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The hairy elbows syndrome: clinical and neuroradiological findings

Sindrome "Hairy Elbolus": Quadro clinico e neuroradiologico

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Key words: hirsutism, hypertrichosis cubiti, infantile spasms, brain overgrowth, hemisphere asymmetry.

Riassunto

La sindrome dei "gomiti pelosi" è un fenotipo raro caratterizzato da un allungamento esagerato dei peli sulla superficie dorsale degli arti superiori. Questa caratteristica spesso si associa a bassa statura, asimmetria facciale, dismorfie, ritardo di crescita uterina, ritardo mentale e del linguaggio. In questo lavoro viene presentato un piccolo paziente con hypertricosis cubiti associata ad un importante coinvolgimento cerebrale caratterizzato da spasmi infantili, disturbi comportamentali e asimmetria degli emisferi cerebrali. Sebbene tale associazione non sia stata mai riportata in letteratura non sappiamo se essa sia casuale o sottostimata. È, comunque, ipotizzabile che il nostro paziente con il coinvolgimento importante del sistema nervoso centrale sia l'espressione più grave del fenotipo comunemente riportato.

Abstract

The hairy elbows syndrome (HES) is a rare congenital phenotype characterized by an abnormal increase in long hairs localized on the upper limbs extensor surfaces. This feature is often associated with short stature, facial asymmetry, dysmorphisms, intrauterine growth retardation (IUGR), and mental and speech delay. We report a case with hypertricosis cubiti associated with infantile spasms, behaviour disorders and cerebral hemisphere asymmetry. Although these findings have not been previously described we are uncertain whether they are unusual or underestimated. However, it is likely that these neurological findings are strongly interrelated leading to a more severe phenotype of the syndrome.

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Introduction

The hairy elbows syndrome (HES) is an uncommon congenital disorder characterized by a remarkable amount of long hairs localized on the extensor surfaces of the upper extremities mainly in the elbow region[1].
Hypertrichosis is not evident at birth; usually, it appears in early childhood and peaks between 5 and 6 years of age followed by a slow decrease and disappearance at puberty.
An autosomal dominant[2] and recessive inheritance trait have both been proposed although most patients previously reported are sporadic cases[2,4-8].
The syndrome has also been described in association with short stature[1-3,5,6,8,12], facial asymmetry and dysmorphic features[2-4,6,8,12], intrauterine growth retardation (IUGR)[5,6,8], mental retardation and speech delay[3,4,6,8,12]. We report additional features including infantile spasms and cerebral hemisphere asymmetry.These associated abnormalities have hitherto never been described to our knowledge.

Case repurt

Our patient, a 5 year 4 month - old male child of healthy unrelated parents, was born after an uneventful pregnancy and spontaneous delivery. His birth weight was 3820 g, height 54 cm, and head circumference 35,5 cm.There was no family history of epileptic disorders or mental and neurological diseases. The child was referred to our department at the age of 8 months because of asymmetric spasms. On admission, neurological and psychomotor examination revealed mild hypo-

tonia of lower limbs and difficulty to sit unsupported. He showed a behavioral regression, including loss of smiling, lack of eye contact, unresponsiveness to voices and/or nonverbal auditory stimuli and indifference to environment EEG recording displayed a hypsarrhythmic pattern.

Since valproate and nitrazepam were ineffective, ACTH therapy was started inducing improvement in seizure control and hypsarrhythmia disappearance but did not adjust behavioral disorders.

At 1 year of age an increasingly long and thick hairs on both elbow regions was observed.

The intellectual assessment (Stanford - Binet scale) at 4 years 3 months revealed a mental retardation (mental age 2 years). The child exhibited use of social gestures and intermittent eye contact. Language skills were poor, his vocabulary included only four single words and his comprehension was strongly dependent on context. Behavioral assessment performed by Rimland's E2 form and Childhood Autism Rating Scale checklist showed mild autistic features (total score -9, and 35.5, respectively).

One year later the child achieved a mental age of 2 years 6 months and a considerable behavioral improvement without autism traits.

He was quiet, smiling and easily engaged in activities, but he played with simple toys, and exhibited a slow lexical development with phonological difficulties.

Neurological examination revealed a head circumference of 50 cm, flat occiput, mild generalized hypotonia and bilateral flat valgus foot.

Magnetic resonance imaging showed hemispheric asymmetry resulting from size increase of left posterior hemisphere associated with mild enlarged left posterior horn of the lateral ventricle (Fig. 1).

The EEG displayed sharp-wave discharges in the left temporal area.

In addition, the child showed long and downy hairs, nearly 8 cm, on the elbow region (Fig. 2), a slight dorsal hypertricosis, slight facial asymmetry, and regular growth.

Chromosome analysis was performed upon cells obtained from peripheral lymphocytes and skin fibroblasts. A normal male karyotype was found in more than 200 metaphases of both cultures; no mosaicism was present.

A biopsy of 11.5x5x5 mm macrosocpically normal of the left elbow skin fragment showed a simple hyertrophy of the piliferi follicle, mantaining the normal spatial relationships with the other components of tissue. Epidermal and dermal layers were otherwise lacking of histological abnormalities.

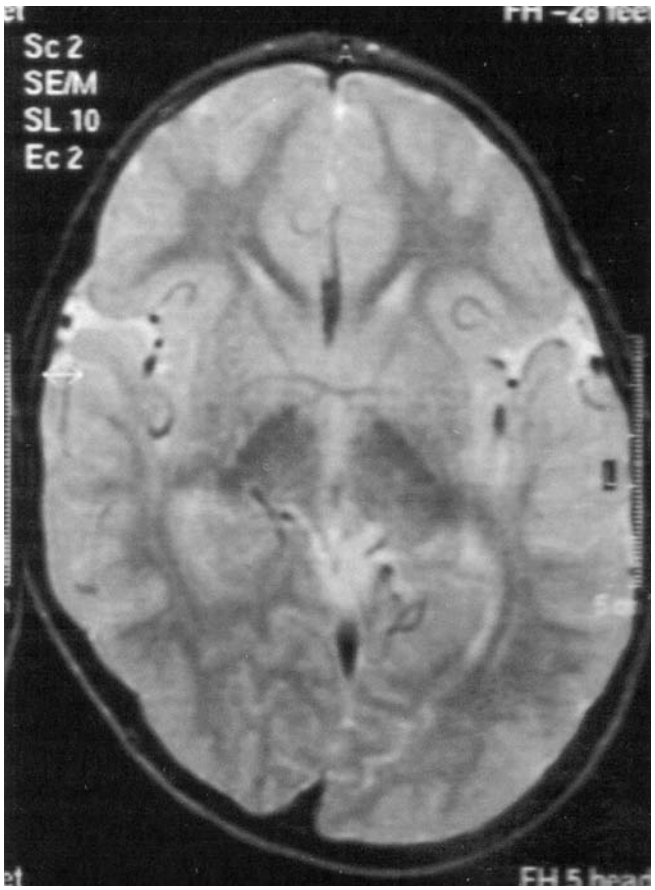

Figure 1
MRI shows hemispheric asymmetry with size increase of left posterior hemisphere and mild enlarged left posterior horn of the lateral ventricle.

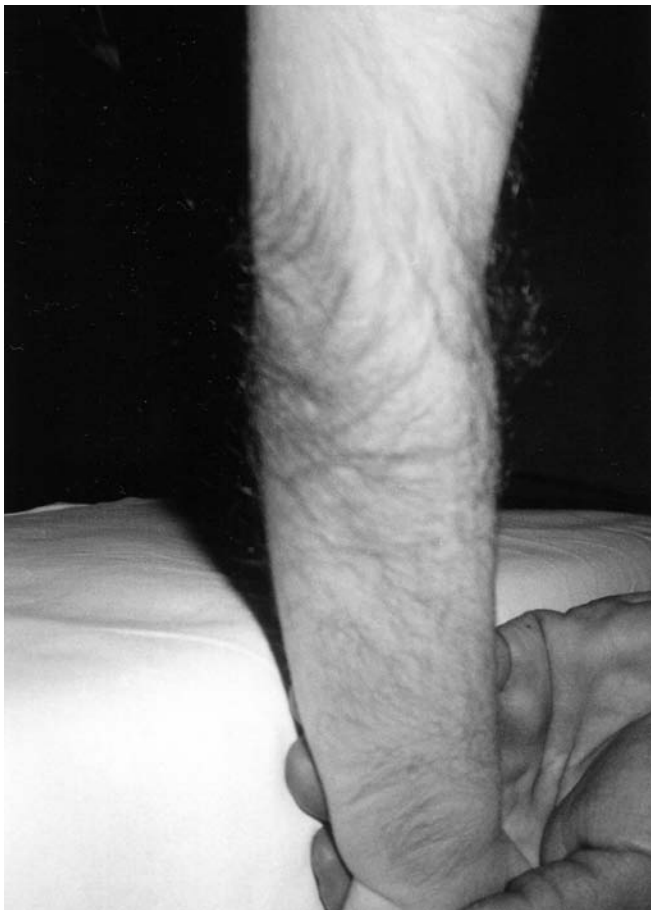

Figure 2
Long and downy hairs on the elbow region.

Discussion

The HES was first recognized by Beighton[1], who reported a localized hypertrichosis confined to the extensor surface of the elbow regions in two siblings from an inbred Amish family. They also had short stature and their parents were heterozygous for the Weill-Marchesani syndrome.

The hypertricosis cubiti is the main marker of the HES and is often associated with short stature[1-3,5,6,8,12]. Most studies remarked somatic abnormalities including IUGR, dysmorphic features, facial asymmetry, and palpebral ptosis[2-5,6,8,12] but did not report relevant neurological data. Hypotonia, deep tendon reflex decrease, mental retardation, and speech delay are the only neurological troubles reported[3,4,6,8]. Recently, neuroimaging findings revealed enlarged lateral ventricles, arachnoid cyst, and subarachnoid space increase in two patients with HES[3,5].

The HES in our case appears with relevant brain involvement including infantile spasms, mental retardation, behavioural disorders and hemisphere overgrowth. Although these findings may be a casual association it is likely that they are strongly linked leading to a more severe phenotype of HES.

Newly, rising attention has been addressed to the overgrowth syndromes and to the role played by the recurrent associated cerebral abnormalities in the pathogenesis of mental deficiency and behaviour disorders[9].

It has been hypothesized that brain volume increase results from a defect in specific developmental events such as excessive amount or growth rate of neurons and/or glial cells, over expression of minicolumns, excessive and premature expansion of dendritic and axonal arborisation, increase of axonal connections, and/or premature myelination[10].

In addition, it has been suggested that abnormal regional growth might depend on abnormalities in the function or expression of neurotrophic factors. However cytogenetic mistiming or apoptotic processes failure could be involved[11].

Unluckily, few neurological data and a smaller amount of neuroimaging features on HSE have been reported in literature, and so we cannot prove whether the brain overgrowth of our case is a sporadic or a common finding of the syndrome. The hypertrophy of the piliferi follicles of the elbows may be interpreted as the result of an overgrowth pattern at that level, possibly pathogenetically related to the brain overgrowth in relation to the common embryological origin of both tissues.

In conclusion, further neuropathological, neuroimaging, and neuropsychological data are needed to better characterize the syndrome and to elucidate the relationships of the different clinical findings in the HES.

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