Effect of Thalidomide in immune mediated paradoxical reaction in childhood CNS tuberculosis

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Introduction

Immune mediated paradoxical reaction (PR) in HIV negative CNS tuberculosis (TB) is frequently encountered.

In CNS TB, tumour necrosis factor- alpha (TNF-α) plays a important role in containing the infection, granuloma formation, CSF pleocytosis and increased blood brain barrier permeability.

High TNF-α levels may lead to exaggerated immune reaction and tissue destruction leading to TB associated paradoxical worsening.

The current retrospective analysis focussed on the indications and response of add-on thalidomide (TNF-α blocker) in childhood CNS tuberculosis with immune mediated paradoxical reaction.

Methodology

Retrospective data analysis

Hospital case records of children with CNS TB being followed up in our hospital were screened for documentation of clinico-radiological immune mediated PR.

PR was defined as worsening of pre-existing tuberculous lesions or appearance of new lesions in patients whose clinical symptoms have worsened after an initial improvement with anti-tubercular therapy (ATT).

Children with PR who did not respond to standard ATT, five day pulse methylprednisolone and dexamethasone (4-6 weeks) were initiated on Thalidomide (THD) and were included for analysis.

Clinical and radiological response was recorded after three months of thalidomide therapy

Patients with drug resistant tuberculosis or with HIV coinfection were excluded.

Demographic, clinical, laboratory and neuroimaging data were entered on an excel sheet and analysed

Observation

Forty-Seven children with TBM were registered during the study period (January 2022 to October 2023).

Seven (14.89%) patients received THD along with 4-drug ATT and steroids. (Table1)

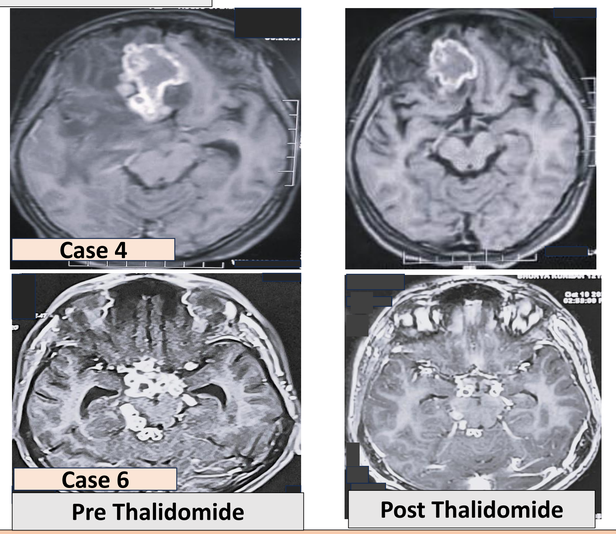
Clinically 3/7 had hydrocephalus (HCP) [Increased tuberculomas +- midline shift (3/4)], despite a functioning ventriculoperitoneal shunt; optico-chiasmatic arachnoiditis (OCA) (4/7)) and 3/7 had significantly increased basal exudates with steroid toxicity.

Mean dose and duration of THD was 4.88mg/kg(3-8 mg/kg) and 3.7months(1-6 months) respectively

Radiological response was observed in 83.6%(5/6) and two-point improvement in PCPC scale at 3 months was seen in 50% (3/6)

Adverse events- SNHL occurred in one child (causality ?multifactorial) and THD was stopped. Transaminitis occurred in two (one had hepatitis A), leukopenia in one (resolved spontaneously).

Age/ gender	Diagnosis	THD dose	THD duration	Clinico-radiological response	Adverse event	PCPC scale
4 y/M	TBM/HCP	3mg/kg	3 months	No response	none	No change
14y/F	TBM/OCA	4mg/kg	5 months	Yes	Transaminitis	No change
10y/F	Disseminated TB/ PR	4.2mg/kg	3 months	Yes	leukopenia	Improved 3 to 1
13/F	Disseminated TB	8mg/kg	4 months	Yes	Transaminitis	Improved from 3 to 1
7y 6 month/F	Disseminated TB	3 mg/kg	4months	Yes	none	No change
11yr5 months/M	TBM/HCP /OCA	6mg/kg	6 months	Yes	none	Improved from 4-2
8yr7month/ M	TBM/HCP /OCA	6mg/kg	1month	-	SNHL	-



Conclusion

A three to six month course of thalidomide at a dose of 4-8mg/kg showed significant radiologic improvement in 84% and clinical improvement in 50% in steroid refractory immune mediated paradoxical reaction in children with CNS TB.

References

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