INFANTILE ONSET OF COCKAYNE SYNDROME WITHOUT PHOTOSENSITIVITY IN A TUNISIAN GIRL

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SYNDROME DE COCKAYNE À DÉBUT PRÉCOCE SANS PHOTOSENSIBILITÉ CHEZ UNE FILLE TUNISIENNE

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RÉSUMÉ

Pré-requis : Le syndrome de Cockayne est une maladie rare de transmission autosomique récessive d'expression clinique variable associant un retard mental et un nanisme. Classiquement, la maladie débute à la deuxième année de vie. L'échec de la synthèse de l'ARN après irradiation par UV-C constitue un outil au diagnostic ; cette anomalie est fortement corrélée à la photosensibilité.
But: Rapporter un cas inhabituel d'un syndrome de Cockayne.
Observation: nous présentons le cas d'une fille de 5 ans atteinte d'un syndrome de Cockayne sans signes de photosensibilité. Le diagnostic a été confirmé par l'échec de la synthèse de l'ARN après irradiation par les UV-C. Le patient est décédé à l'âge de 6 ans d'une pneumonie.
Conclusion: Bien que rare, le syndrome de Cockayne peut se présenter précocement et sans photosensibilité.

MOTS-CLÉS

syndrome de Cockayne, réparation de l'ADN, photosensibilité

SUMMARY

Background: Cockayne syndrome is a rare autosomal recessive disorder with dwarfism, mental retardation, and otherwise clinically heterogeneous features. Classically, the onset of Cockayne syndrome starts in the second year of life. The failure of RNA synthesis to recover to normal rates after UV-C irradiation provides a useful diagnostic test and the clinical feature that correlates most strongly with defective RNA synthesis is photosensitivity.
Aim: To report an unusual case of Cockayne Syndrome.
Case report: A case of a five-year-old girl with Cockayne with an onset in early infancy the girl and without photosensitivity is presented. The diagnosis was confirmed by the failure of RNA synthesis to recover to normal rate after UV-C irradiation. The patient died at the age of 6 of pneumonia.
Conclusion: Although rare, Cockayne syndrome may be presented without photosensitivity and had an early onset.

KEY-WORDS

Cockayne syndrome; DNA repair; mental retardation

متلازمة كوكاين ذات بداية مبكرة عند طفلة تونسية.

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ملخص : متلازمة كوكاين هي مرض نادر ذات مرور صبغي جسدي و يختلف تعبيرها السريري الذي يجمع بين تخلف ذهني و تقزم . يمثل الفشل في تثبيت هؤش بعد التشجيع بواسطة ضبا أداة تشخيص ؛ يرتبط هذا التشوه بالتحسس الضوئي . نستنتج أن هذه المتلازمة يمكن أن تكون بصفة نادرة مبكرة و لا تتزامن مع تحسس ضوئي.

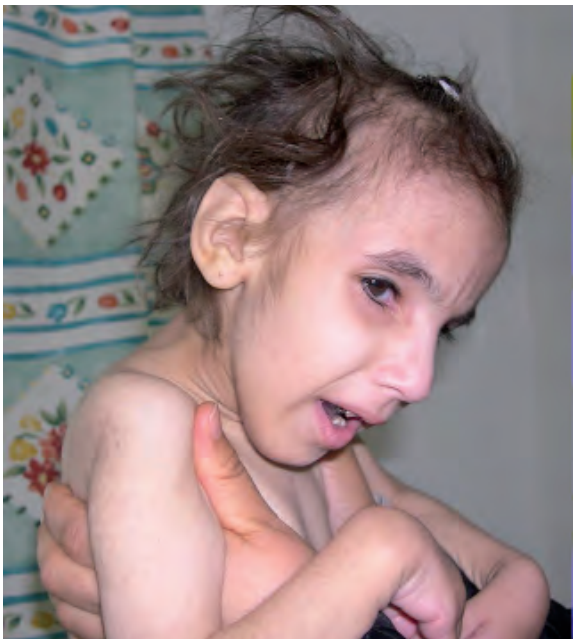
الكلمات الأساسية : متلازمة كوكاين، تحسس ضوئي.

Cockayne syndrome is a rare autosomal recessive degenerative disease with cutaneous, ocular, neurologic and somatic abnormalities. The entity was first described in 1936 by Cockayne. So far, around 150 cases have been reported in the literature [1,2,3]. Classically, the onset of Cockayne begins in the second year of life, however, it is quite rare to report cases with early neonatal onset and death in infancy. The failure of RNA synthesis to recover to normal rate after UV-irradiation which characterizes Cockayne syndrome, is strongly correlated with photosensitivity. We report a case of a five-year-old girl who presented cockayne syndrome with onset in early infancy without photosensitivity.

CASE REPORT

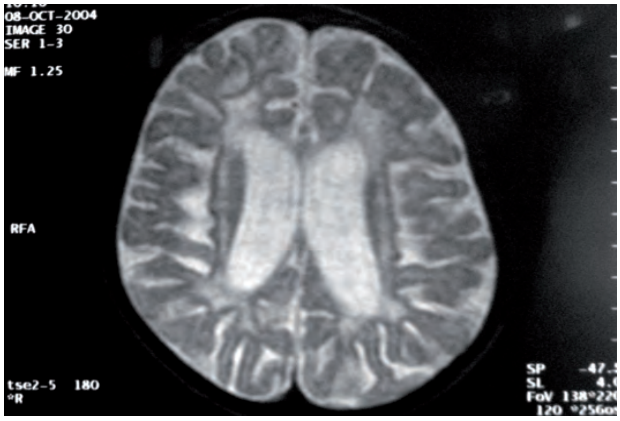
A 5-year-old girl, first sibling of a consanguineous marriage, was admitted to our department to manage pneumonia. She was born at full-term by normal delivery. There was no history of neonatal distress. She had intrauterine growth retardation; her weight was of consanguineous 2 kg, her height was of 49 cm and her head circumference was of 34 cm. She had developmental delay which was noted at 7 months of age. She could not control her head, sit alone, smile or speak.
Upon medical examination: her weight was of 6 kg, her height was of 74 cm, head circumference was of 41 cm. She had large ears, a thin nose and sunken eyes due to the lack of subcutaneous orbital fat and a progeric appearance (figure 1).

Figure 1: Facial dysmorphy



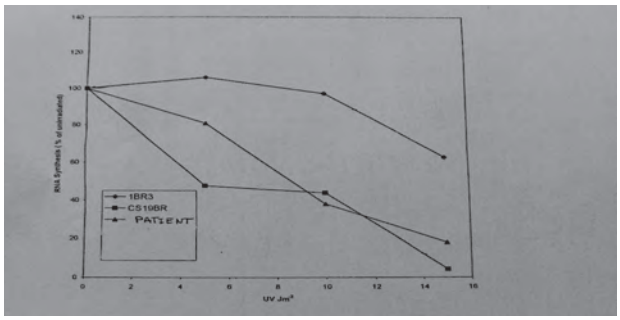
There was a withering away of the temporalis muscles. She had arthrogryposis and hyporeflexia. Photosensitivity, defined as abnormal reaction to sun exposure (as papulovesicular eruption, rash with oedema, or atrophic scars) was not observed in the patient. Chromosome analysis revealed a normal 46 XX.
A magnetic resonance imaging of the brain showed leukodystrophy with cortical atrophy without calcification (Figure 2). Auditory brainstom evolved response revealed bilateral hearing impairment.

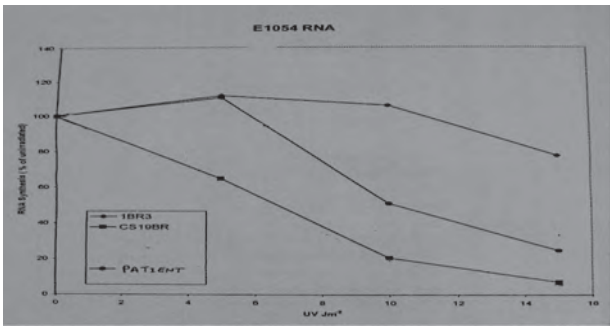
Figure 2: Magnetic resonance imaging of the brain. Axial SE T2 image showing cerebral white mater involvement.



Ophthalmological examination showed bilateral cataract. Electromyography showed peripheral neuropathy.
The response of RNA synthesis to UV was tested in fibroblasts cultured from the patient. After UV irradiation, defective recovery of RNA synthesis was found, confirming the diagnosis of Cockayne syndrome in the patient (Figure 3,4); the patient died at the age of 6 years of pneumonia.

Figure 3 & 4 : RNA synthesis after UV irradiation. The normal control cell line in both graphs E1054 RNA and E1055 RNA is 1BR3 and the known Cockayne syndrome control line is CS19BR in both. Cells from our patient do not recover normally.





DISCUSSION

Cockayne syndrome is a multi-systemic, autosomal recessive disease (MIM 216400) characterised by postnatal growth failure and progressive multi-organ dysfunction. The main clinical features are severe dwarfism (<- 2 SD), microcephaly (<-3 SD), psychomotor delay, sensorial loss (cataracts, pigmentary retinopathy, and deafness) and cutaneous photosensitivity. Nance and Berry have distinguished three clinically different classes of the disease [3]. A classical form (Cockayne syndrome I) which includes the majority of patients, a severe form (Cockayne syndrome II) characterized by early onset and severe progression of manifestations and a mild form, typified by late onset and slow progression of disease. Classical Cockayne syndrome patients show (1) growth failure, (2) neurodevelopmental and neurological dysfunction, (3) cutaneous photosensitivity, (4) progressive ocular abnormalities (pigmentary retinopathy, cataract), (5) hearing loss, (6) dental caries, (7) characteristic wizened facial appearance: bird-like facies. In order to diagnose Cockayne syndrome in an infant, the presence of the first two criteria and a few of the other five criteria are required. The last four features are usually seen in older patients.

Skin findings include photosensitive eruption with erythema and scale, hyperpigmentation, telangiectasia, and subcutaneous lipoatrophy that results in an aged progeric appearance.

There is no cancer proneness [4]. Brain may show several neuropathological abnormalities including hydrocephalus, tigroid-type demyelination, dystrophic calcification, and widespread neuronal loss and gliosis [5].

Our patient had intrauterine growth retardation, a little postnatal neurologic development, a severe clinical form of Cockayne syndrome.

Cockayne syndrome is characterized by a wide clinical variability ranging from prenatal features to normal psychomotor development. Cockayne syndrome has to be also differentiated from other conditions having similar clinical features (DiSanctis Cacchione syndrome, Xeroderma pigmentosa, Bloom syndrome, Rothmund syndrome, Progeria) Almost all Cockayne syndrome cases are due to mutations of the Cockayne syndrome A gene (Cockayne syndrome type A; MIM #216400) on chromosome 5q11on chromosome 5q11 or mutations of the Cockayne syndrome B gene (Cockayne syndrome type B; MIM #133540) on chromosome 10q11 [6].

The cellular diagnostic test for Cockayne syndrome is a failure of RNA synthesis to recover following UV-irradiation [7-9]. The magnitude of this defect appears to be rather uniform in Cockayne syndrome patients and does not correlate with the clinical severity of the disorder. The clinical feature which correlates most strongly with defective RNA synthesis is photosensitivity. This is manifested as a persistent erythema after sun exposure, accompanied in some instances by dermatitis. Photosensitivity was absent in only one case with defective RNA synthesis reported by Lehmann et al [7]. In our case, the diagnosis was suggested by clinical features and confirmed by the failure of RNA synthesis to recover following UV-irradiation. Despite the failure of RNA synthesis to recover after UV-irradiation, our patient does not have photosensitivity.

Treatment for Cockayne syndrome is generally supportive and includes photoprotection, physical therapy, and optimizing nutrition. Genetic counseling should be provided to the parents, as the recurrence risk for future pregnancies is 25%. Prenatal diagnosis should be considered in couples at high risk. It remains the only effective measure to take against this incurable disease [10].

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