

Maternal sirolimus therapy for fetal extensive lymphatic malformation

Selection criteria, sirolimus management, and outcome: a series of 6 cases

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Objective

- To evaluate patient selection, treatment management, maternal-fetal tolerance, pharmacokinetics and outcomes of **maternal sirolimus therapy (MST) in extensive fetal LM** (lymphatic cystic malformations)

Methods

- 15 fetuses referred for extensive LM
- Multidisciplinary selection process
- MST proposed only for extensive lesions at high risk of significant perinatal morbidity

Results

Patient Selection : 15 referrals
Exclusion : 5 Suspected cystic teratoma,
2 Llimited lesion, 1 parental refusal,
1 fetal demise
→ **6 fetuses received MST**

MST protocol

Initiation	24 to > 30 WG
Starting dose	4-6 mg/day
Maximum dose	14 mg/day
Target trough level	10-12 ng/mL
Mean GA at delivery	38.1 WG

Maternal Safety

Mild mucositis (n=2), Hypertriglyceridemia (n=1)

No severe maternal toxicity

No major obstetric complications

Fetal and Neonatal Outcomes

Overall **response rate: 5/6 (83%)**

Pharmacokinetics

- **Effective transplacental transfer** in all cases
- Cord blood concentrations varied considerably
- Fetal levels could be lower, similar or higher than maternal levels
- Suggests substantial **interindividual variability** in placental transfer

Conclusion

- Maternal sirolimus therapy appears feasible and well tolerated
- Significant lesion regression occurred in most fetuses (83%)
- Effective but highly variable transplacental transfer was demonstrated
- Earlier initiation (late second or early third trimester) may improve response
- MST should remain restricted to highly selected high-risk cases managed in expert multidisciplinary centers



Figure 1. MST at 27 WG with an excellent outcome : coronal T2 weighted MR images (A,B) showed an extensive LM involving the hemithorax with inferior extension facing the right liver, a major extension on the right arm. MR follow-up at 37 WG showed major decrease of the lesion (C) confirmed at birth (D)

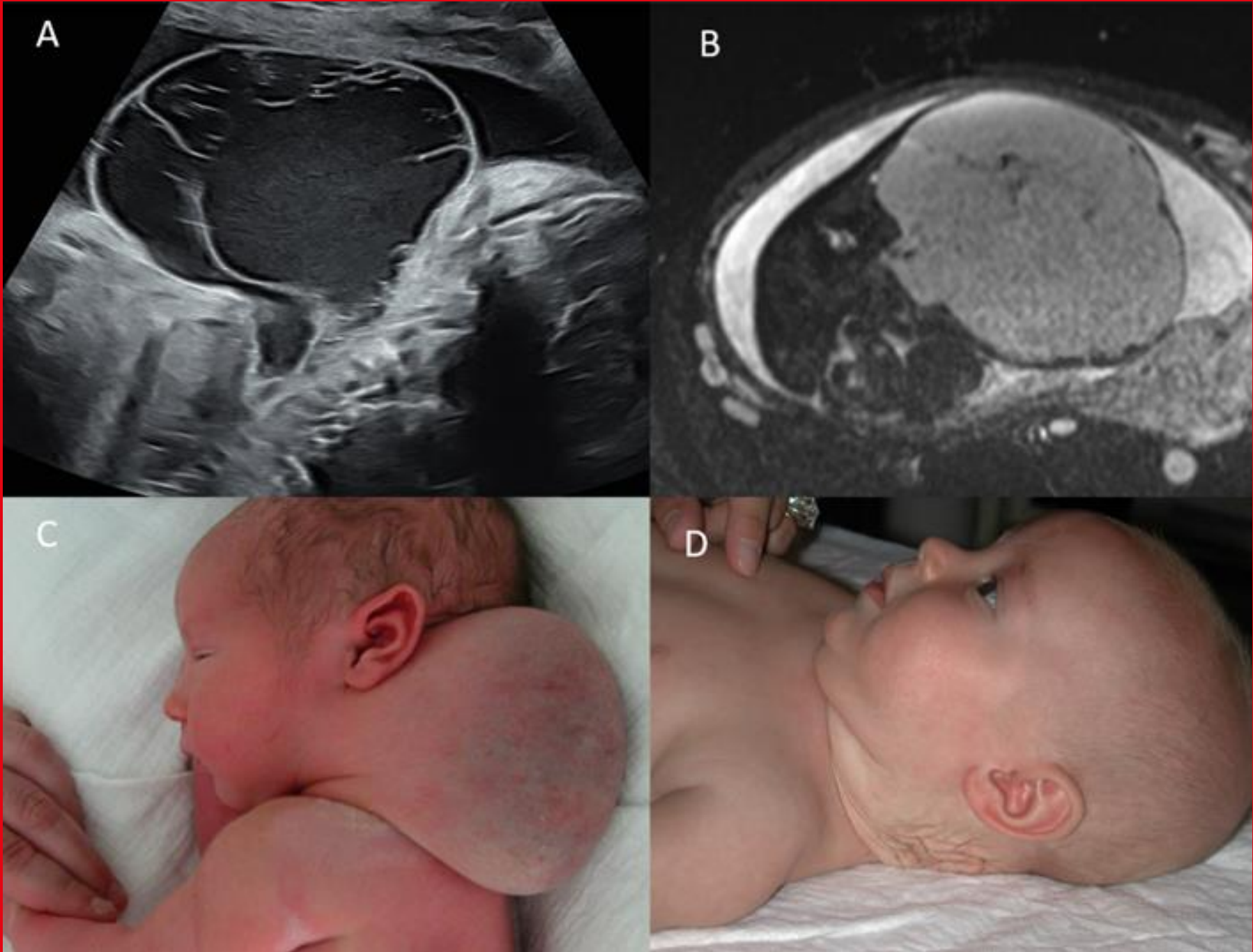


Figure 2. Patient referred for extensive cervico-facial LM not indicated for MST. Prenatal ultrasound at 28 WG and fetal MRI demonstrated a predominantly pedunculated LM without deep cervical extension. Postnatal clinical appearance at birth and clinical evolution 4 months after sclerotherapy with a favorable outcome.