We describe a boy with multiple congenital anomalies/mental retardation (MCA/MR) syndrome. He has growth retardation, microbrachycephaly, coloboma of the iris, and typical facial anomalies including cleft lip/palate. This phenotype overlaps with that described by Richieri-Costa and Guion-Almeida in three Brazilian brothers. The new patient provides further evidence of the existence of this rare clinical entity. Am. J. Med. Genet. 83:419–421, 1999.

**KEY WORDS:** iris coloboma; short stature; microbrachycephaly; cleft lip-palate; mental retardation; Richieri-Costa/Guion-Almeida syndrome

**INTRODUCTION**

Cleft lip/palate, mental retardation, and eye anomalies are reported by the current literature [Ravine et al., 1997] and by the available databases (OMIM, LDDB, POSSUM) as part of many clinical entities, showing different patterns of inheritance.


Herein we report on another patient presenting all the main clinical signs associated with this condition.

**CLINICAL REPORT**

The boy (C.S.) was born in 1983 from a healthy and nonconsanguineous couple. The mother had a healthy daughter from a previous marriage. Pregnancy and delivery were normal; birth weight was 2.4 kg. A cleft lip/palate was noticed at birth. From early infancy until puberty, weight, height, and occipitofrontal head circumference (OFC) were always below the normal standards; neuropsychological development was severely delayed. The child suffered from many episodes of urinary infections. A mild deafness was demonstrated by an audiometric evaluation performed in infancy.

On clinical examination at the age of 14 years height was 121 cm (<3rd centile), weight 22 kg (<3rd centile), OFC 46 cm (<3rd centile), inner canthal distance 2.5 cm (3rd–25rd centile) outer canthal distance 8 cm (3rd–25rd centile).

The patient had microbrachycephaly, long asymmetric face, sparse eyelashes, asymmetric and downslanted palpebral fissures, deep-set eyes, strabismus, coloboma of the right iris, malar hypoplasia, a surgical scar resulting from cleft lip/palate repair, and prominent mandible (Fig. 1 a,b).

Neurological examination showed an atactic gait, generalized hypotonia with joint laxity and increased lower limb tendon reflexes with bilateral foot clonus. The light reaction of the right pupil was decreased. The psychological examination demonstrated absence of language, profound mental retardation, and autistic behavior.

Skeletal X-ray findings were normal; brain CT scan showed mild ventricular enlargement; cardiologic status was unremarkable. Renal ultrasound showed mild left pelvi-calycal dilatation; ophthalmologic evaluations showed the presence of small retinal hemorrhages, in addition to the iris coloboma.

High resolution chromosome analysis showed a normal karyotype. Due to the presence of mental retardation, cleft lip/palate, and iris coloboma, fluorescence in situ hybridization (FISH) with a 22q11 specific probe was performed, but the finding of both target signals
DISCUSSION

We describe the clinical findings in a boy presenting growth and mental retardation, microbrachycephaly, coloboma of the iris, and typical facial anomalies including cleft lip/palate.

A few different conditions present as essential parts of their clinical spectrum the association of oral clefting, coloboma, and mental retardation. To date at least seven clinical conditions can be enumerated, among which two have autosomal dominant transmission [Hussels, 1971; Kingston et al., 1982; Ravine et al., 1997], four are autosomal recessive [Anyane-Yeboa et al., 1983; Baraitser et al., 1982; Fryns et al., 1997; Zunic et al., 1988], and one is X-linked recessive [Abruzzo and Erickson, 1997].

Additional conditions with an unknown pattern of inheritance [Le Marec et al., 1992; Michels et al., 1979; Richieri-Costa and Guion-Almeida, 1992] may be added to the list.

Taking into account the overall clinical picture of our patient and in particular the severity of neurological involvement, none of the above clinical entities appear to overlap completely.

On the other hand, the syndrome described by Richieri-Costa and Guion-Almeida in three Brazilian brothers shares some other important findings with our case as indicated by the comparison, sign to sign, shown in Table I. Nystagmus and retinal coloboma are the only minor signs shared by the three Brazilian sibs but not observed in our patient. Conversely, our patient presents with deafness, which was not recorded in the previous patients, or might have not been investigated for.

Delayed neuropsychological development or simply mental retardation is signaled for the Brazilian sibs, whereas severe neurologic involvement to absence of language characterizes our patient.

Despite these discrepancies, the matching of many clinical features (Table I) and the close similarity of facial changes evidenced by published pictures, cause us to conclude that our patient may likely represent a severe form of the Richieri-Costa/Guion-Almeida syndrome rather than a new syndrome. A severe form could justify the profound neurological involvement in the patient studied, thus expanding the phenotypic spectrum of the Richieri-Costa/Guion-Almeida syndrome.

To our knowledge this is the second report of this clinical entity. Either the Richieri-Costa/Guion-Almeida syndrome is very rare, or it escapes detection, being included among several elusive nosological entities with dysmorphisms and mental retardation, whose genetic cause is unknown.

<table>
<thead>
<tr>
<th>Table I. Comparison of the Clinical Findings Among the Three Patients Reported by Richieri-Costa and Guion-Almeida and the Present Case</th>
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<tbody>
<tr>
<td><strong>Clinical signs</strong></td>
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<td>------------------------</td>
</tr>
<tr>
<td>Short stature</td>
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<tr>
<td>Mental retardation</td>
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<tr>
<td>Microbrachycephaly</td>
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<tr>
<td>Palpebral ptosis</td>
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<tr>
<td>Asymmetric palpebral fissures</td>
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<td>Downslanted palpebral fissures</td>
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<td>Deep-set eyes</td>
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<tr>
<td>Nystagmus</td>
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<td>Strabismus</td>
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<td>Iris coloboma</td>
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<td>Retinal coloboma</td>
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<td>Malar hypoplasia</td>
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<td>Cleft lip/palate</td>
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<td>Prominent mandible</td>
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<td>Deafness</td>
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</table>
The diagnosis of the syndrome in another male patient leaves unresolved the pattern of inheritance, which could be either autosomal or X-linked recessive.

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REFERENCES


Richieri-Costa/Guion-Almeida Syndrome


