 836 IU/mL and ALT 711 IU/mL, total bilirubin 3.8 e direct bilirubin 2.82 mg/dL, albumin 2.3 g/dL, γ -globulin 6.6 g/dL with the characteristic polyclonal peak, haemoglobin 9.8 g/dL, neutrophils $1.28 \times 10^3/\mu\text{L}$ and platelets $111 \times 10^3/\mu\text{L}$. A second US examination described a much enlarged spleen as the only abnormality. During hospitalization a decrease of aminotransferases and bilirubin was observed and the patient was discharged at the end of December with a diagnosis

of "autoimmune cirrhosis": this diagnosis was made in the absence of data on non organ specific autoantibodies, another weak point in the clinical management of this patient. A daily dose of 25 mg of prednisone was started, reduced to 12.5 mg after 3 months. Visceral leishmaniasis was never hypothesized by the physicians of these two local hospitals, probably because of the presence of signs and symptoms of severe liver involvement and the absence of fever.

Until September 2000, the patient was followed at home by his family doctor. There was no fever, aminotransferases and bilirubin were only moderately increased (possibly because of prednisone treatment), laboratory abnormalities remained substantially unchanged but physical conditions progressively deteriorated, asthenia and anorexia increased and over-abundant night sweats persisted. The patients' body weight decreased from 85 to 66 kg. In September 2000 non organ specific auto-antibodies were finally determined and although negative the low dose steroid treatment was confirmed. In October 2000 an abdominal CT examination showed a liver moderately enlarged and a spleen with a longitudinal diameter of 21 cm.

Due to the worsening clinical conditions, the patient was hospitalized in January 2001 in a referral clinical centre to be evaluated for liver transplantation. On admission serum aminotransferases and bilirubin were normal and no sign of portal hypertension was observed at US and EGDS. CT examination showed a normal liver and a spleen with a longitudinal diameter of 23 cm. Antibodies to HIV-1, 2 and serum markers of hepatitis viral infections were negative. The following laboratory abnormalities were recorded: albumin 1.7 g/dL, γ -globulin 4.59 g/dL still with the polyclonal peak, neutrophils $0.290 \times 10^3/\mu\text{L}$, platelets $68 \times 10^3/\mu\text{L}$, hemoglobin 6.5 g/dL, MVC 76 fl, MCH 23.2 pg, MCHC 30.5 g/dL, prothrombin activity 59%. Two units of blood were then transfused.

Visceral leishmaniasis was hypothesized and a 1:1024 antibody title was found. The diagnosis was confirmed by the presence of numerous Leishmaniae in the bone marrow. Previous treatment was discontinued and N-methylglucamine antimoniate was administered for 21 days with no side-effects. Clinical conditions progressively improved and laboratory data became normal or nearly normal in 3 months; γ -globulin decreased

to 3.19 g/dL without polyclonal peak. By April 2001 the patient was considered recovered and turned to a normal life.

The patient was last observed at the end of November 2002. He was in very good clinical condition, his body weight was 82 Kg and the following laboratory data were recorded: albumin 4.21 g/dL, γ -globulin 1.41 g/dL, neutrophils 1.164 $\times 10^3/\mu\text{L}$, platelets 149 $\times 10^3/\mu\text{L}$ hemoglobin 15.4 g/dL, protrombin activity 83%, AST and ALT in the normal range.

DISCUSSION

The possibility of mistaking visceral leishmaniasis for a chronic liver disease was previously described in a clinical report on a patient with a clinical and biochemical presentation resembling liver cirrhosis who died of visceral leishmaniasis because the diagnosis was made too late and treatment with sodium antimony stibogluconate started shortly before death (Mohan A, Vishnuvardhan Reddy, *et al.*, 2007; Prakash A, *et al.*, 2006).

The diagnosis may be difficult even in children who may occasionally show acute hepatitis as a presenting manifestation of visceral leishmaniasis (Hervas JA, *et al.*, 1991).

In the case of visceral leishmaniasis described here the correct diagnosis was delayed by the rarity of clinical presentation, characterized by the concomitance of two rare events, the severe acute hepatic involvement and the absence of fever. These rare events, however, should not divert from a correct diagnosis if other characteristic signs and symptoms and laboratory abnormalities are present.

Funding: The authors have no funding/financial source to disclose.

Competing interests: The authors have declared that no competing interests exist.

REFERENCES

- MOHAN A., VISHNUVARDHAN R., SAMANTARAY J.C., SHARMA S.K. (2007). A rare presentation of visceral leishmaniasis without fever or splenomegaly in an elderly person. *Eur. J. Int. Med.* **18**, 158-160.
- MORAGAS A., SERRANO A., TORÁN N. (1986). Acute form of visceral leishmaniasis in a 3-month-old infant. *Pediatr. Pathol.* **6** (1), 111-117.
- GIANNITRAPANI L., SORESI M., LA SPADA E., TRIPODO C., MONTALTO G. (2009). Progressive visceral leishmaniasis misdiagnosed as cirrhosis of the liver: a case report. *J. Med. Case Reports.* **25**, 3, 7265.
- HERVAS J.A., ALBERTI P., FERRAGUT J., CANET R. (1991). Acute hepatitis as a presenting manifestation of kala azar. *Pediatr. Infect. Dis. J.* **10**, 409-410.
- PAHWA R., GUPTA S.K., SINGH T., NIGAM S. (2004). Acute fulminant visceral leishmaniasis in children - a report of two cases. *Indian. J. Pathol. Microbiol.* **47** (3), 428-430.
- PRAKASH A., SINGH N.P., SRIDHARA G., MALHOTRA V., MAKHIJA A., GARG D., PATHANIA A., AGARWAL S.K. (2006). Visceral Leishmaniasis masquerading as chronic liver disease. *J. Assoc. Phys. India.* **54**, 893-894.
- SAMPAIO M.J., CAVALCANTI N.V., ALVES J.G., FILHO M.J., CORREIA J.B. (2010). Risk factors for death in children with visceral leishmaniasis. *PLOS Neglected tropical diseases.* **2**, 4 (11): e877.
- SINGH N.P., SRIDHARA G., MALHOTRA V., MAKHIJA A., GARG D., PATHANIA A., AGARWAL S.K. (2006). Visceral leishmaniasis masquerading as chronic liver disease. *J. Assoc. Physicians. India.* **54**, 893-894.

