

Unsolved Mystery of Synchronous Metastatic Adenocarcinoma and *Echinococcus* Cystic Infection, a Major Break Through in Clinical Oncology: A Case Report

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Abstract- *Echinococcus* cystic infection is a zoonotic infection caused by the larval stage of cestode species belonging to the genus *Echinococcus*. Through the modulation of the immune system by this parasite, there is an established link of this infection with the metastasis and progression of a tumor. We present a case of a patient with synchronous findings of metastatic adenocarcinoma with unknown primary along with the previous history of echinococcal infection, which highlights the need for prompt management of such infections with a regular follow up of such patients.

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Introduction

Echinococcus is a zoonotic infection caused by the larval stage of cestode species belonging to the genus *Echinococcus*. Although *E. granulosus* was initially regarded as the only causative agent of cystic echinococcosis (CE), it was clear that there were different taxa with differences in adult morphology, host specificity, and pathogenicity (1). Immune system modulation caused by this parasite plays an important role in the metastasis and progression of a tumor (2-3).

Echinococcosis is (one of the 17 neglected tropical diseases NTDs) recognized by the World Health Organization affecting over 1 million people every year and therefore, it is important to carry out research work on this immune modulation caused by *Echinococcus* in order to slow down the progression and metastasis of synchronous tumor present. Therefore, we hereby report a case of a patient with synchronous findings of metastatic adenocarcinoma with unknown primary and echinococcal infection in order to highlight the need to further investigating this association, which might prove a breakthrough in clinical practice.

Case Report

A 35-year-old female patient presented to the

outpatient department of Medicine, Khyber Teaching Hospital, Peshawar with a 1-week history of yellowish discoloration of her skin and sclera, abdominal distention, and pain in her right hypochondrium. She had been drowsy for the last 1 day. According to the attendant, the mother of the patient, she has been losing weight for the last 3 months, which she could not quantify. The mother denied any change in the patient's bowel habits, melena, or hematemesis. She reported that the pain was of gradual onset severe in nature, relieved with painkillers prescribed by the local doctors. She had a similar episode of pain right hypochondrium about 2 months back for which she consulted local doctors. Her medical record showed she was diagnosed with a hydatid cyst of the liver at that time. She refused surgical intervention at that time because of affordability issues and was started on Anthelmintics. She was advised regular follow up for the hydatid cyst, but she didn't because of poor socioeconomic status. Also she did not take her medications regularly because of affordability issues. Her main family concern was her deteriorating condition and progressive weight loss although they have been told previously that she had a mild parasitic infection for which she was using medications regularly and they were of the view that she might not have any other serious illness like cancer since malignant tumor usually has slow progression unlike

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her. Her family history was not significant for similar illnesses or any other illness. There was no previous history of surgical intervention. She had a poor socioeconomic status, her husband was a shepherd, and they had cattles at home.

On examination, she was vitally stable with a BP of 120/80, the regular pulse of 88/min and was afebrile. She was drowsy with severe jaundice. There was no lymphadenopathy. Breast examination was also normal. Her heart sounds were normal. Respiratory examination revealed absent breath sounds in the right middle and lower zone of her chest. The abdomen was grossly distended with a dull note on percussion and positive shifting dullness. She had tender hepatomegaly. The

liver was roughly 4 fingers palpable below the costal margin. The spleen was not palpable. Bowel sounds were audible. There was no pedal edema.

Her investigations revealed microcytic hypochromic anemia, indirect hyperbilirubinemia, and deranged renal function tests. Her LDH was also raised. *Echinococcus* serology came out positive. Laboratory investigations are summarized in Table 1. Ultrasound abdomen and pelvis showed right-sided pleural effusion, gross ascites, and hepatomegaly. Under the suspicion of malignancy, a triphasic CT imaging was carried out, which showed metastatic adenocarcinoma of the liver with scattered nodules in the liver and lungs (Figure 1,2).

Table 1. Laboratory investigations

Laboratory investigations	Patient's values	Reference ranges
Hemoglobin	9.4 gm/dl	12-15gm/dl
Mean Cell Hemoglobin	20 pg	27-32 pg
Mean Cell Volume	80fl	78-98fl
Retic Count	10%	0.5-2.5%
White cell count	4000/cubicmm	4-11 × 1000/cubicmm
Platelets	383000/cubicmm	150-350×1000/cubicmm
Urea	2 mmol/L	1.2-3 mmol/L
Creatinine	2.1 mg/dL	0.8- 1.3 mg/dL
Serum Sodium	138.8 mmol/L	135-145 mmol/L
Serum Potassium	3.9mmol/L	3.5-5 mmol/L
Serum Chloride	96 mmol/l	95-105 mmol/l
Total bilirubin	35 micromol/L with indirect hyperbilirubinemia	2-20 micromol/L
Alkaline phosphatase	450 U/L	50-100 U/L
ESR (erythrocyte sedimentation rate)	60 mm/1st hour	<20 mm/1st hour
LDH (Lactate dehydrogenase)	2000U/L	125-200U/L
Serum Uric acid	5 mg/dL	2-7mg/dL
Prothrombin time	16 sec	10.5-13.5 sec
Activatedpartial thromboplastin time	40 sec	26-36 sec
Stool R/E	Normal, no occult blood found	
Anti-Hepatitis B antigen antibodies/	Negative by ELISA	
Anti HCV antibodies		
Echocardiography	Normal	
Serum Iron	9 micromol/L	10-28micromol/L
Ultrasound abdomen/pelvis	Enlarged liver with multiple hypochoic lesions in the liver along with gross ascites and right-sided pleural effusion.	
CTThorax, abdomen, and pelvis	Metastatic adenocarcinoma of the liver with multiple nodules in the lungs and liver	

Liver biopsy was taken and sent for the histopathological report, which revealed tubular, papillary, or cribriform patterns of columnar cells with basophilic cytoplasm, elongated nuclei, and extensive necrosis. Based upon these investigations, she was diagnosed with metastatic adenocarcinoma of an unknown primary site along with underlying

Echinococcus cystic infection of the liver.

Since she was diagnosed with Stage 4 metastatic adenocarcinoma, her family was counseled regarding her illness and disease prognosis. Oncologist opinion was taken for her management, and as per their decision, she was started on palliative treatment and was prescribed IV analgesics, fluids, antiemetics, and

prophylactic antibiotics for her symptomatic relief. Her intake and output record were maintained, and she was also started on Nasogastric feeding since she was drowsy and had poor oral intake. Unfortunately, before we could investigate her further to identify the primary site of origin of adenocarcinoma, we lost her to cardiac arrest.



Figure 1. Scattered metastatic nodules in the lungs along with right-sided pleural effusion



Figure 2. Multiple hypoechoic lesions in the right and caudate lobe of the liver, the largest one of which is roughly 3x3cm in size with enlarged lymph nodes in the porta hepatis and hilum of the spleen

Discussion

Cancers such as hepatocellular carcinoma, myeloid leukemia, ovarian tumors, adenocarcinoma, and hydatid cyst disease can co-exist, and this link has been reported by several groups (1-3). Since a chronic process is involved in both cancer and parasitic infection, it has been postulated that *Echinococcus* may have a role in cancer metastasis. In the above-reported case, the rapidly progressing tumor and the underlying cystic infection also confirms the role of *Echinococcus* parasite in immunomodulation and thus resulting in rapid growth and metastasis of the concurrent tumor. This parasite can be found worldwide, mostly in tropical and subtropical regions, and the infections in human beings caused by *E. granulosus* is transmitted by domestic animals mainly (4-5).

Mucin-type O-glycans plays an important role in cancer metastasis (6). It has been studied that these molecules also have an important role in the interaction of helminths and their host (7). These molecules have also been shown in parasites such as *Echinococcus*

granulosus, *Taenia crassiceps*, *Mesocestoides voga*, and *Taenia hydatigena* (8). These investigations reveal that mucin-type O-glycans are expressed as a common antigen in both cancer cells and helminths parasites. Immunological cross-reaction of hydatid cyst antigens and cancer patient's sera has been observed previously (9-10). Since this parasite can reside within the liver of their hosts and remain clinically unnoticed for an extended period, therefore, it has been speculated that the meta-cestode must have acquired some means of modulating the human immune response, by counteracting adverse reactions of the host and influencing the physiology of the peri-parasitic area to its own advantage. Moreover, human cancer is strongly associated with alteration and abnormalities of the immune system (11).

Recently, Stadelmann *et al.*, reported that a component of the laminated layer of meta-cestodes *i.e.* *E. multilocularis* phosphoglucose isomerase showed a sequence similarity of 86% with human Phosphatidyl Glycerol Inositol (PGI) in terms of the amino acid sequence (12). Mammalian PGI is a multi-functional protein that plays an important role in tumor metastasis, acting as a cytokine, growth factor, and inducer of angiogenesis (13).

Based on this, there is a possibility that *Echinococcus* may induce the development and metastasis of a tumor in human beings. Also, modulation of the immune system by this parasite is another hypothesis in favor of a link between this infection and metastatic tumor. This clearly indicates an immunological link between cystic echinococcosis and cancer that influences the metastatic behavior of tumor cells.

In conclusion, it should be kept in mind that Cystic echinococcosis (CE) infection may play a role in metastasis of primary cancer, especially in developing countries like Pakistan, where the disease is prevalent. Therefore, such patients must be managed properly for the concurrent cystic infection, and regular follow up must be advised.

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