

# ECHINOCOCCUS MULTILOCULARIS - NOVI ZONOTSKI PATOGEN U SRBIJI, PATO-HISTOLOŠKE ODLIKE KOD HUMANIH SLUČAJEVA

## ECHINOCOCCUS MULTILOCULARIS - A NEW ZONOTIC PATHOGEN IN SERBIA, PATHOHISTOLOGICAL FEATURES IN HUMAN CASES

Dušan Lalošević<sup>1</sup>, Mirjana Živojinov<sup>1</sup>, Aleksandra Đikić Rom<sup>1</sup>

<sup>1</sup> Medicinski fakultet Univerziteta u Novom Sadu, Medicinski fakultet Univerziteta u Beogradu

### SAŽETAK

Uvod: Na teritoriji Srbije kod ljudi postoji cistična ehinokokoza koju izazivaju dva molekularno slična agensa: *Echinococcus granulosus sensu stricto* kao i *E. canadensis*. Od decembra 2022. znamo i da postoji kod ljudi infekcija sa *E. multilocularis s. alveolaris*, uzročnika multilokularne ili alveolarne ehinokokoze čoveka. Dijagnoza alveolarne ehinokokoze se obično postavlja na operativnom materijalu, najčešće jetre, koja je operisana pod sumnjom na tumor. Zato smatramo važnim da se istaknu razlike između cističnog i multilokularnog ehinokoka na patološkom materijalu.

Prikaz serije bolesnika: Do sada su potvrđena tri slučaja alveolarne ehinokokoze iz Srema i četiri iz Sandžaka. Prvi i treći slučaj iz Srema sa lokalizacijom na jetri su operisani, drugi slučaj je inoperabilan zbog veličine lezije, ali je histološki u biopsiji dokazan ehinokok, a serološki je utvrđena multilokularna vrsta. Slučajevi multilokularne ehinokokoze iz Sandžaka takođe su imali lokalizaciju na jetri a dijagnoza je postavljena postoperativno.

Patohistološka analiza izvršena je kod 4 slučaja multilokularne ehinokokoze, dva sa područja Sandžaka i dva iz Srema i komparirana sa serijom slučajeva hidatidne ehinokokoze iz rutinske patološke dijagnostike. Patohistološke odlike multilokularne ehinokokoze su, za razliku od cistične, brojne male ciste infiltrativnog rasta.

Zajednička odlika kod cistične i multilokularne ehinokokoze su ehinokokne membrane, koje se prepoznaju kao višeslojne, od paralelno postavljenih slojeva. Međutim, membrane kod cističnog ehinokoka su znatno deblje, dok su kod multilokularnog tanke i izvijane.

Glavna razlika između ovih vrsta je da cistični ehinokok ima pravilnu jednu ili više cisti koje polako rastu ekspanzivno, dok multilokularni ima jako veliki broj malih nepravilnih cisti milimetarske veličine koje ponekad mogu dostići i centimetar, ali to je najčešće rezultat njihovog slivanja dok je tip rasta infiltrativni.

Pericista kod cističnog ehinokoka je debela vezivna membrana, dok je kod multilokularnog izražena destruentna fibroza i opsežne nekroze kako parenhima organa, tako i tkiva ehinokoka, pri čemu nastaje jedna ili više većih pseudocisti kolikviranjem nekroze.

Metastaziranje je registrovano kod jednog slučaja multilokularne ehinokokoze u regionalni limfni čvor jetre, kao i radiološki suspektne metastaza u plućima.

Kod sva četiri slučaja multilokularne ehinokokoze morfološka dijagnoza je potvrđena molekularnim metodama. Kod jednog drugog slučaja ehinokokoze kičmenog stuba, odnosno paravertebralne muskulature, morfološka dijagnoza vrste ehinokoka nije bila sigurna, ali je molekularna analiza dokazala cističnu ehinokokožu.

Zaključak: Tri humana slučaja do sada su dokazana iz regiona Srema, gde je 2016. godine dokazana enzootija multilokularne ehinokokoze kod lisica i šakala. Prvi slučaj humane multilokularne ehinokokoze iz Sandžaka objavljen je 2022. godine, mada u radu nije navedena tačna vrsta ehinokoka. Time je otklonjena prva zabluda da humanih slučajeva multilokularne ehinokokoze nema u Srbiji. Druga zabluda bila je da nikada ne postoji formiranje protoskoleksa kod humanih slučajeva multilokularne ehinokokoze. Od četiri pacijenta, kod jednog su nađeni protoskoleksi, mada je morfološka i molekularna dijagnoza multilokularne ehinokokoze potvrđena.

### ABSTRACT

Introduction: On the territory of Serbia, there is cystic echinococcosis in humans, which is caused by two molecularly similar agents: *Echinococcus granulosus sensu stricto* and *E. canadensis*. Since December 2022, we also know that there is infection in humans with *E. multilocularis s. alveolaris*, the causative agent of multilocular or alveolar echinococcosis in humans. The diagnosis of alveolar echinococcosis is usually made on surgical material, most often the liver, which was operated on under suspicion of a tumor. Therefore, we consider it important to highlight the differences between cystic and multilocular echinococcosis on pathological material.

Case report series: So far, three cases of alveolar echinococcosis from Srem region, Northern Serbia, and four from Sandžak, from the South, have been confirmed. The first and third cases from Srem with localization of lesion in the liver were operated on, the second case was inoperable due to the size of the lesion, but histologically in the biopsy *Echinococcus* was proven, and serologically the multilocular species was determined. Cases of multilocular echinococcosis from Sandžak also had localization in the liver and the diagnosis was made postoperatively.

Pathohistological analysis was performed in 4 cases of multilocular echinococcosis, two from the Sandžak area and two from Srem and compared with a series of cases of hydatid echinococcosis from routine pathological diagnostics. Pathohistological features of multilocular echinococcosis in contrast to cystic, are numerous small cysts of infiltrative growth.

A common feature of cystic and multilocular echinococcosis is the echinococcal membranes, which are recognized as multilayered, consisting of parallel layers. However, the membranes in cystic echinococcus are significantly thicker, while in multilocular they are thin and twisted.

The main difference between these types is that cystic echinococcus has one or more regular cysts that slowly grow expansively, while multilocular has a very large number of small irregular cysts of millimeter size that can sometimes reach a centimeter, but this is most often the result of their merging, while the growth type is infiltrative.

The pericyst in cystic echinococcosis is a thick connective membrane, while in multilocular, there is pronounced diffuse fibrosis and extensive necrosis of both the organ parenchyma and the echinococcal tissue, with one or more larger pseudocysts forming by coalescing necrosis.

Metastasis was registered in one case of multilocular echinococcosis in the regional lymph node of the liver, as well as radiologically suspicious metastasis in the lungs.

In all four cases of multilocular echinococcosis, the morphological diagnosis was confirmed by molecular methods. In another case of echinococcosis of the spinal column, i.e. of the paravertebral muscles, the morphological diagnosis of the echinococcal species was not certain, but molecular analysis proved cystic echinococcosis.

Conclusion: Three human cases have been proven so far from the Srem region, where enzootic multilocular echinococcosis was proven in foxes and jackals in 2016. The first case of multilocular echinococcosis from Sandžak was published in 2022, although the exact species of echinococcus was not specified in the paper. This dispelled the first misconception that there are no human cases of multilocular echinococcosis in Serbia. The second misconception was that protoscoleces formation never occurs in human cases of multilocular echinococcosis. Out of four patients, protoscoleces were found in one, although the morphological and molecular diagnosis of multilocular echinococcosis was confirmed.