Mildly Elevated Transaminases: Excellent Diagnostic Clue for Anicteric Leptospirosis

Sir,

Leptospirosis is a zoonosis with protean manifestations, being endemic in almost whole of India and contributes to significant morbidity and mortality in the population. Microscopic agglutination test (MAT) is the gold standard serologic test because of excellent specificity. IgM ELISA and PCR are other tests available for diagnosis of Leptospirosis. MAT is available only in reference laboratories and other tests even if available are positive after one week of illness and are beyond the meagre resources that most patients can afford. Clinicians are left with little options but to treat the patients empirically.

Analysis of the last 22 patients admitted to our hospital, diagnosed anicteric leptospirosis on the basis of clinical and serological criteria and discharged after successful treatment revealed a remarkably consistent finding of mild elevation of serum transaminases (AST/ALT: 44/54 - 67/78 U/L) in 20 of these patients. Interestingly none of these patients had raised serum bilirubin levels. Elizabeth F Daher et al studied 210 patients and reported 82.4% of their patients showed elevated transaminases in anicteric leptospirosis. V Chauhan et al too reported elevated liver enzymes in 12 out of 13 patients studied.

It would be prudent to say that mildly elevated transaminases along with a consistent history is an excellent diagnostic clue for anicteric leptospirosis in resource poor settings and can aptly be described as “Poor man’s MAT”.

References

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Reply from Author

Sir,

Dr. Rajesh Deshwal stated that leptospirosis is now endemic in most parts of India and microscopic agglutination test (MAT), which is the gold standard serologic test is not available anywhere except for the reference labs. The patients have to be treated empirically before the results of the tests are available.

Dr. Deshwal has presented 20 patients of anicteric leptospirosis diagnosed based on clinical and serologic criteria showing mild elevation of transaminases without elevated bilirubin levels. In his letter he says that similar findings were present in the studies of Elizabeth F Daher et al and V Chauhan et al.

Regarding our study that he has quoted, I would like to say that we had jaundice in 10 out of 13 patients and elevated transaminases in 12 out of 13 patients, therefore only two patients were anicteric leptospirosis. Main presentation in our cases was Weil’s disease, so, it is difficult to draw conclusions from only two patients of anicteric leptospirosis. As far as the study of Elizabeth F Daher et al is concerned this study also had Jaundice in 94.5% patients out of total 201 patients.

MAT is a highly specific test, though sensitivity is poor, whereas mildly raised transaminases in anicteric leptospirosis can be highly sensitive but have poor specificity for leptospirosis, thus these two tests are not comparable. In my view it will not be prudent to call it “Poor man’s MAT” due to poor specificity, but it can definitely be used as a whistle blower for leptospirosis in the first week of illness. However, on the contrary, we need to be more vigilant in those patients who have disproportionately raised bilirubin levels(>3.5 mg%) compared to only mildly raised transaminases and suspect leptospirosis in such patients as quoted by Elizabeth F Daher et al.

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Scleroderma Cardiac Disease

Sir,

We read with interest the Pictoral CME titled “Scleroderma Cardiac Disease”, published in the September 2010 issue of JAPI.

While the author needs to be complemented for bringing out this interesting but rare association of cardiac involvement in Progressive Systemic Sclerosis, there are certain inaccuracies which we would like to highlight and clarify.

The authors, while describing the echocardiography findings, have mentioned that the septal leaflet of tricuspid valve was displaced towards the apex. The authors have not mentioned the extent of displacement and whether this has any bearing on the case. This finding is seen in Ebstein’s anomaly which clearly is not the case. Besides the authors have not mentioned the TR derived RVSP and IVC derived RA pressure apart from tricuspid annulus measurement. We thus could not infer whether the TR was primary or secondary to pulmonary involvement. The presence of right ventricular hypertrophy and obliteration of RV apex as mentioned in the findings could be secondary to pressure overload of the right ventricle due to pulmonary hypertension, usually seen in systemic sclerosis. The authors report a normal HRCT chest but no information has been given on pulmonary function test and diffusion capacity of lungs which would be helpful in this regard. Similarly, restrictive pattern of tricuspid inflow velocity is not enough to diagnose endomyocardial fibrosis. Endomyocardial biopsy is the gold standard for settling the final diagnosis in this situation. Cardiac CT scan and MRI are also useful in delineating myocardial involvement in systemic...
sclerosis.

Besides this, the findings of anterolateral ischemia on ECG at rest but no LV wall motion abnormality on echo cannot be explained.

Cardiac involvement in systemic sclerosis is usually secondary to pulmonary hypertension and prognostically very important. A clear understanding of this association is vital to proper screening of patients with systemic sclerosis for initiation of appropriate therapy.

References

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Reply from Author

Sir,

Thanks to Dr Ravi R Kasliwal for reading the article ‘Scleroderma cardiac disease’ with interest and bringing some points for further clarification.

Cardiac involvement in progressive systemic sclerosis (PSS) is usually secondary to pulmonary hypertension; however primary cardiac involvement is also seen.

Our patient did not have any lung parenchymal abnormality detected in high resolution (HR) CT scan of thorax. Her pulmonary function test had restrictive pattern due to thickening of skin of chest wall. Diffusion capacity of lung was not done. Pulmonary function test had restrictive pattern due to thickening of skin of chest wall. Our patient did not have any lung parenchymal abnormality detected in high resolution (HR) CT scan of thorax. Her pulmonary function test had restrictive pattern due to thickening of skin of chest wall. Diffusion capacity of lung was not done.

In 2-D echocardiography, septal leaflet of tricuspid valve of the patient was displaced towards the apex (15 mm). This is due to retraction of valve downward due to endomyocardial fibrosis (EMF). The patient had huge right atrial (RA) enlargement and reduced right ventricular (RV) cavity size. Differential diagnoses are Ebstein anomaly, right ventricular EMF and tricuspid atresia. The patient had no other features of Ebstein anomaly. Tricuspid atresia was absent. Colour Doppler study revealed tricuspid regurgitation (TR).

In RV hypertrophy due to pulmonary hypertension, RV cavity size is usually normal or slightly increased. In presence of TR, features of volume overload should be present with RV cavity dilatation. In contrary to it, our case had reduced RV cavity size and obliteration of cardiac apex.

Assessment of RA pressure, RV systolic pressure (RVSP) and TR gradient are helpful in differentiating RV hypertrophy due to pulmonary hypertension from myocardial or endomyocardial fibrosis of RV (RVSP≥ TR gradient + RA pressure). In pulmonary hypertension RVSP is elevated and TR gradient is high. In RV systolic failure in pulmonary hypertension, RVSP may be low but then RV will be hugely dilated. In RV myocardial fibrosis or EMF, RA pressure is elevated with normal or reduced RVSP and TR gradient is low as in our case (21 mm Hg). Low TR gradient with reduced RV cavity size is against the pulmonary hypertension in our patient.

In echocardiography ventricular thickening, obliterated apex, dilated atrium and strong echoes emanating from endocardial surface give idea regarding EMF. In proper clinical setting, it is sufficient enough to diagnose EMF, though endomyocardial biopsy is the gold standard. Cardiac CT or MRI are superior to echocardiography but are not cost effective and they are not readily available.

ST – T changes in surface ECG may not always be reflected as left ventricular (LV) wall motion abnormality on echocardiography at rest. ECG also may not be reliable as an indicator of myocardial ischemia always, especially in association with other cardiac, systemic or metabolic disorders.

Cardiac involvement either primary or secondary to pulmonary hypertension has bad prognostic significance in PSS. Awareness is needed for its proper and early diagnosis.

Reference

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Swine Flu Encephalitis - First Adult Case Report from India

Sir,

48 year old man, known diabetic, presented with history of fever not associated with chills for 2 days, cough and breathlessness, difficulty in walking and slurring of speech for one day. On examination, the patient was confused, talking irrelevant. His vitals were BP 120/76mmHg, Pulse 82/min, afibrile, oxygen saturation 92%. Chest examination revealed occasional rhonchi bilaterally, cardiovascular and abdominal examination were normal. Neurological examination revealed patient was confused, disoriented and slurring of speech which was cerebellar type. Cranial nerve, sensory and motor system examinations were normal. Patient was swaying towards left side. Left knee, heel, shin test was impaired. There was no neck stiffness and Kernig’s was negative Provisional diagnosis of viral encephalitis was considered. The patient’s haematological and biochemical parameters were within normal limits. MRI brain with contrast was normal. H1N1 RT-PCR was sent from throat swab in view of complaints of mild dyspnoea. CSF examination revealed total cell count of 85 with 100% lymphocytes, protein was 89.3g% and glucose was 80 mg/dl. Herpes simplex PCR was sent, which was negative. Patient was empirically started on injectable Acyclovir and supportive treatment. H1N1 serology came positive and patient was started on Oseltamivir 75 mg twice daily and Acyclovir was discontinued. Patient improved neurologically with 48 hours. A repeat CSF was done after 10 days was normal.
Discussion

Neurologic complications, including seizures, encephalitis, encephalopathy, have been described previously in association with respiratory tract infection with seasonal influenza A or B viruses (1–2), but not with novel influenza A (H1N1) virus.

The Center for Disease Control in the US has published the first report on central nervous system complications from swine flu in children, based on case studies from Texas1 All four boys, whose ages ranged from 7 to 17, recovered fully during hospitalization. All four had fever, three had encephalopathy, and two had seizures. The onset of the neurological symptoms after respiratory disease ranged from one to four days. All received a five-day course of oseltamivir.

Another case is of a 7 years old healthy boy from Thailand, presented with seizure and confirmed for new H1N1 influenza infection and meningitis is confirmed due to positive viral RNA in CSF. This case developed the neurological symptoms within 2 days after onset of fever and was treated with oseltamivir in the hospital for 10 days and got full recovery.2 The first case of encephalitis reported in a 8 year old child from Pune, India. Patient had proven H1N1 infection with seizures, CSF pleocytosis, abnormal EEG and focal CT changes.3

The swine flu encephalitis is very rare and the possibility of virus to enter thorough blood brain barrier into the neurological system seems to be difficult (due to the larger size of virus). The possible explanations for this could be that there might be occulted pathology of blood brain barrier in this boy. Second, this case might be misdiagnosed of an aseptic meningitis and the positive CSF might be due to contamination. The report from CDC in USA also noted for no detection of viral RNA in cases with neurological presentation as well. It should be noted that the encephalitis due to swine flu has never been reported in adult with complete blood brain barrier and should not be detected in the future. This is contrary to the case report by us and the possible mechanism might be antibodies against the virus in the CSF or hyperactivated cytokine response may play a role in pathogenesis, as supported a report acute encephalopathy associated with influenza A infection in 3 adults where it was detected high cerebrospinal fluid (CSF) and plasma concentrations of CXCL8/IL-8 and CCL2/MCP-1 (CSF/plasma ratios > or =3), and interleukin-6, CXCL10/IP-10, but no evidence of viral neuroinvasion.3

References


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There are Infections other than TB Please!

Sir,

We read with great interest the case report titled, “Unusual presentation of brain abscess with uncommon organism in an immunocompetent person.”1 The report highlights that infections other than TB have to be kept in mind too. We commend the authors for making the etiologic diagnosis and successfully managing the patient. However we wonder whether the entire illness was due to Listeria and whether the patient had an initial partial response due to the drugs directed against TB having activity against Listeria.

Although brain abscess due to Listeria is commonly associated with immunocompromised hosts, its occurrence in immunocompetent individuals is well documented. This patient, who had no apparent immunocompromise, did have initial brain stem symptoms and abscesses. Rhomboencephalitic presentation of Listeriosis is described in healthy people. This occurs due to inoculation of bacteria into the oral mucosa when abrasive food is chewed and phagocytosis of bacteria by macrophages leads to invasion of the cranial nerves.2 Retrograde spread through nerve axons occurs allowing the bacteria to reach the CNS and spread intercellularly to the parenchyma. Abscesses located in the thalamus, pons and medulla are more common with Listeria than with other bacteria.3

Rifampicin and quinolones have good in vitro activity against listeria.4 We do not know whether the patient received a quinolone as part of ATT, which is an unfortunate, but all too common practice.

The patient’s initial presentation with confusion and ataxia was considered indicative of TB meningitis in this case report. TB is often suspected and treated in our country on rather flimsy grounds. Since TB is a common infection, empirical treatment works most of the time, thus reinforcing the physician’s belief. However there is a very real possibility of missing another infective etiology or a non infectious disease by this approach. Some of the drugs used as ATT do have a wider range of antibacterial activity and may produce a partial response. Hence making a positive diagnosis of TB should be attempted as far as possible in every case. Awareness among clinicians of these considerations and greater availability of TB MGIT culture and molecular methods of diagnosis is the need of the hour.

The diagnosis of Listeria infections is impossible without Gram stain and culture. So it is imperative to obtain samples for microbiological diagnosis from the site of infection as was done in this case. Empirical therapy cannot cover the entire range of differential diagnoses. In many instances the risk and cost of an invasive procedure is far less than that of ineffective and toxic empirical therapy.

References

Reply from Author

Sir,

In regards to the case report titled “Unusual presentation of brain abscess with uncommon organism in an immunocompetent person”, the letter aptly titled “There are infections other than TB please!” further stresses on the fact although TB is one of the commonest infectious diseases in our country, diagnosing TB on flimsy grounds can lead to misdiagnosis of various other infective and non-infective etiologies. Also, many a time, TB coexists with various other diseases, so a less than expected recovery with anti tubercular drugs should prompt us to look for other etiologies.

Now, in respect to the doubts raised, the patient was diagnosed to have TB meningitis in another institute and the reports were not available to us. The typical clinical picture of listeria meningitis is one of a biphasic illness with a prodrome of fever, headache, nausea, and vomiting that lasts about 4 days, followed by the abrupt onset of asymmetrical cranial nerve deficits, cerebellar signs, and hemiparesis and/or hemisensory deficits. Listeria usually presents as acute and more frequently as subacute meningitis (with illness developing over several days) with only a single case of chronic meningitis due to listeria reported till date in a HIV infected patient. No such history was present during the initial phase of illness when the patient was diagnosed to have TB and an illness of 6 months duration were negatives for considering it as a case of listeriosis from the onset.

Also there was clinical improvement of patient on Cat I anti tubercular (no. quinolone was used). Although rifampin is quite active in vitro against L. monocytogenes and is known to penetrate into phagocytic cells; the clinical experience is minimal, and the addition of rifampin to ampicillin was not more effective than ampicillin alone in animal models. Listeria monocytogenes (Lm) is a Gram-positive, facultative anaerobic bacterium that primarily causes sepsis and meningitis and even with appropriate antibiotic therapy, this entity has a high morbidity and mortality (24%-62%). Thus it is unlikely for the patient harboring listeria meningitis for more than 6 months to survive due to rifampin, a drug with unproven clinical efficacy and later on recover completely with proper treatment.

Finally we would like to reinforce that listeria should be considered as an etiologic agent in the following situations: 1. elderly or immunocompromised patients 2. fluctuating mental status, seizure and movement disorder 3. cerebritis, brain abscess (cortical, thalamus,pons or medulla) or brainstem encephalitis 4. high CSF/blood glucose ratio 5. hyponatremia.

References

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