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General Medicine

UNVEILING NAIL PATELLA SYNDROME: A MULTIFACETED GENETIC TALE OF CLINICAL CHALLENGES AND MANAGEMENT STRATEGIES TO PREVENT COMPLICATIONS

Dr Arvind Radhakrishnan MBBS (2020) MD General Medicine 2nd Year, Chettinad Medical College and Research Institute

Dr Asha Maria Xavier MD General Medicine , Assistant Professor, Chettinad Medical College and Research Institute

Dr J Vigneshwaran DNB General Medicine, Professor, Chettinad Medical College and Research Institute

ABSTRACT Nail Patella Syndrome (NPS), a rare autosomal dominant genetic disorder occurring in approximately 1 in 50,000 live births, underscores the importance of early identification and intervention in outpatient settings due to its potential systemic complications, including glaucoma and glomerulonephritis. A 35-year-old female presented to the GM OPD with complaints of fatigue. On examination, she exhibited several clinical findings suggestive of NPS: fixed flexion deformity of the elbow, nail pterygium, and absent distal interphalangeal (DIP) joint creases in both upper and lower limbs. Fundoscopy revealed cupping in the right eye without visual defects. Urine routine examination showed no proteinuria. Radiological investigations further supported the suspicion of NPS: X-ray of the elbows revealed bilateral radial subluxation, while X-ray of the knees showed hypoplastic and inferiorly displaced patellae bilaterally. Additional imaging included X-ray of the pelvis, revealing bilateral iliac horns, and X-ray of the thorax, indicating a hypoplastic right scapula and thoracic vertebral scoliosis. Tonometry revealed elevated intraocular pressure, with readings of 27mmHg in the right eye and 25mmHg in the left eye. These findings collectively suggest a diagnosis of NPS. The clinical spectrum of NPS includes nail pterygium, triangular lunula, nail dysplasia, loss of DIP crease, fixed flexion deformity in the elbow, hypoplastic and inferiorly dislocated patella, kyphosis, scoliosis, hypoplastic scapula, glaucoma, and glomerulonephritis. In this patient, the diagnostic tetrad for NPS was observed: fingernail dysplasia, absent or hypoplastic patella, posterior iliac horns, and subluxation of radial heads on X-ray, associated with the LMX1B gene on chromosome 9q33.3. Systemic complications arise from abnormal collagen IV regulation, leading to glaucoma and glomerulonephritis. Management included antiglaucoma medication and yearly urine examination and tonometry. Early detection of genetic disorders like NPS allows for comprehensive counseling and proactive management to mitigate long-term consequences such as vision loss and chronic kidney disease.

KEYWORDS : Nail Patella Syndrome, genetic disorder, glaucoma, glomerulonephritis

INTRODUCTION

Nail Patella Syndrome (NPS), a rare autosomal dominant genetic disorder occurring in approximately 1 in 50,000 live births, presents with a distinctive array of clinical features. This syndrome, also known as Hereditary Onychoosteodysplasia and Fong's disease, underscores the importance of early identification and intervention in outpatient settings due to its potential systemic complications, including glaucoma and glomerulonephritis. First described in the early 20th century, NPS is characterized by a range of musculoskeletal and nail abnormalities that can be detected through careful clinical and radiological examination.

Case Report

A 35-year-old female presented to the GM OPD with complaints of fatigue. On examination, she exhibited several clinical findings suggestive of Nail Patella Syndrome (NPS): fixed flexion deformity of the elbow, nail pterygium, and absent distal interphalangeal (DIP) joint creases in both upper and lower limbs. These findings are significant as they represent some of the hallmark signs of NPS, which can often be overlooked or misdiagnosed in primary care settings. Fundoscopy revealed cupping in the right eye without visual defects, an important observation given the potential for glaucoma in NPS patients. Urine routine examination showed no proteinuria, indicating that the patient's kidneys were not currently affected by the disease. Radiological investigations further supported the suspicion of NPS: X-ray of the elbows revealed bilateral radial subluxation, a common skeletal abnormality in NPS patients. X-ray of the knees showed hypoplastic and inferiorly displaced patellae bilaterally, another classic feature of the syndrome. Additional imaging included X-ray of the pelvis, revealing bilateral iliac horns, which are pathognomonic for NPS, and X-ray of the thorax, indicating a hypoplastic right scapula and thoracic vertebral scoliosis. Tonometry revealed elevated intraocular pressure, with readings of 27mmHg in the right eye and 25mmHg in the left eye, confirming the presence of ocular hypertension, a precursor to glaucoma. These findings collectively suggest a diagnosis of Nail Patella Syndrome.

DISCUSSION

The clinical spectrum of Nail Patella Syndrome encompasses a range of features, including nail pterygium (Fig 1), triangular lunula, nail dysplasia, loss of distal interphalangeal (DIP) crease (Fig 2), fixed flexion deformity (FFD) in the elbow due to subluxated radial head, hypoplastic and inferiorly dislocated patella (Fig 3), kyphosis, scoliosis, hypoplastic scapula, glaucoma, and glomerulonephritis (1). In our patient, the diagnostic tetrad for Nail Patella Syndrome was observed, which includes fingernail dysplasia, absent or hypoplastic patella, presence of posterior iliac horns (Fig 5), and subluxation of radial heads on X-ray. These features align with the genetic abnormality associated with the condition, specifically the LMX1B gene located on chromosome 9q33.3 (2,3,4). The LMX1B gene plays a critical role in limb and kidney development, and mutations in this gene disrupt normal development, leading to the characteristic features of NPS. The systemic complications of Nail Patella Syndrome arise from abnormal regulation of collagen IV expression, leading to impaired aqueous outflow and subsequent glaucoma, as well as decreased protein for actin cytoskeleton necessary for normal podocyte functioning, resulting in glomerulonephritis (5).

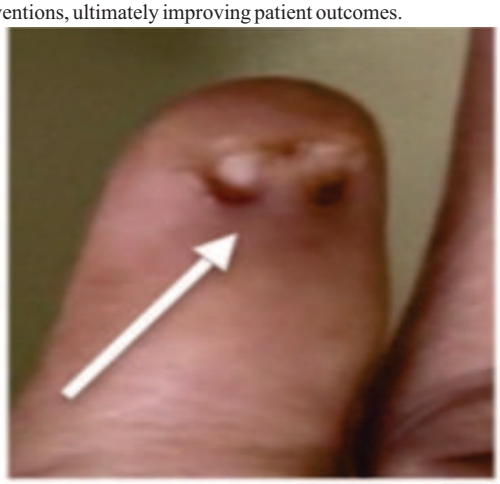
Management for the patient included initiation of antiglaucoma medication (6) and advising yearly urine routine examination and tonometry (7) to monitor for complications. Early intervention with antiglaucoma medications is crucial in preventing the progression of ocular hypertension to glaucoma, thereby preserving vision. Regular monitoring of kidney function through urine examination helps in the early detection of glomerulonephritis, allowing for timely intervention to prevent chronic kidney disease. Genetic counseling is also an important aspect of management, as NPS is inherited in an autosomal dominant pattern. Family members of the patient may benefit from genetic testing and counseling to understand their risk of developing NPS and its associated complications.

In addition to medical management, physical therapy can be beneficial for patients with musculoskeletal abnormalities. Exercises to improve joint mobility and muscle strength can help manage symptoms and improve the quality of life. Occupational therapy may also be recommended to assist patients in performing daily activities more effectively, considering the limitations imposed by the skeletal deformities.

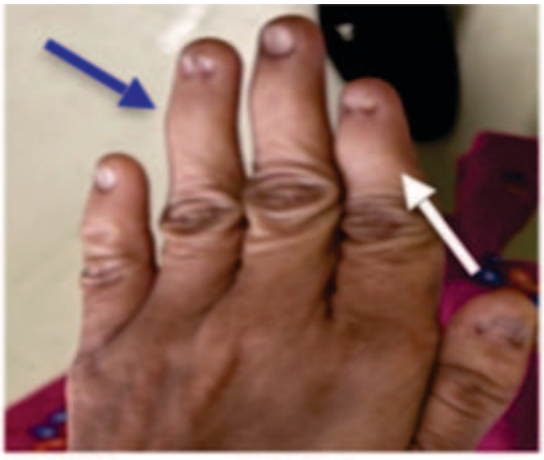
CONCLUSION

Glaucoma constitutes 10% of blindness cases (8), while Glomerulonephritis ranks as the third most prevalent cause of chronic

kidney disease. Early detection of genetic disorders such as Nail Patella Syndrome (NPS) enables healthcare providers to offer comprehensive counseling to patients regarding potential systemic complications (9). This proactive approach aims to mitigate long-term consequences such as vision loss and chronic kidney disease. By recognizing the characteristic signs and symptoms of NPS, healthcare professionals can initiate appropriate diagnostic and therapeutic interventions, ultimately improving patient outcomes.

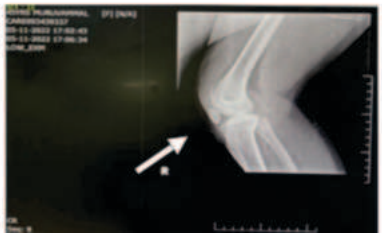


(1)Nail pterygium

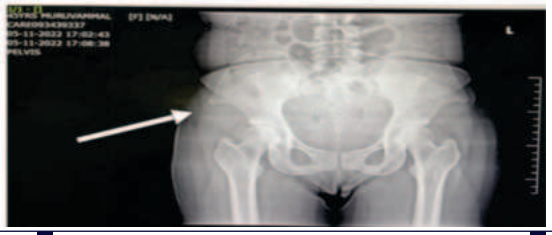


(2)Absent DIP crease

[3]Hypo-plastic patella right knee



5]Presence of iliac horns



Furthermore, advancements in genetic research and molecular diagnostics have the potential to enhance our understanding of NPS and its underlying mechanisms. As more is learned about the LMX1B gene and its role in NPS, targeted therapies may be developed to address the root causes of the condition, rather than merely managing its symptoms. Continued research and clinical observation will be essential in refining the management strategies for NPS and improving the quality of life for affected individuals.

In summary, Nail Patella Syndrome is a complex genetic disorder with significant implications for patients 'ocular, renal, and musculoskeletal health. Through early diagnosis, vigilant monitoring, and a multidisciplinary approach to management, healthcare providers can help mitigate the impact of this condition and support patients in leading healthier, more fulfilling lives.

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