African Journal of Urology (2018) **24**, 339–341

African Journal of Urology

Official journal of the Pan African Urological Surgeon's Association
web page of the journal

www.ees.elsevier.com/afju
www.sciencedirect.com

BPH and Prostate Diseases
Case report

Benign prostatic hyperplasia in a 23 year old man with progeroid syndrome

M. Ahmed [*], **A.T. Lawal**, **A. Bello**, **A. Abubakar** [1], **H.Y. Maitama**

Division of Urology, Department of Surgery, Ahmadu Bello University/Ahmadu Bello University Teaching Hospital, Zaria, Nigeria

Received 6 April 2018; received in revised form 21 May 2018; accepted 10 July 2018; Available online 13 October 2018

KEYWORDS
BPH;
Bladder outlet obstruction;
Progeroid syndrome;
Premature aging

Abstract
Introduction: Progeroid syndromes are characterized by accelerated aging and early development of diseases typically associated with aging. Premature development of tumors including BPH, maybe observed in these patients, which can lead to significant bladder outlet obstruction.
Observation: The index patient was a 23 year old man who presented to us with lower urinary tract symptoms (LUTS), features of obstructive nephropathy and was noticed to have been aging rapidly. He had features of premature aging, bilateral cataract and enlarged benign prostate (BPH). He eventually succumbed to obstructive nephropathy and urosepsis.
Conclusion: Progeroid syndromes may be associated with premature development of obstructive BPH.

Introduction

Premature aging diseases are well documented in the literature, however their exact aetiology remains to be fully unraveled. They have also stimulated interest in the search for the exact mechanism/s of normal aging process; consequently this has lead to better understanding of aging. To date more than 75 syndromes with features of premature aging are recognized and collectively referred to as **Progeroid Syndromes**, by analogy with progeria [1]. Progeria also called "Hutchinson Gilford Syndrome", is a clinical aging syndrome that was first described in 1886, it becomes evident in early childhood and progresses rapidly, ending in death at an early age (13–17) [2]. However, over the cause of time many early aging syndromes

* Corresponding author at: Division of Urology, Department of Surgery, Ahmadu Bello University/Ahmadu Bello University Teaching Hospital, Zaria, Kaduna State, Nigeria.
E-mail addresses: darm313@yahoo.com, ahmedmuhammed@abu.edu.ng (M. Ahmed).
[1] Bayero University/Aminu Kano Teaching Hospital, Kano, Kano State.
Peer review under responsibility of Pan African Urological Surgeons' Association.

https://doi.org/10.1016/j.afju.2018.07.004

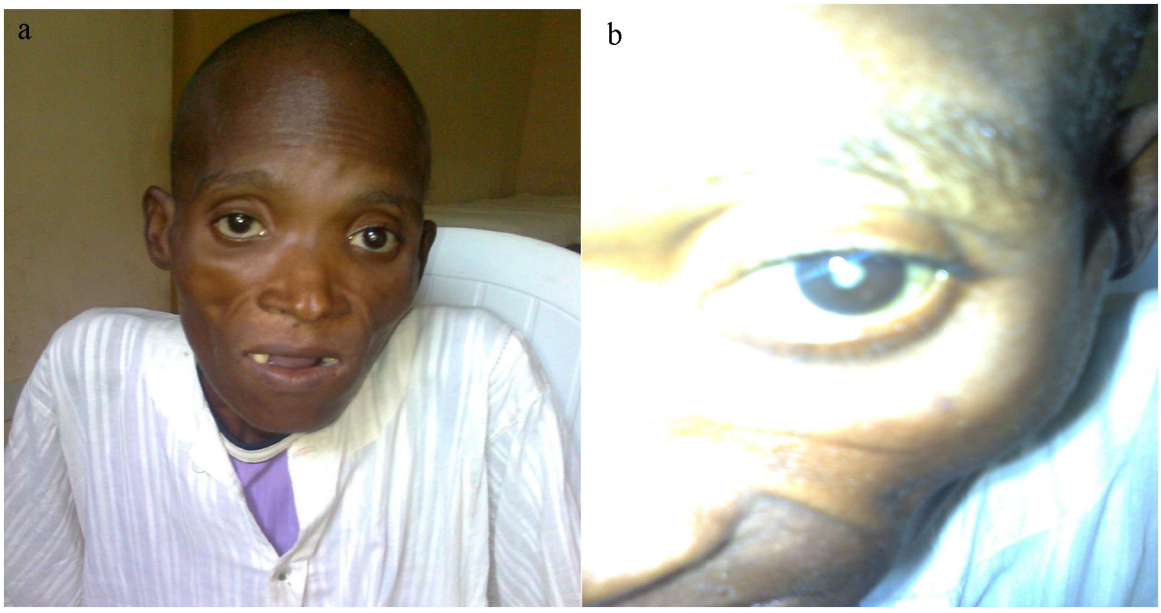

Figure 1 (a) A 23 year old man who looks elderly, with, greying, balding, wrinkled skin, teeth loss and bilateral cataract. (b) A closer image of cataract in one of the eyes.

were described with varied presentations and manifestations giving rise to the term "Progeroid syndromes". The premature aging syndromes described in literature to date include; Hutchinson Gilford syndrome, Werner syndrome, Ataxia telangiectasia, Xeroderma pigmentosum, Cockayne syndrome, Fanconi syndrome & Bloom and Rothmund Thomson syndrome [1].

There are disease conditions typically associated with normal aging, one of the common diseases is benign prostatic hyperplasia (BPH); it is characterized by stromal and epithelial proliferation of the transition zone of the prostate [3]. BPH is typically begins from middle age, it has not been demonstrated histologically in men younger than 30 years and most clinical BPH are seen beyond forty years [3]. BPH is thought to be initiated by senescent epithelial cells located in the prostate. These cells secrete the cytokines IL-1α and IL-8 that stimulate stromal growth factor secretion, which in turn correlates with proliferation of the non-senescent epithelial cells [4–6]. Progeroid syndromes are characterized by premature senescence, which affects many organs including the prostate [2,7], thus the potential development of BPH in patients with accelerated aging disorders.

Case summary

We reviewed the case records of a 23 year old man after obtaining written informed consent from the next of kin and ethical clearance from our hospital's health research ethics committee (HREC). He presented to our outpatient clinic from a peasant rural community with progressive obstructive and irritative lower urinary tract symptoms (LUTS) of over a year. He subsequently developed malaise, anorexia and bilateral lower limbs swelling. There was no history of trauma to the pelvis or perineum and no history of haematuria. He was noticed to be aging faster than usual, with progressively worsening vision and generalized asthenia.

Examination revealed an elderly looking man (Fig. 1(a)) with balding, and thin sparse hair with marked greying, he had wrinkled atrophic skin, bilateral cataract (Fig. 1(b)), multiple missing teeth and bilateral pitting pedal oedema. He had a painless distended bladder up to the umbilicus and the prostate was moderately enlarged with benign features.

A diagnosis of obstructive nephropathy secondary to BPH in a patient with progeroid syndrome was made. Ultrasound confirmed the enlarged prostate (42 g) with a postvoid residual urine of about 1000 ml. Serum urea, electrolyte and creatinine were markedly deranged. The patient was catheterized and maintained on continuous bladder drainage. However, on follow up visit, there was no significant improvement of renal function despite continuous bladder drainage, he subsequently developed urosepsis and progressively deteriorated until he ultimately succumbed a month after diagnosis.

Discussion

Progeroid syndromes have variable manifestations but they all have accelerated aging as a common denominator. Progeroid syndromes may either be Unimodal or Segmental; unimodal progeroid syndromes affects only a single organ unlike the segmental progeroid syndromes that manifest in several organs. The common characteristics of segmental progeroid syndromes is the concurrent onset of premature aging in several organs, which may involve the skin and the skeletal system with osteoporosis and degenerative diseases features, early onset arthritis, vascular diseases, diabetes mellitus, marked atrophy of subcutaneous fat. Other manifestations include; neurodegenerative diseases, increased incidence of various tumors, increased incidence of autoimmune diseases, impaired immune function and increased predisposition to infection [1,8]. The index patient had multiple organ involvement (skin, eyes, hair, dental and prostate); which manifested as accel-

erated aging, early balding and greying, atrophic degenerative skin (wrinkled skin), dental loss, bilateral cataract (Fig. 1(a)) and prostatic enlargement consistent with segmental progeroid syndromes.

In order to ensure uniformity of description of these syndromes with diverse manifestations, criteria for diagnosis were developed. The criteria are divided into clinical and genetic criteria [1,2]. The clinical criteria include; one or more tumours, which are typical in older age group (BPH in our patient), premature development of grey hair, hair loss, impaired memory; other criteria are; increased susceptibility to slow virus disease, pigment disorders or regional fibrosis in the skin, altered distribution of adipose tissues, hypogonadism, degenerative vascular disease/hypertension, osteoporosis, arthritis/other degenerative bone diseases and cataracts. The genetic criteria include; genomic instability and non-constitutional chromosomal aberrations, defects in stem cell population or in the proliferation of stem cells and mitochondrial changes in one or more tissues [1,9]. Our patient had most of these clinical criteria, however we could not establish the genetic component.

Cellular senescence (aging) is an established key factor in the pathogenesis of the manifestations of progeroid syndromes [7]. The role of telomeres in cellular senescence and apoptosis has been an area of extensive investigation. Research has demonstrated that irreversible growth arrest (cell senescence) is to a large extent a consequence of short telomeres, which activate DNA damage response pathways. Many progeroid syndromes in mice and humans were shown to originate from mutations that disrupt DNA repair and/or DNA damage responses, resulting in an increased incidence of tumours that usually occur at a decreased latency. Several evidences have been presented to confirm that premature and rapid cellular senescence is linked with increased rates of telomere shortening [8–10].

Benign prostatic hyperplasia is a disease associated with aging, it is a manifestation of progressive proliferation of the transition zone of the prostate [3,5,6]. It has been shown by several studies on aging process that, this proliferation is probably due to the presence of senescent epithelial cells in the prostate. The mechanistic process of cellular proliferation is believed to be induced by cytokines (IL-1α and IL-8) secreted by the senescent cells, which stimulate the production stromal growth factors and consequently induction of proliferation of non senescent epithelial cells [4,6,11,12]. The overall effect of the activation of the senescence pathways in the prostate is progressive enlargement of the transition zone (BPH), which manifested in the index patient. This patient progressed to develop bladder outlet obstruction and eventually obstructive nephropathy, which contributed in part to the deterioration in health of the patient and eventual death.

Conclusion

The hallmark of progeroid syndromes is accelerated aging and the early development of diseases typically associated with aging. Premature (23 years in the index patient) development of BPH maybe observed in these patients and can lead to significant bladder outlet obstruction and obstructive nephropathy. This report provides additional evidence for the pivotal role of senescence pathways in the pathogenesis of progeroid syndromes and BPH.

Conflict of interest

None.

Authors' contribution

Dr. Ahmed Muhammed: Case summary, literature review, manuscript writing, final article preparation and submission. Corresponding author.

Dr. Lawal Ahmad Tijjani: Case summary, Literature search and manuscript drafting.

Dr. Ahmad Bello: Case review, manuscript writing and critical review.

Dr. Abubakar Abdulkadir: Literature search, manuscript drafting and critical review.

Prof. Maitama Hussaini Yusuf: Contribution Final critical manuscript review and proof.

Source of funding

None.

Consent from the patients

Obtained.

References

[1] Homack S, Hill CR, Reynolds CR. Progeroid syndromes. In: Handbook of Neurodevelopmental and Genetic Disorders in Adult; 2005. p. 458–76.
[2] Kudlow BA, Kennedy BK, Monnat RJ. Werner and Hutchinson–Gilford progeria syndromes: mechanistic basis of human progeroid diseases. Nat Rev Mol Cell Biol 2007;8(5):394–404.
[3] Lepor H. Pathophysiology of benign prostatic hyperplasia in the aging male population. Rev Urol 2005;7(Suppl. 4):S3–12.
[4] Bavik C, Coleman I, Dean JP, Knudsen B, Plymate S, Nelson PS. The gene expression program of prostate fibroblast senescence modulates neoplastic epithelial cell proliferation through paracrine mechanisms. Cancer Res 2006;66(2):794–802.
[5] Lee KL, Peehl DM. Molecular and cellular pathogenesis of benign prostatic hyperplasia. J Urol 2004;172(5):1784–91.
[6] Castro P, Giri D, Lamb D, Ittmann M. Cellular senescence in the pathogenesis of benign prostatic hyperplasia. Prostate 2003;55(1):30–8.
[7] Jeyapalan JC, Sedivy JM. Cellular senescence and organismal aging. Mech Ageing Dev 2008;129(7–8):467–74.
[8] Ramírez CL, Cadiñanos J, Varela I, Freije JMP, López-Otín C. Human progeroid syndromes, aging and cancer: new genetic and epigenetic insights into old questions. Cell Mol Life Sci 2007;64(2):155–70.
[9] Kyng KJ, Bohr VA. Gene expression and DNA repair in progeroid syndromes and human aging. Ageing Res Rev 2005;4(4):579–602.
[10] Diderich K, Alanazi M, Hoeijmakers JH. Premature aging and cancer in nucleotide excision repair-disorders. DNA Repair (Amst) 2011;10(7):772–80.
[11] de Magalhães JP. How ageing processes influence cancer. Nat Rev Cancer 2013;13(5):357–65.
[12] Coutinho H, Falcão-Silva VS, Gonçalves G, da Nóbrega R. Molecular ageing in progeroid syndromes: Hutchinson-Gilford progeria syndrome as a model. Immun Ageing 2009;6(1):4.