TITLE: Extracellular vesicles from *Sporothrix brasiliensis* are an important virulence factor that induce an increase in fungal burden in experimental sporotrichosis

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ABSTRACT: Sporotrichosis is a mycosis that affects the skin, lymphatic system and other organs in humans and animals. The disease has a worldwide distribution, with endemic areas in Brazil, and is caused by a complex of species, including *Sporothrix brasiliensis*. Some fungi release extracellular vesicles (EVs) that can interact with the host cell and modulate the host immune response. The aim of this study was to analyze the participation of *S. brasiliensis* EVs in the modulation of dendritic cells (DCs) and in the control of infection *in vivo*. Our results showed that *in vitro*, the EVs isolated from *S. brasiliensis* induced an increase in the phagocytic index and fungal burden in DCs. In addition, we were able to analyze the composition of the EVs, finding 70-kDa and 100-kDa components. Besides that, to verify the protein composition of EVs, we performed LC-MS/MS. We found a total 63 proteins in *S. brasiliensis* and some proteins related to several processes, such as metabolism and transport, were identified. We described heat shock protein, major facilitator superfamily transportes, serine, cell wall glucanase and uncharacterized proteins. These proteins can also act as virulence factors in infection. Then, the EVs were inoculated into BALB/c mice before subcutaneous infection with yeast, and the lesion was analyzed. An increase in fungal burden and lesion diameter were observed after 21 days in mice inoculated with a high concentration of EVs. However, after 35 days, we observed a regression of the lesion, which persisted until 42 days after infection. Interestingly, we observed an increase in fungal burden in these mice. These results suggest that EVs can play an important role in virulence and modulation of the host immune system during experimental *S. brasiliensis* infection.

Keyword: Extracellular vesicles, *Sporothrix brasiliensis* and sporothricosis