Investigation and Diagnosis of SRS

Child Growth Foundation
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Does the patient meet the clinical criteria for diagnosis of SRS (NH-CSS)?

- Yes (score ≥4/6) Or No, but continued clinical suspicion (score 3/6)*
- No (score <3/6)

No → Diagnosis not confirmed

Yes → Molecular testing for 11p15 and upd(7)mat[1]

- Positive → Molecular diagnosis confirmed - the patient has SRS
- Negative → Does the patient have relative microcephaly?
  - Yes → Diagnosis not confirmed Consider differential diagnosis **
  - No → Consider differential diagnosis **

Consider differential diagnosis ** → Are the clinical features consistent with a differential diagnosis?

- Yes → Molecular testing as per differential diagnosis
- No → Consider additional molecular testing:
  - CNV and/or 14q32 analysis followed by upd(16)mat, upd(20)mat or CDKN1C or IGF2 mutation analysis
  - Alternative tissue analysis

Consider additional molecular testing:

- Positive → Alternative molecular diagnosis[2]
- Negative → What is the NH-CSS score?
  - ≥5/6 → Clinical SRS[3]
  - 4/6 → Does the patient have relative macrocephaly and protruding forehead?
    - Yes → Clinical SRS[3]
    - No → Diagnosis not confirmed
  - 3/6 → Diagnosis not confirmed

Taken from 'Diagnosis and management of Silver–Russell Syndrome: first international consensus statement'

DOWNLOAD STATEMENT

- Diagnostic questions
- Recommended molecular tests
- Diagnosis not confirmed
- Diagnosis of SRS confirmed

* Studies have excluded 11p15 LOM and upd(7)mat in patients with intrauterine growth retardation and postnatal growth retardation alone; some patients, particularly those with upd(7)mat or children under 2 years, score 3/6 (see text for details).
[1] Arrange CNV analysis before other investigations if patient has notable unexplained global developmental delay and/or intellectual disability and/or relative microcephaly.
[2] Insufficient evidence at present to determine relationship to SRS, with the exception of tissue mosaicism for 11p15 LOM. ||Unless evidence of catch-up growth by 2 years.
[3] Previously known as idiopathic SRS. CNV, copy number variant; LOM, loss of methylation; NH-CSS, Netchine-Harbison clinical scoring system; SRS, Silver–Russell syndrome.
** See clinical criteria for diagnosis of Silver Russell Syndrome