The Term "Partial Extensively Drug Resistance" in Tuberculosis is Superfluous

The paper by Shah and Rahangdale on drug resistant tuberculosis (TB) in children is an eye opener to some neglected aspects of TB problem in India [1]. However, the term "partial XDR" as coined by the authors is eye-catching but superfluous; all of their study strains were MDR (multidrug resistant) with fluoroquinolone resistance.

Primary MDR TB in children, as illustrated by Shah and Rahangdale has already become a difficult problem. If a child acquires infection from an MDR TB adult, preventive chemotherapy with isoniazid or rifampicin or a combination will be ineffective.

Extensively drug-resistant (XDR) TB in adults in India is an emerging problem, already an emergency in our opinion, but not yet 2.4% of all MDR cases as mentioned by the authors. As far as we can verify, the World Health Organization has recognized only 1 case of XDR TB in India, while many such cases have been reported in the literature [2]. We strongly recommend to the Indian Academy of Pediatrics to urgently develop policy options for community level prevention of TB and take them up with the national TB control program at the highest level.

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Rituximab Usage in Children: A Double Edged Sword!

We read the recent article on Rituximab by Borker, *et al*. with great interest [1]. This letter reports our experience with Rituximab in children for various indications. A brief tabulation of Rituximab usage in eleven children admitted in our unit from 2006 to 2011 is presented in ***Table* I**. We have previously reported 5 of these 11 patients [2]. Rituximab has good efficacy but some severe side-effects which we highlight in this report.

We report 2 cases of autoimmune hemolytic anemia (AIHA), the first being an infant refractory to steroid and intravenous immunoglobulin (IVIG) who is now transfusion independent at 6 months post-therapy with Rituximab and cyclophosphamide. The second patient who presented with AIHA, nephritis, inflammation and asplenia did not respond to Rituximab. She died of her disorder which was later diagnosed as only the second reported case of human heme-oxygenase-1 deficiency [3].

Rituximab based immune tolerance induction (ITI) in the case of Hemophilia-A with inhibitors (high responder) succeeded in clearing inhibitors 3 months post-ITI.

Of the 3 cases associated with lympho-proliferative disorders, the first was a girl with Epstein-Barr virus induced post-transplant lympho-proliferative disorder (PTLD) post-matched-sibling donor stem-cell transplant for Familial Hemophagocytic Lympho-histiocytosis. Rituximab produced a dramatic improvement in her PTLD. The two cases of mature B-cell Lymphoma responded well to chemotherapy combined with Rituximab.

The child with acute lymphoblastic leukemia with refractory immune thrombocytopenic purpura (ITP) (one of 5 children with ITP) maintained platelet counts >100,000/μL following Rituximab therapy. The disseminated tuberculosis which he developed at the end of treatment could be partly attributed to Rituximab-associated CD20+ cell depletion.

The four other cases of ITP non-responsive to IVIG,

TABLE I DETAILS OF RITUXIMAB USAGE IN CHILDREN FOR VARIOUS INDICATIONS

Indication	*Age/ sex*	*Dosage/Schedule*	*Response*	*Side effects*	*Replacement IVIG*	*Outcome*
AIHA	1 yr/ M	Std.D × 4 wks + Cy × 8 doses	DCT negative Transfusion free	Not significant	Yes	Alive
AIHA with HO-1 def	11yr/F	Std.D × 3 wks + Pred/ Cy × 2 doses	No response	Not significant	No	Died (primary disease)
Hemophilia-A with inhibitors	13 yr/ M	Std.D × 4 wks + Cy × 2 doses	Inhibitors negative at 3 months	Not significant	No	Alive
FHLH with EBV-PTLD	1½ yr/ F	Std.D × 4 wks + Pred for GVHD	PTLD subsided	Not significant	Yes	Alive
DLBCL	16 yr/ F	375 mg/m^2 with each cycle of R-CHOP × 2 cycles	Partial Response	Not significant	No	Alive
Burkitt's lymphoma	5yr/M	Std.D/ MPC842 chemo cycle × 4	CR	Not significant	No	Alive
ALL with ITP	3yr/M	Std.D x 4 wks	Sustained rise in plts	Diss. TB (responded to ATT)	Yes	Alive
Chronic ITP	10yr/F	Std.D x 4 wks + CSA/Pred	Sustained rise in plts	CNS white matter changes	No	Alive with PML
Chronic ITP	7yr/M	Std.D x 4 wks	Sustained rise in plts	Not significant	No	Alive
Chronic ITP	8yr/M	Std.D x 4 wks	Plts raised for 6-8 months then decreased	Not significant	No	Alive
Chronic ITP	8 yr/ F	Std.D x 4 wks +Aza	Plts increased	CMV infection	Yes	Died (CMV pneumonitis)

AIHA- Auto-immune hemolytic anemia; ALL- Acute lymphoblastic leukemia; ATT- Anti-tubercular therapy; Aza- Azathioprine; CMV- Cytomegalovirus; CNS- Central nervous system; CSA- Cyclosporin-A; Cy- Cyclophosphamide; DCT- Direct Coombs' test; Diss.- Disseminated; DLBCL- Diffuse large B-cell lymphoma; EBV- Epstein-Barr virus; FHLH- Familial hemophagocytic lymphohistiocytosis; GVHD- Graft versus host disease; HO-1- Heme oxygenase-1; ITP- Immune thrombocytopenic purpura; IVIG- Intravenous immunoglobulin; PML- Progressive multifocal leukoencephalopathy; Pred.- Prednisolone; Plts- Platelets; R-CHOP- Rituximab with CHOP chemotherapy; Std. D.- Standard dose of Rituximab (375 mg/m^2/wk); TB- Tuberculosis.

Intravenous anti-D, steroids and cyclosporine received Rituximab and all responded with an increase in platelets >l00,000/mm^3. Three patients sustained their response but two of them developed Rituximab therapy associated infectious complications (***Table* I**). The fourth showed a decline in platelet count after a transient increase for about eight months.

As this data illustrates, Rituximab has wide and effective applications in pediatric haematology-oncology. However, adequate caution is warranted to pre-empt and institute early therapy, if required, for opportunistic infections which may arise due to resultant immunosuppression. Also, progressive multifocal leukoencephalopathy (PML) is a rare but real complication of Rituximab use and close clinical observation is essential [4].

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