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A Rare Case of Cockayne Syndrome

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Authors' contributions

This work was carried out in collaboration between all authors. Author Satish Sivan gave the case details. Authors UV and Soundarya Srinivasan wrote the first draft of the manuscript. Author MN contributed for the relevant images for the manuscript. Each author was involved in the collection of data (articles) for the review of literature, critically reviewing for the relevant points for the manuscript. Authors Soundarya Srinivasan and MN wrote the draft for submission. Author Soundarya Srinivasan wrote the revised manuscript based on reviewers comments. After discussion among all the authors the final manuscript was written. All authors have approved the final manuscript for submission.

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Case Study

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ABSTRACT

Background: Cockayne syndrome is a rare autosomal recessive congenital disorder characterized by growth failure, impaired development of the nervous system, abnormal sensitivity to sunlight (photosensitivity), and premature aging.
Case: In this report we present a 24 year old male with decreased height, weight & reduced head circumference measuring 124 cm, 20 kg and 20 cm respectively. Cachectic dwarfism, ataxic gait,

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mental retardation, sunken eyes, hypoplastic maxilla, and parrot beak shaped nose giving “bird like facies” were other key features observed in our patient. Oral examination revealed congenital missing teeth and multiple dental caries teeth are also seen. Magnetic resonance imaging and computed tomography findings were also contributory to our diagnosis.

Conclusion: This case report aims to rekindle and emphasis the diagnostic features of Cockayne syndrome & highlights the role of various investigations done by both medical & dental professionals to diagnose and manage the patient.

Keywords: Cockayne syndrome; bird like facies; cachetic dwarfism; mental retardation.

1. INTRODUCTION

Cockayne syndrome (CS) is one of the several Progeroid Syndromes (PSs) that has been reported and studied for the past several decades. PSs mimic clinical and molecular features of aging [1]. Based on the several studies reported the pathophysiology of progeroid syndrome can be attributed to the mutations in the genetic coding for DNA repair mechanism or genes involved in biological pathways. Several other human disorders occur due to defect in DNA repair mechanism [2,3].

CS is characterized by retarded growth, cachectic dwarfism, premature aging, mental deficiency, microcephaly, intracranial calcifications, neurologic deficits, retinal pigmentary abnormalities, sensori neural hearing loss, and photosensitivity. Oral manifestations like increased dental caries, missing or impacted permanent teeth are also reported. It manifests defective repair of damage induced in DNA by ultraviolet light [2,3].

As per the reports of David MW et al. [4] Cleaver et al. [5] and Jaarsma et al. [6] in the year 2013 suggested that the pathology of Cockayne syndrome can be attributed to the multiple mechanisms such as the DNA repair deficiency, transcription dysregulation, altered redox balance and mitochondrial dysfunction. Conceivably each of these mechanisms participates during a different stage in life of a Cockayne syndrome patient. Endogenous reactive oxygen is considered as an ultimate cause of DNA damage that contributes to Cockayne syndrome pathology. Mutations of two genes, the CKN1 or ERCC8 (Excision-Repair Cross- Complementing Group 8), and the ERCC6 (Excision-Repair Cross Complementing, Group 6), located on chromosomes 5 and 10q11 respectively can be the cause of CS [2,3,7,8].

As the pathology of Cockayne syndrome lies in the molecular level, the modern molecular diagnostics such as DNA repair assay, Complementation groups (research basis only), DNA sequence analysis, Deletion/duplication analysis, Carrier testing, Prenatal diagnosis & preimplantation genetic diagnosis plays an imperative role in the diagnosis of the same [3,7-10]. However the biochemical analysis cannot be ignored as it aids diagnosis. Hyperinsulinemia and hyperlipoproteinemia has been observed in most of the cases reported till date [2,11]. Growth hormone levels and functions of T lymphocytes and mixed lymphocytes are normal. However deficiency of growth hormones also been reported [11]. Whereas thymic hormone levels are significantly reduced or undeductable [2].

The management of Cockayne Syndrome in actual fact is merely supportive care. Treatment of Cockayne syndrome includes symptomatic management, prevention of secondary complications, avoidance of risk factors and periodic follow up. Despite the lack of effective treatment and progressive course of the disease, a correct diagnosis is very important to assist the family with the caretaking of the child and genetic counseling should be done to prevent recurrence of the condition in the family [10,12,].

Since 1936, when Cockayne described the first case of Cockayne syndrome, more than dozen cases have been reported in the world. Most of the cases showed the diagnostic features such as growth disturbances either before birth or after birth, ophthalmic involvement as cataracts or retinal pigmentation, severe neurologic dysfunction from birth, sensorineural hearing loss, cutaneous photosensitivity and dental caries. Over the past several decades some cases were reported and studied but the incidences of CS with oral manifestations are very rare [3,7-21].

2. PRESENTATION OF THE CASE

A male patient aged 24 years came to the dental hospital with chief complaint of pain in his decayed tooth with stunted growth of face. His

family history revealed that his mother had consanguineous marriage. He had low birth weight of about 2 kg and crawled lately at the age of 2 years and walked at the age of 4 years with stammering speech and aversion to light.

General examination revealed ataxic gait, cachectic dwarfism with height and weight measuring 124 cm, 20 kg respectively & head circumference measuring 20 cm. He was mentally retarded with abnormal speech & low pitched voice. Ophthalmological examination revealed photophobia with optic atrophy. Auditory examination revealed sensorineural hearing loss. Multiple cystic lesions were seen over the chest. (Fig. 1).

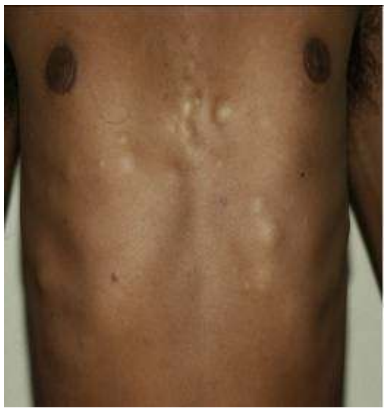

Fig. 1. Chest shows evidence of multiple cysts like lesions

Extraoral examination revealed microcephaly, loss of subcutaneous fat tissue in face, sunken eyes, hypoplastic maxilla, relatively small mandible, large ears, parrot beak shaped nose giving them classical “bird like facies” appearance (Fig. 2). Intra oral examination revealed multiple dental caries in relation to teeth number 4, 12, 24, 25, 33, 37 with congenitally missing teeth number 12, 22; bud shaped uvula (Fig. 3).

OPG showed multiple dental caries, multiple root stumps with increased caries activity, relative micro-dontia and slight increase in the density of mandible (Fig. 4). Lateral skull radiograph revealed micro-cephaly, small orbits with increase in the gonial angles and marked density of calvarium. Postero anterior skull views show obliterated paranasal sinuses. Plain X-ray of the chest showed decrease in the total length of spine and thoracic kyphosis (Fig. 5).

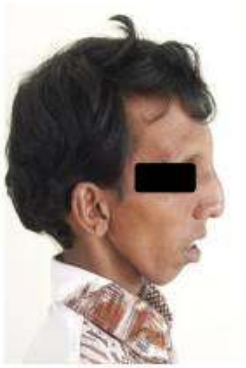

Fig. 2. Lateral profile of face

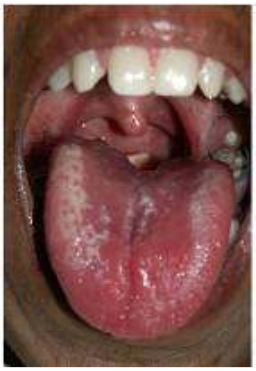

Fig. 3. Intra oral examination

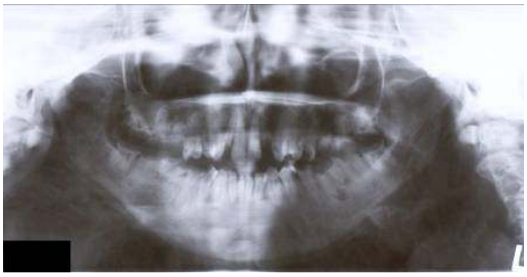

Fig. 4. OPG

Computed tomographic examination of head revealed obliterated paranasal sinuses, dilated ventricles, and calcification of falx cerebri (Fig. 6).

Magnetic resonance imaging revealed atrophy of cerebellum and basal ganglion calcification and electro retinogram examination revealed “salt and pepper” retinal hyperpigmentation. MR T2 weighed image showed progressive generalised cerebral and cerebellum atrophy with brainstem thinning (Fig. 7).

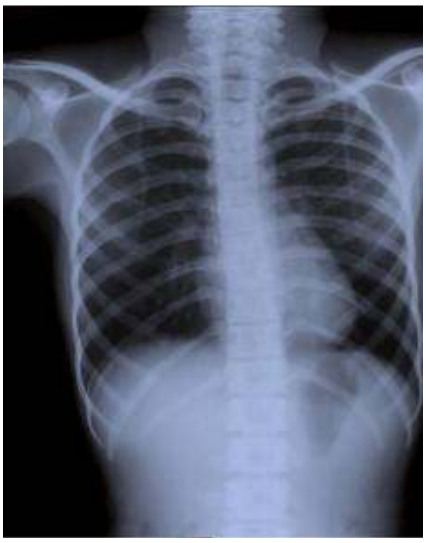

Fig. 5. Plain X-ray of the chest

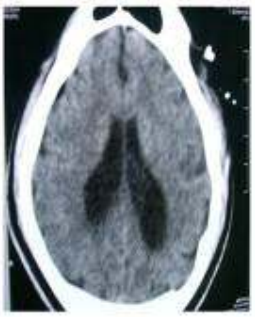

Fig. 6. Axial computed tomography of skull

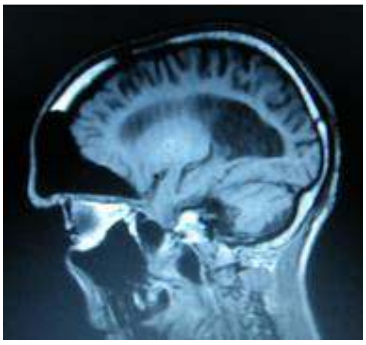

Fig. 7. Magenetic resonanace T2 weighed image

3. DISCUSSION

Similar to the cases reported by Guardiola A et al. [14] in 1999, Maria et al. [3] and Sonmez et al. [7], in 2006 patient presented in this case report also showed all the diagnostic features of the Cockayne syndrome. Our patient reported to the dental hospital for pain in decayed tooth. His cachectic dwarfism, ataxic gait and delayed psychomotor skill development during his growth after birth suggested a striking thought for the diagnosis of Cockayne syndrome. Ataxic gait was characteristic of the cases reported by Maria et al. [3] Firosh K et al. [8] and Raghavendra et al. [19] in 2006, 2008 and 2012 respectively. The growth percentile of patient presented in this case report was also compromised as it was evident from his height and weight. This was a characteristic feature of Cockayne syndrome patients reported till date.

As reported by Arun N et al. [20] in 2005 patient presented in this case report also showed characteristic facial appearances such as, loss of subcutaneous fat, sunken eyes, large ears, parrot beak shaped nose giving classical 'bird like facies'. Further intra oral examination revealing multiple dental caries was similar to Robert AB, [13] case reported in 1991. Photosensitivity was also a characteristic feature found in patient presented in this case report as suggested by most of the cases reported, and this is supported by Jabre P et al. [15] case reported in 1999. Jabre's case also showed retinopathy and mental retardation as reported in our case. Majority of the cases showed thoracic kyphosis stunted bone growth as reported by Sun-Kyu et al. [11] in 1994.

The MRI findings of patient presented in this case report was similar to Praveen M [21] case reported in 2012. Literature search also showed that salt and pepper retinal hyperpigmentation, basal ganglionic calcifications as found in patient presented in this case report was also characteristic of the cases reported by Hamdani et al. [16] in 2000 and Arun N et al. [20] in 2005. Similar findings were also reported by Simone MK et al. [13] in 2000, Olaciregui et al. [17] in 2001 and Kaissi et al. [18] in 2005. According to neuroimaging studies by Koob et al. [22] in 2010 computed tomography imaged brain calcifications, cerebral atrophy, and white matter hypoattenuation. Calvarial thickening was observed either with or without association with dilation of facial sinuses Magnetic Resonance imaging studies revealed infra- and supratentorial cerebral atrophy with predominantly white matter loss and abnormal white matter signal intensity [7,8,16,17,19,20]. The search for cases reported with multiple cyst like lesion seen over the chest as seen in patient presented in this case report ends in remote cases.

We considered the Bloom syndrome, Hartnup disease, Xeroderma pigmentosum, Rothmund-Thomson syndrome and Progeria for differential diagnosis [2]. Although dwarfism, photosensitivity and delayed development of psychomotor skills suggest Bloom syndrome and Xeroderma pigmentosum for the differential diagnosis, other characteristic features such as unusual facies, microcephaly, retinal pigmentation, basal ganglionic calcification all adds to the support of the diagnosis of Cockayne syndrome. And also absence of multiple cutaneous malignancies excludes the diagnosis of Xeroderma pigmentosum further [2,10]. Presence of retinal changes excludes Rothmund – Thomson syndrome and Progeria from the list. Further except for the short stature Progeria does not feature photosensitivity [2].

As suggested by Vincent Laugel patient presented in this case report can be diagnosed as classic Cockayne syndrome. Thus correlating the clinical findings of patient presented in this case report with the literature allowed us to arrive at the diagnosis of Cockayne syndrome [23].

4. CONCLUSION

Cockayne syndrome is an uncommon, distressing autosomal recessive disease akin to progeria. Craniofacial and oral anomalies and dental caries are universal finding in the syndrome. While life expectancy is pretty short for these individuals, the pediatric dentist plays a major role in managing the Cockayne syndrome patient. Early dental assessment and parental counseling have the paramount importance. Precautionary dental regimens must be independently planned and implemented because of reduced mandibular motion. Dietary counseling is very important because of a predisposition for dental caries and low weight. Regular examinations and prevention of the dental disease must be emphasized. Suitable and safe dental care for patients with CS can be rendered after medical consultation.

CONSENT

All authors declare that 'written informed consent was obtained from the patient for publication of this case report and accompanying images.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Claire LN, Pierre C, Nicolas L. Molecular bases of progeroid syndromes. Human Molecular Genetics. 2006;15(2):R151–61. PMID - 16987878
2. Robert JG, Michael C, Raoul CMH. Syndromes of head and neck. 4th ed. Newyork. Oxford University Press. 2001;596-600.
3. María LAS, Edgar HZ, Luis AMP, Beatriz CAB. Cockayne's syndrome: A case report. Literature review. Med Oral Patol Oral Cir Bucal. 2006;11:E236-8. PMID-16648759.
4. David MW, Vilhelm AB. Special issue on the segmental progeria cockayne syndrome. Mech Ageing Dev. 2013; 134(0):159–160. DOI: 10.1016/j.mad.2013.04.002
5. Cleaver JE, Bezrookove V, Revet I, Huang EJ. Conceptual developments in the causes of cockayne syndrome. Mech Ageing Dev. 2013;134(5-6):284-90. DOI: 10.1016/j.mad.2013.02.005. (Epub 2013 Feb 18)
6. Jaarsma D, van der Pluijm I, van der Horst GT, Hoeijmakers JH. Cockayne syndrome pathogenesis: Lessons from mouse models. Mech Ageing Dev. 2013;134(5-6):180-95. DOI: 10.1016/j.mad.2013.04.003 (Epub 2013 Apr 13)
7. Sonmez FM, Celep F, Ugur SA, Tolun A. Severe form of cockayne syndrome with varying clinical presentation and no photosensitivity in a family. J Child Neurol. 2006;21(4):333-7. PMID - 16900932
8. Khan F, Chemmanam T, Mathuranath PS. Cockayne syndrome. Ann Indian Acad Neurol. 2008;11(2):125–6. PMID – 19893654.
9. Hamel BCJ, Raams A, Schuitema- Dijkstra AR, Simons P, et al. Xeroderma pigmentosum-cockayne syndrome complex: A further case. J Med Genet. 1996;33:607-10. PMID – 8818951.
10. Anitha SM, Sundip S, Jayaram R, Reagan M and Vasanth K. Cockayne syndrome: A

rare case report. Int J Med Health Sci. 2014;3(1):92-94.
11. Park SK, Chang SH, Cho SB, Baek HS, Lee DY. Cockayne syndrome: A case with hyperinsulinemia and growth hormone deficiency. Journal of Korean Medical Science. 1994;9:74-7.
PMID – 8068222
12. Karam SM, Costa JC, Jardim L, Pires RF, Lehmann AR, Giugliani R. Cockayne syndrome: Report of a Brazilian family with confirmation of impaired RNA synthesis after UV-irradiation. Genetics and Molecular Biology. 2000;23(2):273-5
13. Boraz RA. Cockayne's syndrome: Literature review and case report. Pediatric Dentistry. 1991;L3:227-30.
PMID – 1832221.
14. Guardiola A, Alvares-da-Silva CR, Grisolia JR, Silbermann R. Cockayne syndrome. Case report. Arq Neuropsiquiatr. 1999;57(1):106-10. (Portuguese)
PMID – 10347735.
15. Jabre P, Mezzina M, Megarbane A. Cockayne syndrome in Lebanon. Description of 3 cases and review of the literature. J Med Liban. 1999;47(2):144-7. (French)
PMID – 10410472.
16. Hamdani M, El Kettani A, Rais L, Benhaddou M, Hda N, Rachid R, et al. Cockayne's syndrome with unusual retinal involvement (report of one family). J Fr Ophtalmol. 2000;23(1):52-6. (French)
PMID – 10660649
17. Olaciregui O, Yoldi ME, Gurtubay IG, García-Bragado F, Carrera B, Gila L, et al. Clinical and neuropathological study of two brothers with cockayne syndrome. Rev Neurol. 2001;33(7):628-31. (Spanish)
PMID – 11784950.
18. Kaissi AA, Safi H, Ghachem MB, Henaoui L, Chehida FB. Congenital dysplastic hips, spinal column abnormalities, fractures and progressive neurological manifestations in Tunisian family with cockayne syndrome. Annals of African Medicine. 2005;4(2):83-7.
19. Raghavendra MN, Anuradha P, Suresh KV, Yusuf AA, Mounesh KCD. Cockayne's syndrome: A case report. 2012;10(1):42-6.
20. Arun N, Shiv BB, Jamuna M. Cockayne syndrome. Nepal Journal of Neuroscience. 2005;2:140-1
21. Praveen M. A rare case of cockayne syndrome – MRI features. JCDR. 2012;6(9):1582-3.
22. Koob M, Laugel V, Durand M, Fothergill H, Dalloz C, Sauvanaud F, et al. Neuroimaging in cockayne syndrome. AJNR Am J Neuroradiol. 2010;31:1623–30.
DOI 10.3174/ajnr.A2135
23. Laugel V. Cockayne syndrome. 2000 Dec 28. In: Pagon RA, Adam MP, Ardinger HH, et al. editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2014.
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