Nigerian Journal of Clinical Practice
March 2007 Vol.10 (1): 91- 94

TWENTY-ONE-YEAR-OLD MALE WITH CONGENITAL ANOMALIES, OBSTRUCTIVE UROPATHY AND CHRONIC RENAL FAILURE: IS THIS A CASE OF TOWNES BROCKS SYNDROME?

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ABSTRACT

Townes Brocks syndrome is an autosomal dominant multiple malformations syndrome comprising of ear anomalies/hearing loss, limb defects, anal, genitourinary, eye, spine anomalies, heart defects and sometimes mental retardation.

This report presents the case of a 21-year-old secondary school leaver as a likely case of Townes-Brocks syndrome. He was born with congenital abnormalities consisting of fixed flexion deformities of hands, wrist and elbows, urethral meatal stenosis, scoliosis and aortic stenosis. He was diagnosed with obstructive uropathy at the age of 19 years and subsequently developed chronic renal failure.

The report aims to highlight the need for early recognition of potentially preventable conditions, which, if left unattended to, can lead to unnecessary fatality.

INTRODUCTION

Obstructive uropathy, a common cause of impaired renal function, is a potentially reversible condition when promptly diagnosed and appropriate treatment instituted. Congenital urinary tract abnormalities such as pelvi-ureteric dysfunction, vesico-ureteric reflux, urethral valves, phimosis and meatal stenosis are some causes of obstructive uropathy. They impede urine flow, cause urinary outflow obstruction and obstructive uropathy eventually.

Townes Brocks syndrome (TBS) is an autosomal dominant multiple malformation syndrome with variable expression[1]. Townes and Brocks first described the syndrome in 1972, characterized by external ear malformations with sensorineural hearing loss, limb anomalies and anorectal malformations[2]. Since this first report many more cases have been reported and the features of the syndrome have been widened to include more abnormalities.

The major clinical features of TBS now include ear abnormalities/hearing loss, limb defects, anal anomalies, genitourinary anomalies, growth and development problems, heart defects, as well as eye and spine abnormalities [1,3-10]. It has been suggested that the diagnostic criteria for TBS should include two or more of these major features[11]. The genitourinary anomalies that have been described in TBS include unilateral or bilateral hypoplastic/dysplastic kidneys, renal agenesis, multicystic kidney, uretero-pelvic stenosis, posterior urethral valves, vesico-ureteric reflux, meatal stenosis, bifid scrotum and hypospadias [3-5,12-15]. In several patients with TBS renal failure or impaired renal function has been reported [4,5,7].

TBS is a rare disease and, to our knowledge, there are no reports of the syndrome in Nigerian patients. This report is to draw attention to this disease which, although rare, can be a cause of CRF in our patients.

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Case Report

Mr. I. O, a 21-year-old man, was referred to the Renal Unit by the Urologist as a case of chronic renal failure (CRF) secondary to obstructive uropathy. He presented with complaints of leg and facial swelling, oliguria associated with exertional dyspnoea, paroxysmal nocturnal dyspnoea, orthopnea, cough productive of frothy sputum, easy fatiguability, nausea and vomiting. He claimed he had been in good health and coping with his daily activities until these symptoms set in. He was not a known diabetic or hypertensive and there was no history of use of mercury containing soaps or creams, non-steroidal anti-inflammatory drugs or herbal medications. He was delivered in 1983 as a breech presentation following an uneventful full-term pregnancy. At birth, he was noticed to have skeletal deformities with fixed flexion of elbows, wrists and fingers. For this he was managed by an Orthopaedic Surgeon with several applications of plaster of Paris for remodeling until the patient could manage to use the limbs. His mother denied use of native herbs or unprescribed drugs during pregnancy. She noticed from the patients' childhood that he had some

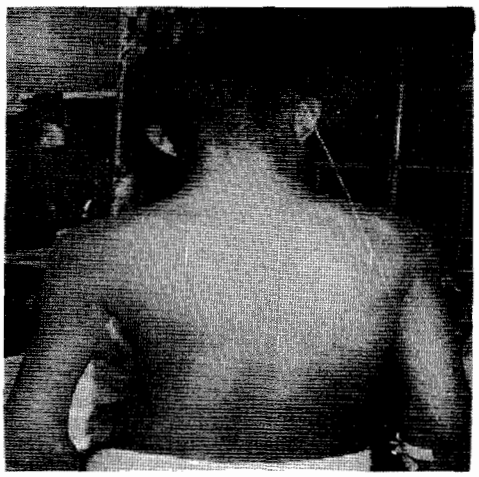
difficulty passing urine and had to strain slightly to void urine. This symptom was considered not severe enough to warrant a medical consultation. However, as he grew older urinary symptoms progressively worsened to include increasing dysuria, hesitancy, feeling of incomplete voiding of urine, poor stream on micturition, supra-pubic discomfort, urge incontinence, increased frequency of micturition and enuresis. He wore cloth pads to help him cope with urinary symptoms, particularly while in school and at night. In 2003, at the age of 19 years, he had a herniorhaphy for an inguinoscrotal hernia and as part of the surgical consultation he had a bouginage and insertion of an indwelling urethral catheter for the first time. The urinary symptoms abated but subsequently worsened to the extent that he developed urinary retention subsequently warranting a urological consultation. His urinary retention was relieved with a suprapubic cystostomy. A renal ultrasonography at this stage showed right kidney measuring 11.8cm x 5.1cm and left kidney 11.3 x 6.0cm, with pelvicalyceal dilatation, hydroureters and thickened bladder wall, all consistent with obstructive uropathy. Urethrocystoscopy revealed a tight meatal stenosis, normal prostatic urethra; no membrane/valve was seen. A meatotomy was done and an indwelling Foley's urethral catheter was introduced and the suprapubic catheter removed 2 days after. At this admission he had a serum urea of 135 mg/dl, creatinine of 5.6 mg/dl, calcium of 6.6 mg/dl, a haematocrit of 16% and evidence of urinary tract infection with klebsiella specie. He had blood transfusion, was given calcium supplements and cefuroxime. He improved and haematocrit appreciated to 31%. He was discharged home to continue management as an outpatient. However, after an initial outpatient clinic attendance where the urethral catheter was changed he was lost to follow-up. He was readmitted about two years later with index complaints and with an indwelling urethral catheter. There was paucity of information as regards medical care, particularly care of urethral catheter, for the previous two years.

He was one of 7 children and there is no similar illness amongst siblings or parents. He was however the shortest in his family. He attained milestones at the right times and coped well with his primary and secondary school education. He was an above average student and obtained six credits in the Senior Secondary Certificate Examination. He was awaiting the University Matriculation Examination results for University entry. He neither smoked cigarettes nor drank alcohol.

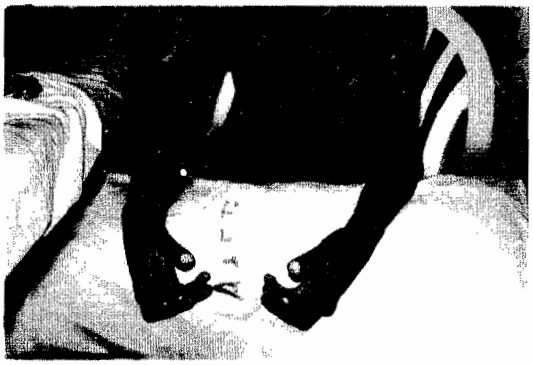
A clinical assessment at this index presentation revealed a chronically ill-looking intelligent young man with a urethral catheter in-situ. He was short for his age, with facial puffiness, pallor, mild dehydration, digital clubbing, sacral and bilateral pitting pedal oedema. The pulse rate was 90 beats/minute, blood pressure 170/120 mmHg, had a raised jugular venous pulsation, accentuated aortic component of the second heart sound and an ejection systolic murmur of aortic stenosis. There was ascites and a right inguinal scar. The right hemi-thorax was flattened and he had vertebral scoliosis to the right (Photogragh 1). He had fixed flexion deformity of the wrists and fingers, wasting of the thenar and hypothenar muscles and small muscles of the hands (Photograph 2). There was hypotonia of the upper limb muscles, difficulty in supination of the forearms and wrist, valgus deformity of the knees and pes planus. He had no external ear deformities and no hearing loss.

A urine examination revealed turbid urine with 3^{+} of proteinuria, haematuria and pyuria. He had a haematocrit of 22%, serum urea 205 mg/dl, creatinine 7.1mg/dl, potassium 5.5 mmol/L, calcium 4.4mg/dl, phosphate 6.3mg/dl. Hepatitis B surface antigen, antibodies to hepatitis C virus and human immunodeficiency viral screening were all negative. Renal ultrasonography revealed shrunken kidneys with right and left kidneys measuring 7.0cm × 3.0cm and 7.4 cm × 3.4cm respectively. He was managed as a case of CRF with 40gm protein and low salt diet, frusemide 160 mg bd, nifedipine ® 20 mg bd captopril 12.5mg calcium carbonate, subcutaneous erythropoeitin 4,000 units twice weekly, anti-emetics and haematinics. He also had cefuroxime 125mg bd for urinary tract infection. There was an initial improvement but he subsequently became increasingly breathless and developed retrosternal pain with a pericardial friction rub; these features were ascribed to uraemic pericarditis. He was commenced on haemodialysis but died after two sessions of dialysis.

1. Photograph 1 showing vertebral scoliosis



Photograph 2 showing flexion deformity of wrists and fingers



DISCUSSION

The differential diagnosis in this patient includes TBS, the VATER association, Baller Gerold syndrome, (BGS), oculoauriculovertebral spectrum (OAV) and the cat eye syndrome. All these syndromes have overlapping features but there are specific and important ones that differentiate them from TBS. For example, patients with the VATER association have tracheo-oesophageal fistula or vertebral anomalies, all BGS patients have craniosynotosis while vertebral anomalies are a prominent part of OAV. All these differentiating features are absent in TBS. Also the mode of inheritance and chromosomal studies help to differentiate them from TBS.

Presence of abnormalities such as limb defects, genitourinary abnormalities, spine abnormalities and heart defect are features in support of a likely diagnosis of TBS. He was born with fixed flexion deformities of the hands, wrist and elbows. The hand defects were still evident on presentation to us despite the orthopaedic management quite early in his life. The meatal stenosis, though diagnosed much later in patient's life, was present right from birth as urinary symptoms were noticed quite early in his life. The meatal stenosis left unattended to for many years ultimately led to renal impairment.

Scoliosis has been reported in three patients with TBS and all three had associated mental retardation [7, 10]. This patient had scoliosis but was not mentally retarded. From his academic achievements he had normal intelligence. This is not unusual, as normal intelligence has been reported in TBS patients[1]. The association between TBS and congenital heart defect is not fully proven. However, defects like tetralogy of Fallot, ventricular septal defect, truncus arteriosus and pulmonary atresia have been described in some sporadic cases of TBS [4,9,15]. Although, we were unable to do an echocardiograghy (for logistic reasons), there was clinical evidence of aortic stenosis.

TBS is an autosomal dominant disorder and the gene for the syndrome has been mapped to 16q12.1 [12]. Although the syndrome is familial, a few sporadic cases have been reported [16]. All the family members could not be assessed, but family history and clinical assessment of parents and one sibling did not reveal similar illness or abnormalities. This may be a sporadic case of TBS. The presence of aortic stenosis is in support of this, as cardiac abnormalities have only been described in sporadic cases of TBS. Chromosomal studies would have been useful in making a definitive diagnosis in this case, but the facilities for such studies were unavailable.

CRF in this patient could have been prevented if the congenital meatal stenosis was identified and corrected early in his life. Although the urinary symptoms were noticed even in the first year of life, his parents, rather than seek appropriate medical attention decided to use palliative measures of making the young boy wear cloth pads even up to secondary school age. It was only at the age of nineteen years that a urological consultation was sought for. Appropriate measures instituted early may have prevented uropathy and consequent renal failure.

This report underscores the need for early identification and management of congenital conditions that are potential sources of renal failure. Continuous medical education for medical personnel and enlightenment of parents will go a long way in attempts to reduce potentially preventable medical conditions.

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