INTRODUCTION

Hydatid disease or Echinococcosis or Hydatosis is a zoonotic, parasitic disease transmitted to human beings by larval forms of tapeworms (Echinococcosis), which are usually found in the small gut of carnivore animals. The main culprit parasites for human infections are E. Granulosus and E. Multilocularis leading to Cystic Echinococcosis (CE) and Alveolar Echinococcosis (AE) respectively. The minimum presumed worldwide human burden of Cystic Echinococcosis measures about 280,000 disability-adjusted life years or approximately per annum loss of US 190,000,000 US dollars. If untreated or inadequately treated, Alveolar Echinococcosis is documenting mortality of >90% within 10–15 years of diagnosis. The mortality rate from Cystic Echinococcosis (approximately 2–4%) is inferior to Alveolar Echinococcosis but it may show upsurge substantially if medical management are scarce.

CYSTIC ECHINOCOCCOSIS (CE)

A single organ involvement is documented in 80% patients, where liver is the predominant organ involved having a solitary cyst (80%) followed by lungs (20%). The germinal layer of E. Granulosus creates brood capsules and proto-scoleces into a central cavity occupying clear hydatid fluid. This hydatid fluid is bounded immediately by an acellular laminated film followed by host response. There may be “daughter” vesicles of variable dimensions in the vicinity of “mother” or initial hydatid cyst.

Pathogenesis:

Radiologic surveys documented that cysts may grow in size from 1–50 mm yearly or may remain static for decades. During course of time, these cysts may also tend to rupture instantly, collapse or even vanish. These cysts usually are asymptomatic till they avail a specific size and mostly these cysts induce pressure symptoms. Abrupt clinical presentation is mostly the result of instant rupture of these cysts. Liver cysts are documented to grow at a slower pace as compared to lung cysts.

Diagnostic tools:

Ultrasound is the modality of choice for the diagnosis of CE involving abdominal organs. In 1995, the WHO in collaboration with Informal Working Group on Echinococcosis (IWGE) devised a classification system for CE. This classification comprises of:

- Active CE (CE1, CE2)
- Transitional CE (CE3)
- Inactive CE (CE4, CE5)

This classification system proceeds from early to late stages of CE: CE1 & CE2 are initial stages whereas CE4 & CE5 are late stages of CE infections (Fig-1). WHO-IWGE classification is currently widely used classification for CE infections worldwide. Presence of calcification is not a valid criterion of non-viable cyst.
Conventional Radiography is valuable in the diagnosis of thoracic and bony involvement of CE.

Serological Tests: Antigen detection of this parasite contributes no effective clue to viability of CE. The sensitivity of serologic tests to detect serum antibody for CE (either by indirect hem-agglutination, ELISA, or latex agglutination tests) along with antigen assays in hydatid fluid sample ranks from 85–98% for hepatic hydatosis, 50–60% for pulmonary and 90–100% for multi-organ hydatosis. These serologic tests are easily available in all the good laboratories across Pakistan.

Treatment of CE:

Management recommendations for CE are multifaceted and depend on hydatid cyst’s characteristics, existing medical and surgical competence/equipment and compliance of patients to follow-up during course of this disease. The current management varies on individualized circumstances, staging, characteristics and extent of the disease. These management options include:

I. Conservative, radical and laparoscopic techniques

II. Percutaneous approaches including PAIR (Puncture, Aspiration, Injection of scolicidal agents and Re-aspiration)

III. Chemotherapy with Albendazole or Mebendazole as alternative option.

The main indications for drug treatment of CE are:

- Non-operable cases having primary hepatic or pulmonary echinococcosis
- Multiple cysts affecting two or more viscera and peritoneal structures
- Prevention of relapses after surgery or PAIR
- Pre-surgical use to diminish the hazard of relapse of CE and make the surgery easier by reducing the intracystic pressure

The main contra-indications of chemotherapy are:

- Big cysts (>10 cm)
- Calcified/ inactive hydatid cysts
- Medical disorders significantly compromising liver and bone marrow functions as these medications are hepatotoxic and myelotoxic
- First trimester of pregnancy is a contraindication and chemotherapy in 2nd or 3rd trimester is rarely recommended. Although literature failed to document any abnormal birth outcome with albendazole in pregnant ladies, usage of ABZ in pregnancy

Figure No.1: WHO-IWGE classification of CE
should be very cautious keeping in mind the benefit versus risk ratio.\textsuperscript{15} The drug of first choice to treat CE is albendazole (ABZ) either alone or in combination with percutaneous treatment. It is recommended in a dose of 10–15 mg/kg. body weight daily in two divided doses along with high fat diet to maximize its bioavailability. It should be given uninterruptedly against the old monthly regimens in 1980’s.\textsuperscript{16} Drug-drug interactions are important. Medications that increase the level of ABZ are: dexamethasone, praziquantel, cimetidine and antiepileptic drugs (carbamazepine, phenytoin, and phenobarbital). All these drugs enhance bioavailability of ABZ with increased levels of its active metabolite.\textsuperscript{17}

The best approach for a GP/Health professional is to refer these patients of CE to a nearby well-qualified medical specialist/hepatologist for proper management and follow-up.

Management of asymptomatic CE detected during screening:

Mass screening is not recommended on ethical grounds without the consent of community under study and elaborative concept regarding medical care should be offered to individuals having suspicion of CE. If willing, they can undergo specific serologic and clinical assessments for confirmation of diagnosis and selection of those requiring treatment. Infected individuals, who are not candidate of urgent treatment, need careful monitoring on regular basis.\textsuperscript{18}

**ALVEOLAR ECHINOCOCCOSIS (AE)**

Alveolar Echinococcosis (AE) is a serious disease due to larvae of E. Multilocularis and manifests as infiltrative growth mimicking tumor like conditions. Its management evolves around different options including chemotherapy and entails specialized clinical expertise.\textsuperscript{19} All patients with suspicion of AE needs timely referral to a nearby well- experienced AE treatment center. Prompt diagnosis is of prime significance for proper managements as early diagnosis can minimize morbidity and mortality of this disease.\textsuperscript{20}

**Disease Progression of AE:**

Primarily, liver is the first organ to be infected by the larval stage of this parasite. The right hepatic lobe shows predominance, however, hepatic hilum along with one or two lobes may also be affected. These hepatic lesions may vary in size from few mm to > 15 cm in diameter. Primary extra-hepatic involvement of these larvae is rare.\textsuperscript{21} These larvae of E. Multilocularis then disseminate from liver to other structures by infiltration or metastasis.

**Pathogenesis of AE:**

AE infection comprises of initial incubation period of asymptomatic phase lasting from 5-15 years to be followed by chronic course of this disease. The clinical features are usually of cholestatic jaundice and epigastric pain (in approximately 1/3 of cases each) while the remaining (1/3 of cases) AE patients are diagnosed incidentally during medical check-up for lethargy, weight loss, organomegaly or abnormal lab reports.\textsuperscript{22} There is high mortality rate amongst non-treated/inadequately treated patients of AE. Clinical reports are documenting 5-year mortality of 70% and 10 year mortality of 94%.\textsuperscript{23} However, immune response of human body can degenerate and even kill the larvae of AE and these dead calcified larvae can be recognized during mass screening programs.\textsuperscript{24}

**Diagnosis of AE:**

AE is diagnosed on the basis of clinical manifestations, epidemiological data and morphology of lesions under imaging modalities in combination with immunological and other lab investigations. Ultrasonographic findings are useful in 70% of AE cases.\textsuperscript{21} However, CT/MRI and MRCP can be useful in occasional situations.\textsuperscript{25} PCR of biopsy specimen may
detect Echinococcus specific nucleic acids and even viability of these lesions.\textsuperscript{26} The diagnostic sensitivity and specificity of E. Multilocularis antigens ranges from 90–100\% and 95–100\% respectively.\textsuperscript{27} However, these tests are expensive and are not easily available in Pakistan.

**Diagnostic criteria of AE:**

At least one of the following four diagnostic criteria is required to diagnose AE:

i. Distinctive organ lesions identified by imaging techniques (abdominal U/S, CT, MRI)

ii. Detection of Echinococcus species specific serum antibodies by high sensitivity serological tests and confirmed by a high specificity serological test

iii. Histopathologic findings compatible with AE

iv. Detection of E. Multilocularis nucleic acid sequence in a clinical scenario\textsuperscript{28}

**Treatment of AE:**

The following concepts are generally considered in the management of AE:

I. Radical surgery of the whole lesion is first option in all operable patients

II. Chemotherapy after radical resection is indicated for a limited time

III. Chemotherapy of prolonged duration is compulsory if: lesion is incompletely resected, non-operable conditions including post-interventional procedures and post-liver transplant AE patients. Two BMZ (MBZ and ABZ) are preferentially used for chemotherapy of AE. The dose of ABZ is same as recommended in CE (10–15 mg/kg, in daily 2 divided doses with high fat diet). In daily clinical practice, a total dose of 800 mg/day is given orally to adults in 2 divided doses.

Non-interrupted ABZ therapy for AE is well tolerated and is being in clinical practice for more than 20 years.\textsuperscript{29}

For GP’s and other health care providers, referral to a well qualified experienced medical specialist/Hepatologist or nearby recognized AE treatment center is highly recommended.\textsuperscript{30}

Regular follow-ups for adverse events are necessary. All types of treatment modalities require regular long-term follow-up by U/S and CT/or MRI scans at interval of 2–3 years. Progress of disease is manifested as enlargement of lesions with passage of time. Serologic tests interpretation in AE patients managed with chemotherapy without radical resection is complex and needs careful interpretation and well experienced medical specialist/Hepatologist consultation.\textsuperscript{31}

**CONCLUSIONS**

- Echinococcal infection is common in this part of the world.
- Early and timely diagnosis can prevent morbidity and mortality associated with this disease.
- Clinical findings, serologic tests along with radiologic-imaging are important tools for diagnosis.
- Chemotherapy with BMZ plays a vital role in all management modalities and continuous therapy is recommended along with follow up for any adverse events.
- General practitioners and other health care providers are advised to refer timely any suspected case of CE/AE and monitor these CE/AE patients undergoing chemotherapy for any side-effect/complication along with timely consultation by a well-experienced medical specialist/Hepatologist.
REFERENCES