Paradoxical Ascites During Anti-tuberculous Chemotherapy

Sir,

A paradoxical response is a possibility in a patient who responds inadequately or shows unexpected worsening while on antituberculous drugs (ATT).[1,2] In order to avoid an unnecessary and potentially dangerous modification of the drug regimen, the importance of recognizing this phenomenon early cannot be overemphasized.

A 20 years old female was admitted in the medical ward with the evening rise low grade fever, weight loss and pain in abdomen for one month duration in January 2010. Her pulse, blood pressure and respiratory rate were within normal range. Her body temperature was 101°F and weight was 40 kg. Ascites was present. Haemoglobin was 10.3 gram/dl. Leucocytes count was 9100/cmm (Neutrophils = 77%, Lymphocytes = 31%, Monocytes = 2%) and erythrocyte sedimentation rate (ESR) 26 mm after first hour. Blood sugar, renal function tests (RFTs), liver function tests (LFTs), stool and urine analysis were normal. Anti-nuclear antibody (ANA) was negative. Mantoux test was 16 mm. Blood culture showed no growth of microorganism. Ascitic fluid protein was 5.4 gm/dl, albumin 2.8 gm/dl, glucose 84 mg/dl, adenosine deaminase (ADA) 143 units, Leucocytes 11300/cmm (Neutrophils = 80%, Lymphocytes = 20%), AFB smear negative and culture sterile.

Chest X-ray was normal. Plain X-ray abdomen showed distended bowel loops. Ultrasound abdomen showed mild to moderate ascites.

Patient refused to undergo laparoscopy. With the suspicion of TB ascites, patient was put on category-I anti-TB drugs. After 28 days of treatment, patient was readmitted because of increasing ascites, though fever subsided and patient gained weight. On examination, her vital signs were normal, weight increased to 45 kg and ascites was also increased. Complete blood count, RFTs and LFTs were normal. Ascitic fluid findings were Leucocytes 3650/cmm (Neutrophils = 03%, Lymphocytes = 93%), protein 6.0 g/dl, albumin 2.9 g/dl, ADA 78 units and Lactate dehydrogenase (LDH) 278 IU/l. Repeat USG showed mild splenomegaly and gross ascites.

As there was no evidence of non-compliance, adverse drug reaction, drug resistance, secondary infections and any other pathology, paradoxical response to anti-TB treatment was suspected. Patient was put on tablet Prednisolone 40 mg per day tapered in 4 weeks. She improved significantly but developed body ache after 4 weeks of second visit. Her uric acid was 6.3 mg/dl and repeat USG showed minimal ascites. Patient completed intensive phase of treatment and was advised to start continuation phase of treatment.

ATT stopped after 6 months. She gained 15 kg of weight. She remained under regular follow-up, and no relapse was reported till date.

A paradoxical response in a patient infected with TB is generally defined as the clinical or radiological worsening of pre-existing TB lesions or the development of new lesions in a patient who initially improves with anti-tuberculosis therapy.[1-3] Since a rapid and accurate diagnostic test is lacking, the diagnosis of the paradoxical phenomenon can only be ascertained when other differential diagnoses such as secondary infections, inadequate ATT resulting in drug resistance, poor compliance, and adverse reactions due to therapy are excluded.[4,5]

The median time for development of a paradoxical response is 60 days (14 – 270 days) in HIV-negative patients.[5] Systemic corticosteroids in moderate doses for a short duration are usually effective against paradoxical responses in tuberculosis.[4]

REFERENCES

1. Bloch S, Wickremasinghe M, Wright A, Rice A, Thompson M, Kon OM. Paradoxical reactions in non-HIV tuberculosis presenting as endobronchial obstruction. *Eur Respir Rev* 2009; **18**:295-9.
2. Chopra V, Singh UP, Chopra D. Contralateral paradoxical pleural effusion during anti-tuberculosis chemotherapy. *Lung India* 2008; **25**:124-5.
3. Cheng SL, Wang HC, Yang PC. Paradoxical response during anti-tuberculosis treatment in HIV-negative patients with pulmonary tuberculosis. *Int J Tuberc Lung Dis* 2007; **11**:1290-5.
4. Janmeja AK, Das SK. Cervico-mediastinal lymphadenopathy as a paradoxical response to chemotherapy in pulmonary tuberculosis. *Respiration* 2003; **70**:219-20.
5. Vincent CC. Paradoxical response during anti-tuberculosis therapy. *Med Bull* 2006; **2**:20-1.

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"T2 Shine Through Effect" of Vasogenic Oedema on DWI

Sir,

I am writing this letter after reading an interesting case report published in JCPSP 2012, Vol. 22 (6): 398-400 by Sameera Ehtisham and Haleema A. Hashmi titled "Posterior Reversible Encephalopathy Syndrome. I take this opportunity to elaborate a very important imaging aspect that will greatly enhance readers' understanding.

Diffusion weighted imaging (DWI) and ADC (Apparent diffusion coefficient), are key sequences to differentiate cytotoxic from vasogenic oedema and remain a gold standard for the early diagnosis of an acute infarct. DWI interpretation is never reliable without description of corresponding ADC signal. Acute cytotoxic oedema results in diffusion restriction and appears bright on DWI. To establish the diagnosis of cytotoxic oedema (infarct), ADC map must have corresponding low signal. Vasogenic oedema increases water diffusion, however DWI appearance is variable.[1]

DWI is an echo planar imaging sequence and carries hybrid imaging characteristics being sensitive to both diffusion and tissues T2 effects. Suppose if we freeze the diffusion sensitivity of DWI, the vasogenic oedema would always appear bright for T2 prolongation. However, if on the other hand, we freeze the T2 character of DWI, the vasogenic oedema will always appear hypointense (black) on DWI for its increased diffusivity. Since realistically both the opposing characters are operational in DWI, the Vasogenic oedema appearance depends on their net effect. Depending on which character predominates in a certain microstructural environment, the vasogenic oedema may appear as hypointense, isointense or hyperintense on DWI images.[2] This is the reason one finds conflicting reports in literature regarding vasogenic oedema appearance on DWI.[3-5] Regardless of DWI appearance, the vasogenic oedema always appears hyperintense on ADC images in contrast to hypointense cytotoxic oedema. If vasogenic oedema appears hyper intense on DWI, it is due to the predominance of T2 prolongation effect over increased diffusion in certain clinical and imaging settings. This effect is called "T2 shine through" (Table I).[3,4] As such, a combination of DWI and ADC hyperintense signal favours vasogenic oedema with T2 shine through effect. If vasogenic oedema appears hypointense or isointense, there is no question of "T2 shine through" as nothing is bright or shining on DWI images (Table I).

In short, in certain clinical and imaging settings of vasogenic oedema, DWI-robust T2 hyperintense MR signal may shine through the relatively less strong and opposing hypointense signal for increased diffusivity. This is like the Sun occasionally shining through a relatively thin cloud layer on a rainy day.

Table I: Vasogenic oedema appearance options on DWI and ADC. T2 and diffusion related signals may cancel each other's effect on DWI. The resultant signal will be sum of T2 hyperintensity and increased diffusion related hypointensity. The resultant appearance will be net effect. *T2 shine through (see text).

T2	Diffusivity	DWI	ADC
⇑⇑	⇑⇑	Isointense	Hyperintense
⇑	⇑⇑	Hypointense	Hyperintense
⇑⇑	⇑	Hyperintense*	Hyperintense

REFERENCES

1. Srinivasan A, Goyal M, Al Azri F, Lum C. State-of-the-art imaging of acute stroke. *Radiographics* 2006; **26**:S75-95.
2. Schaefer PW, Grant PE, Gonzalez RG. Diffusion-weighted MR imaging of the brain. *Radiology* 2000; **217**:331-45.
3. Doelken M, Lanz S, Rennert J, Alibek S, Richter G, Doerfler A. Differentiation of cytotoxic and vasogenic oedema in a patient with reversible posterior leukoencephalopathy syndrome using diffusion-weighted MRI. *Diagn Interv Radiol* 2007; **13**:125-8.
4. Schaefer PW, Buonanno FS, Gonzalez RG, Schwamm LH. Diffusion-weighted imaging discriminates between cytotoxic and vasogenic oedema in a patient with eclampsia. *Stroke* 1997; **28**:1082-5.
5. Schwartz RB, Mulkern RV, Gudbjartsson H, Jolesz F. Diffusion-weighted MR imaging in hypertensive encephalopathy: clues to pathogenesis. *AJNR Am J Neuroradiol* 1998; **19**:859-62.

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Reply of author:

It was already stated in the discussion that the patho-physiology of PRES is not well understood.

The radiology part was written in consultation with the institute's radiologist and with due referencing.

Authors being non-radiologists, a discussion on the details of sequences as described by the author of the letter is beyond their scope. They have only described the clinician's understanding and thank the author for so much effort to enlighten the readers.

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Letter to Editor Regarding the Case Report "Posterior Reversible Encephalopathy Syndrome (PRES)"

Sir,

We read with interest the case report titled "posterior reversible encephalopathy syndrome (PRES)" published in JCPSP.[1] Following observations were made.

1. There is no known association of intracranial aneurysm with posterior reversible encephalopathy syndrome (PRES). Conventional angiography (CA) being an invasive procedure, carrying high cost and having significant mortality and morbidity, (2 – 3%) has no established role in the management of PRES. It may be used in selected cases rather than often, if the results of noninvasive imaging tests are equivocal and suspicion of an aneurysm or intravascular thrombosis is high. The diagnostic yield of multi-detector head CT angiography (CTA) is comparable to conventional angiography.[2]

2. The statement that "Diffusion weighted images may show foci of high signal intensity in cortex that is either undergoing infarction or at high risk of infarction. ADC values in these areas are normal or slightly elevated", is misreported and is not factually correct. In addition, no reference is cited for this statement. Diffusion weighted imaging (DWI) is the gold standard sequence to diagnose an established acute infarct and is typically normal in areas either undergoing infarction or at high risk of infarction. In addition to establish the diagnosis of an infarct, ADC must be low in corresponding DWI bright areas rather than low or normal. If a DWI bright area also appears bright on ADC maps; it does not favour diffusion restriction to suggest acute ischaemic infarct but represents vasogenic oedema. As such, the DWI differentiates cytotoxic oedema, confirmatory for an ischemic infarct, from vasogenic oedema, indicative of PRES.[3]

3. It appears as if MRI examination was performed without contrast since there is no mention of contrast dose and no contrast images were provided. Further, the authors relied on MR venography (MRV) to exclude acute venous sinus thrombosis. Non-contract MR/MRV has little value in excluding acute venous sinus thrombosis because blood clot appears as a flow void on time of the light MRV like flowing blood in a patent sinus and will be easily overlooked. Contrast MRI/MRV accurately excludes acute venous sinus thrombosis and helps to avoid this pitfall. In addition, contrast is helpful to avoid other direction related non-contract MRV pitfalls. Acute venous sinus thrombosis, unlike PRES, results in haemorrhagic infarcts rather than vasogenic oedema. The MR angiography (MRA) findings in PRES are non-specific and may be seen in various other etiologies such as vasculitis and vasospasm.[4] MR spectroscopy and diffusion tensor imaging (DTI) findings are non-specific and currently have limited role in imaging and management of patients with PRES.

REFERENCES

1. Siddique TS. Posterior reversible encephalopathy syndrome. *J Coll Physicians Surg Pak* 2012; **22**:168-70.
2. Kaufmann TJ, Huston J 3rd, Mandrekar JN, Schleck CD, Thielen KR, Kallmes DF. Complications of diagnostic cerebral angiography: evaluation of 19,826 consecutive patients. *Radiology* 2007; **243**:812-9.
3. Bartynski WS. Posterior reversible encephalopathy syndrome, part 2: controversies surrounding pathophysiology of vasogenic oedema. *Am J Neuroradiol* 2008; **29**:1043-9.
4. Srinivasan A, Goyal M, Al Azri F, Lum C. State-of-the-art imaging of acute stroke. *Radiographics* 2006; **26**:S75-95.

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Editor's note:

The content of the letter was communicated to the author of the case report. Despite multiple reminders, the letter remains unanswered and hence published as such.