ANALYSIS OF P62 ACCUMULATION IN PATIENTS WITH ALPHA-1-ANTITRYPSIN DEFICIENCY WITH DIFFERENT DISEASE OUTCOME
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α1-antitrypsin deficiency (α1ATD) is related to inherited point mutation in allele Z, which alters protein(ATZ) folding [1]. It causes ATZ accumulation with different clinical disease characteristic, ranging from absence of hepatic symptoms, via liver inflammation to cirrhosis, requiring liver transplantation [2]. Unfortunately markers letting prognosis of liver disease are missing. p62 protein is involved in the packing and delivery of misfolded proteins for their clearance through autophagy in mammalian cells [3]. It was found in tumor cells that the accumulation of p62 is an evidence of autophagy deficiency [4]. The aim of our study was to analyse of p62 accumulation in hepatocytes of α1ATD patients (pts) with unfavourable or good prognosis.

Liver tissue samples divided into groups: I – α1ATD pts with unfavourable prognosis; II – α1ATD pts with good prognosis and group III – pts with biliary atresia as control group were investigated. Paraffin 4 µm thick sections were labelled with rabbit monoclonal anti – p62 antibody (1:400, Cell Signalling), next Alexa Fluor 488 goat anti- rabbit (1:500, Life technologies). Localizations of p62 in portal and central zone of the liver lobule sections were investigated with confocal microscope (FV-1000, Olympus). Morphometric method (CellSense program, Olympus) was used to quantify positive reactions (more than 2 pixels).

Obtained morphometric results are demonstrated in Table 1. Statistical analysis of p62 localization revealed in group I no difference between both zones, in group II high accumulation in portal zone, in group III high accumulation in central zone. Significant differences were found between group I and II in both localisations, between group II and III in central zone.

Table 1. Results of p62 accumulation in patients with α1ATD unfavourable (I), good (II) prognosis and biliary atresia (III).

<table>
<thead>
<tr>
<th>Lobular zone</th>
<th>Portal</th>
<th>Central</th>
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<tr>
<td>Group of patients</td>
<td>I</td>
<td>II</td>
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<td>% mean of hepatocytes with accumulation of p62 (±SD)</td>
<td>49,76 (±22,85)</td>
<td>28,33 (±17,74)</td>
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In conclusion accumulation of p62 is diversifying patients with good and unfavourable prognosis of α1ATD.

References: