Diagnosing Rubella: Fallacies and Pitfalls

Sir,

Congenital rubella is a preventable disease, which could be controlled by immunization. Serological surveys in India indicate that up to 45% of women of child-bearing age are susceptible to rubella and potentially at risk of infection during pregnancy. Since primary infection with rubella in the first four months of pregnancy carries a major risk of foetal damage, correct and early diagnosis of rubella is of vital importance.

Clinically diagnosis of rubella could be missed due to following reasons:

1. Rubella is a mild viral exanthematous infectious disease, which follows a typically benign clinical course.
2. The infection may present atypically with minimum lymphadenopathy and an evanescent rash.
3. Typical rubelliform rashes may also be induced by other viruses like enteroviruses, chikungunya virus, Ross river virus and Parvo virus B19.

Diagnosis of Rubella could be confirmed by viral culture but the process is difficult and the facilities for culture are lacking in most of the laboratories. Hence, serodiagnosis is considered the most useful and reliable method for detection of infection. Acute rubella infection is usually established by demonstration of seroconversion in paired sera or by demonstration of rubella-specific IgM antibodies in a single specimen. IgM antibodies usually attain their maximum concentration within 10-14 days after the onset of illness but the duration of response is variable. In general, following primary infection, they persist for 6-12 weeks although some patients may exhibit a more prolonged response, which may extend for as long as a year.

ELISA is a rapid and reliable method of measuring rubella specific IgM antibodies in the serum sample of patients with acute rubella infection. However, there are several pitfalls. All assays for specific IgM antibodies occasionally give false positive results. Low concentration may occur in infections like infectious mononucleosis, Parvo virus B19 infection and CMV infection and also if rheumatoid factor is present. A further problem is to distinguish primary rubella from reinfection. Reinfection is diagnosed when an antibody response is shown in someone who has previously had natural rubella or successful immunization. It has been recommended by a working party of the Medical Research Council’s subcommittee on Rubella Vaccine that evidence of re-infection would be accepted if a person with pre-existing rubella antibodies showed a significant rise in antibody concentration or a rubella specific IgM response, or both. Distinction between primary infection and re-infection could also be done on basis of avidity of specific IgG antibodies. High avidity suggests recent re-infection. But avidity assays have not yet been elucidated in routine use.

Rubella specific IgM response during re-infection is usually lower and more transient than primary infection. Asymptomatic re-infection in early pregnancy is very unlikely to be associated with foetal infection. However, if it is accompanied by significant viraemia, transmission to foetus can cause significant damage.

In our study conducted on 380 females of reproductive age, IgM antibodies were present in 26/380 (6.84%). However, further analysis of these females showed that 21 of them were seronegative for IgG antibodies indicating primary infection. Five of them had IgG antibodies along with IgM antibodies indicating re-infection in them. Correct diagnosis of primary rubella or re-infection in patients without symptoms may thus be difficult. Hence, we emphasize the fact that a proper National Immunization Policy should be formulated to immunize adolescent females against rubella before they contemplate pregnancy.

N Jindal*, N Singla**, A Aggarwal*
*Department of Microbiology, Govt. Medical College, Amritsar. **Department of Microbiology, Govt. Medical College and Hospital, Sector 32 Chandigarh.

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Unilateral Chorioretinitis: An Initial Manifestation of Subacute Sclerosing Panencephalitis

Sir,

SSPE is a devastating neurologic disorder associated with persistent measles virus infection of the nervous system with an invariably fatal outcome. A wide variety of visual disorders have been associated with SSPE including papilledema, retinitis, chorioretinitis, optic nerve pallor, homonymous visual field deficits, and cortical blindness. Adult-onset patients are more likely than children to present with purely ophthalmologic complaints rather than the classical personality changes as their first symptom of disease. We report an interesting case of SSPE who developed acute onset unilateral chorioretinitis as an initial manifestation.

Panencephalitis

Unilateral Chorioretinitis: An Initial Manifestation of Subacute Sclerosing Panencephalitis

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preceding the neurological symptoms by three and a half years!

A 16-year-old Hindu male born of a non-consanguineous marriage, from a rural background was noted to have subtle forgetfulness and impaired concentration in routine activities for past 6 months. This was associated with progressively increasing jerky movements of the axial musculature and limbs, sometimes with falls, three episodes of generalized seizures, and progressively decreasing scholastic performance at school, impaired calculation, visuospatial abnormalities and recent memory impairment. About three and a half years prior to this he had developed acute onset painless vision loss over right eye and within four hours only finger counting was possible at one feet distance.

This was not associated with any constitutional symptoms, any systemic manifestations or any other focal neurological deficit at that time or in the past. Patient was not investigated for it and nor did he take any specific treatment. Vision loss had improved for the past 2-3 months and now he was able to count fingers from a 1 meter distance. Patient had a past history of measles infection at the age of one and a half years. The attendant could not recall details about vaccination. Family history was negative for any progressive neurodegenerative disorder and or epilepsy.

General examination was normal. His MMSE was 21/30. Detailed Higher mental function testing revealed mainly parieto-occipital dysfunction followed by temporal and subtle frontal lobe dysfunction. Cranial nerve testing revealed RAPD right eye, diminished visual acuity right eye with finger counting possible at 3 feet distance, temporal pallor of the disc with macular and perimacular pigmentation surrounded by an atrophic scar. Patient had a characteristic periodic predominant axial myoclonus recurring after every 15 seconds. Routine biochemical parameters were normal, HIV and VDRL were negative. CT scan of the brain was normal. EEG revealed characteristics periodic complexes consistent with a diagnosis of SSPE. CSF revealed normal cell count end sugar with mildly raised proteins. Serum and CSF antimeasles IgG antibody titre was significantly elevated. Based on the clinical symptomatology, characteristic periodic complexes, CSF picture, with a background history of childhood measles infection a diagnosis of SSPE was made.

Although high (50%) of ocular involvement usually occurs concurrently with the neurological features, yet vision loss as an early feature, preceding the appearance of typical myoclonus and cognitive decline by months and even as long as eight years has been described especially with increasing age of presentation. Our patient is also unusual that he had a three and a half year gap between the ocular and neurological manifestations. Possibly the patient’s immunologic system was able to contain and abort a presumable measles viral retinitis in his right eye but failed in doing so three and a half years later leading to neurological manifestations.

Because of high percentage (50%) of ocular involvement in SSPE, which may antedate the other symptoms by even years and no definitive treatment available, any child or adult presenting with unexplained or atypical vision loss must be necessarily enquired about childhood measles infection and vaccination otherwise a potentially devastating disorder may be missed!

*Resident Doctor; **Lecturer; ***Professor and Head, Department of Neurology, Institute of Medical Sciences, Banaras Hindu University, Varanasi – 221 005.
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Ocular Changes in Infectious Diseases

Sir,

Ophthalmoscopy is a very important bedside test by which a person can diagnose, give the differential diagnoses in undiagnosed patient and once diagnosed can also give the prognosis in various infectious and noninfectious diseases. Ophthalmoscopic changes are well described in non-communicable diseases ie hypertension, diabetes mellitus congenital/hereditary metabolic disorders etc. but it is not so in cases of infectious diseases because of variability of incidence, prevalence/epidemics from place to place, emergence of newer infections and last but not least the infectious diseases are mainly the burden of third world countries which are mostly resource poor.

Ocular/Ophthalmoscopic changes are well described in some infections ie malaria, infective endocarditis, cysticercosis, HIV to name few of them. In the July 2005 issue of JAPI (53;656-57) - the detailed report of five cases by Mehta is worth praise. We have earlier studied ocular changes in more than 400 patients of plasmodium falciparum malaria in which all categories of patients ie uncomplicated and complicated/prenicious syndrome cases were included. According to the available literature from 1879 to 1996 there were varying results in different studies which could be due to geogrpahical factors, variable strains of the plasmodial species, varying
definition of various indices of severity, smaller number of patients population in the studies. so we conducted a larger prospective study and finally it was concluded that ophthalmoscopic abnormalities per se are not associated with mortality statistically except disc pallor (which could be due to fewer number of patients with disc pallor) but there was a trend towards worse prognosis. It was also concluded that some fundus findings ie retinal hemorrhages in malaria endemic areas may give a possible diagnosis of malaria if peripheral blood film is negative and otherwise there is strong suspicion of malaria.2,3

Our findings were similar to the findings to Dengue patients described by Mehta with regards to morphology and recovery point of view ie subconjunctival haemorrhage, retinal haemorrhage, Roth's spots but maculopathy was not observed in our study.2,3 So the ocular findings are probably reflection of underlying anaemia, thrombocytopenia and bleeding tendency.

As there are frequent outbreaks of Dengue from time to time in various parts of India so we agree with the author’s comment that an effort should be made to detect and document the findings in larger number of patients whenever there is an opportunity. We would like to add further to the author’s comment that the ocular lesions be studied in all verities of Dengue fever and not only in patients of Dengue hemorrhagic fever as we did in our study on malaria patients to become more wise.

Shubhakaran*, Rekha Jakhar**
*Department of Neurology, MG Hospital. **Department of Obs and Gynae, Dr. SN Medical College, Jodhpur - Rajasthan. Received : 23.8.2005; Accepted : 15.9.2005

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Reply From the Authors
Sir,

I am grateful for the interest and appreciation shown by Dr. Shubhakaran et al to my correspondence.1

1. The authors have made a significant contribution to literature both by reporting the varied fundus findings of a large cohort of patients of malaria2 and by excellent reviews.3 I agree with their conclusion that fundoscopy may be of help in the diagnosis of malaria especially when the peripheral blood smears may be negative.

2. The subconjunctival and intraretinal hemorrhages are likely due to an underlying thrombocytopenia that is well reported in these patients. The maculopathy is an infrequently reported finding with only a few cases being reported worldwide. The exact etiopathogenesis is still unclear but possibly represents direct tissue invasion. A larger series would be needed to elucidate whether any of these findings are risk factors towards a worse outcome.

3. All these patients were admitted, mostly in the intensive care units, and were thus examined by us. Mild or subclinical infections often seek no treatment or are treated empirically as “pyrexia of unknown origin (PUO)” and do not undergo fundoscopy. I agree that these findings, if available would be an interesting study.

4. Ophthalmoscopy remains an underutilized tool by physicians and further studies will help establish the role of fundoscopy in PUO.

Salil Mehta
Lilavati Hospital, Bandra, Mumbai 400 050. Received : 23.8.dengue 2005; Accepted : 15.9.2005

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Erratum
In the Editorial entitled “Whose life is it, anyway? The evolving face of Euthanasia” published in JAPI 2005;53:279-281, the 5th paragraph should read as “When the person who is killed has made and expressed a wish to be killed” it is termed as Voluntary Euthanasia.

- Editor