Original Article

Common antigens between hydatid cyst and cancers

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Abstract

Background: Different research groups reported a negative correlation between cancers and parasitical infections. As an example, the prevalence of a hydatid cyst among patients with cancer was significantly lower than its prevalence among normal population. Tn antigens exist both in cancer and hydatid cyst. This common antigen may be involved in the effect of parasite on cancer growth. So in this work, common antigens between hydatid cyst and cancers have been investigated.

Materials and Methods: Different hydatid cyst antigens including hydatid fluid, laminated and germinal layer antigens, and excretory secretory antigens of protoscolices were run in SDS PAGE and transferred to NCP paper. In western immunoblotting, those antigens were probed with sera of patients with different cancer and also sera of non-cancer patients. Also, cross reaction among excretory secretory products of cancer cells and antisera raised against different hydatid cyst antigen was investigated.

Results: In western immunoblotting, antisera raised against laminated and germinal layers of hydatid cyst reacted with excretory secretory products of cancer cells. Also, a reaction was detected between hydatid cyst antigens and sera of patients with some cancers.

Conclusion: Results of this work emphasize existence of common antigens between hydatid cyst and cancers. More investigation about these common antigens is recommended.

Key Words: Cancer, common antigen, hydatid cyst

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INTRODUCTION

An adverse relationship between some parasitic infections and cancer in human population has been reported by different research groups.[1-3] Anticancer activity of some parasites such as *Trypanosoma cruzi,*[4-10] *Toxoplasma gondii,*[11-18] *Toxocara canis,*[19] *Acantamoeba castellani,*[20] and *plasmodium Yoelii*[21] have been shown in experimental animals. *In vitro* investigations also revealed that some parasites such as *Trypanosma cruzi,*[9,22] hydatid cyst protosciles,[23] and *Toxoplamagondii*[11,24] show anticancer activities. Moreover, it has been shown that cancer-associated mucin-type *O*-glycan compositions are made by parasites.[25,26]

Unusual *O*-glycans such as the α-*N*cetylgalactosamine-*O*-serine/threonine (Tn), sialyl-Tn or Thomsen-

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Friedenreich (TF) antigens presented in cancer cells have important roles in metastasis, cell adhesion, and invasion.[27] Parasite *O*-glycans and mucin-like molecules seem to have important functions in the interaction of helminthes and their hosts.[28] It has been shown that mucin-type *O*-glycan structures of cancers are expressed by helminthes. As an example, the adult worm of *Schistosoma mansoni* and its schistosomula express Tn antigen.[26] In other studies, expression of Tn antigen in adult and larval stages of *Echinococcus granulosus* was shown.[25] Another carbohydrate antigen, called Tk, is expressed at the surface of human colorectal carcinomas. This antigen was found in *Taenia crassiceps, Mesocestoides voga*, and *Taenia hydatigena.*[29] More carbohydrate antigens such as sialyl-Tn antigens and TF antigens have also been recognized as common antigens of cancers and parasites.[25,30-32] We considered these unusual *O*-glycan antigens as common antigens of cancers and parasites. These antigens received great attention because antibody response to them yields protection against certain cancers.[33,34] Moreover, these antigens may be involved in anticancer activities of some parasites.[35] So in this work, immunological cross reaction between cancers and hydatid cyst, larval stage of *Echinococcus granulosus*, has been investigated.

MATERIALS AND METHODS

In this experimental study, *Echinococcus granulosus* hydatid cysts were collected from sheep or cattle from a slaughter house in Isfahan, Iran. Hydatid fluid was aspirated, collected, and examined for the presence of protoscolices. The fluids were then centrifuged at 2000×g, for 2 min, and the supernatant was concentrated using the lyophilizer apparatus and kept at -20 as hydatid fluid antigen. The sediment which was compact protoscolices washed with isotonic saline, sonicated, and kept at -20 as crude protoscolice antigen. Also, culture medium was added to compact alive protoscolices, and following 48 hours incubation was centrifuged at 2000×g, for 2 min and the supernatant was used as excretory secretory molecules of protoscolices (ES antigen). Laminated and germinal layers were removed from the cyst, homogenized, and then sonicated and kept at -20 as laminated and germinal layers antigen.

Polyspecific rabbit antisera were raised against four hydatid cyst antigens by injecting 4 rabbits fortnightly with 1 ml of emulsions containing equal volume of each antigen and ferund's adjuvant (complete for the first and incomplete for the boosters). Polyacrylamide gel electrophoresis with sodium dodecyl sulfate (SDS-PAGE) was performed as described by Laemmli[36] under non-reducing condition using the BIO RAD apparatus. Western immunoblotting was performed as described by Towbin *et al*.[36] using the BIO RAD apparatus. Pooled sera for each cancer was prepared by mixing 0.5 ml of 10 individual patients sera. For preparing cancer cell ES antigens, Baby Hamster Kidney (BHK) cell line was purchased from Pasture institute cell bank in Tehran, Iran. 6 million cells were incubated in 5 ml culture medium for 48 hours. Then they were centrifuged at 2000×g for 5 min and the supernatant was kept as excretory secretory antigen of cancer cells.

RESULTS

Different hydatid cyst antigens including: hydatid fluid, crude antigen of protoscolices, excretory secretory antigen, laminated and germinal layers antigens were run in SDS-PAGE and were transferred to NCP papers. Each antigen probed with pooled sera (10 sera for each cncer) of patients with (i) breast cancer, (ii) colon cancer, (iii) blood cancer, (iv) normal sera. Breast cancer sera reacted with a band in hydatid fluid antigen about 40-50 KDa. This reaction was not clear for other cancers and was not observed with normal sera.

Also, hydatid cyst fluid antigen was probed with different cancer sera in western immunoblotting. Results of this experiment revealed that breast cancer sera reacted with hydatid cyst antigen [Figure 1].

In another experiment, excretory secretory products of cancer cells were probed with different rabbit antisera in western immunoblotting. Antiserum raised against laminated and germinal layer of hydatid cyst reacted strongly with excretory secretory products of cancer cells [Figure 2].

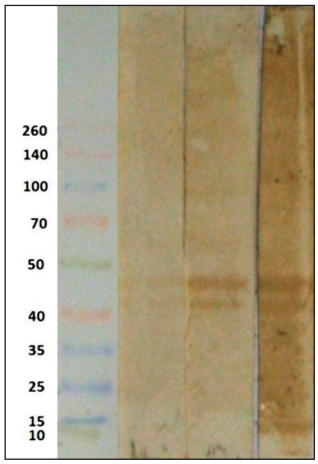

Figure 1: Western immunoblotting of hydatid cyst fluid antigen probed with (from left) normal sera, sera of patients with breast cancer and a patient serum with hydatid cyst

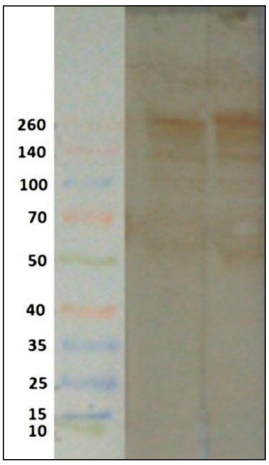

Figure 2: Western immunoblotting of cancer cells ES antigens probed with the sera of rabbits raised against hydatid cyst Laminated and germial layers antigen (both lanes)

DISCUSSION

In this investigation, it has been shown that rabbit antisera raised against hydatid cyst antigens specially laminated and germinal layers antigen reacted with excretory secretory products of cancer cells. Also, patient's sera with cancers especially breast cancer reacted with antigens of hydatid cyst.

Mucin-type *O*-glycans have important roles in cancer metastasis.[27] These molecules have also important functions in the interaction of helminthes and their hosts.[28] Nyame *et al*. showed that mucin-type *O*-glycan structures of cancers are expressed by the adult worm of *Schistosoma mansoni*.[26] These molecules have also been shown in another parasites such as *Echinococcus granulosus, Taenia crassiceps, Mesocestoides voga*, and *Taenia hydatigena*.[29] According to these investigations, mucin-type *O*-glycans are expressed in both cancer cells and helminthic parasites. These findings are consistent with our results and emphasize existence of common antigens both in cancers and helminthes. Tn antigens which exist both in cancers and parasites are glycosylated molecules so the cross reaction between cancer patient's sera and hydatid cyst antigen may be related to carbohydrate branches of the glycoproteins.

Immunological cross reaction of hydatid cyst antigens and cancer patient's sera has been reported in previous investigations.[37,38] In a study, only 6.3 of 270 cancer patients sera reacted with hydatid fluid antigens in ELISA. However, the cross reaction was not detectable in western immunoblotting with the 8 kDa band.[38] The smallest 8 kDa subunit of antigen B is a peptide band while we assumed that immunological cross reaction between hydatid cyst antigens and cancer patient's sera may be mainly related to carbohydrate branches of glycoproteins. In the present investigation, we did not get antibody reaction against 8kDa band in western blotting, instead the reaction was against 40-50 kDa bands. Moreover, the majority of sera of patients with breast cancer reacted with these bands in western blotting.

In conclusion, in this study for the first time we showed that a mutual cross reaction exists between antigens of hydatid cyst and excretory secretory products of cancer cells. More investigation is needed to confirm that this cross reaction is related to carbohydrate molecules.

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