Investigation and Diagnosis of SRS

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

- Yes (score ≥4/6)
- No (score <3/6)

Or
- No, but continued clinical suspicion (score 3/6)*

Molecular testing for 11p15 and upd(7)mat¹

- Positive
- Negative

Diagnosis not confirmed

Does the patient have relative microcephaly?

- Yes
- No

Diagnosis not confirmed

Consider differential diagnosis **

Are the clinical features consistent with a differential diagnosis?

- Yes
- No

Molecular testing as per differential diagnosis

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

Diagnosis not confirmed

What is the NH-CSS score?

- ≥5/6
- 4/6
- 3/6

Does the patient have relative macrocephaly and protruding forehead?

- Yes
- No

Clinical SRS³

Diagnosis not confirmed

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* 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.