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Diagnostic challenge of cutis Verticis Gyrata (CVG) in a patient presenting clinical features of Noonan or turner syndrome

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ABSTRACT

Cutis Verticis Gyrata (CVG) is an uncommon condition, often classified as primary (idiopathic) or secondary to other diseases or syndromes. Its pathogenesis remains poorly understood, and its association with genetic syndromes is particularly rare. Noonan and Turner syndromes are distinct genetic disorders with characteristic phenotypes and multiple systemic involvements. This report aims to highlight the diagnostic complexities when CVG presents in the backdrop of these syndromes. A 38 years old patient was presented with chief complaints of receding hairline, dropping eyelids, cerebral deformations with deep furrows and thickened dermis. On the basis of patient's complaints, Noonan or turner syndrome was considered as possible diagnosis. This particular report presents a case of patient suffering from CVG having history of noonan and turner syndrome. With the detailed MRI, histology etc. CVG was finally confirmed. The novelty of this case lies in its rarity, diagnostic complexity, and the need for a multidisciplinary approach to unravel and manage the intersecting conditions. It contributes valuable insights to the existing medical literature, enhancing our understanding of the interplay between dermatological and genetic conditions. Patients with Noonan and turner syndrome exhibit clinical signs and symptoms that are strikingly similar to those of CVG, suggesting that this presents a significant diagnostic problem. An unfavorable outcome could arise from delayed or incorrect diagnosis. Because of this, it is recommended that healthcare fraternities should include uncommon illnesses like CVG as differential diagnosis. Considering CVG in differential diagnosis is crucial for early identification, accurate diagnosis, and comprehensive management. It ensures that associated systemic and genetic conditions are not overlooked and that patients receive holistic and personalized care.

1. Background

Cutis Verticis Gyrata (CVG) is a rare benign cutaneous progressive condition that resembles cerebral sulci and gyri, with deep furrows and convoluted folds on the scalp. Typically, the vertex and occipital regions of the scalp are most commonly involved. Also it can lead to cosmetic concerns and psychological impact due to its noticeable appearance. Severity of this condition increases over time. This condition is common in young adults and teenagers [1]. This condition is further divided into three types that are primary essential, secondary and primary non-essential CVG. In the later stages of this disease, patient may complaint about painful folds, unusual odour due to deposition of skin's usual secretions. Roughly 12.5% of occurrences of CVG are related to cerebriform intradermal nevus (CIN), an uncommon cause of CVG. This condition is also known as bulldog scalp syndrome [2]. These furrow on the scalp maybe with symmetric or asymmetric that depends on individual patient. Primary essential CVG is often idiopathic in nature. However, secondary CVG can be associated with a variety of genetic syndromes including Turner syndrome and neurodevelopmental disorders also. Genetic testing for CVG can provide valuable insights, especially when CVG represents the common clinical features of other genetic syndromes. CVG mimics number of other conditions such as noonan and turner syndrome, pachydermoperiostosis, isolated scalp collagenoma, acromegaly [3]. These conditions are vague and may cause a false positive. In most cases, the diagnosis of CVG is established by ruling out other medical diseases such as Turner syndrome and

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noonan. Certain tests, like MRIs, skin biopsies, EEGs, and chromosomal analyses, can be used to make a confirmation diagnosis. The patient's health is at risk due to unclear signs and characteristics, incorrect diagnoses, and delayed diagnoses [4,5]. Noonan syndrome is a genetic disorder predominantly caused by mutations in the RAS-MAPK signaling pathway, which plays a crucial role in cell growth and development. Patients with Noonan syndrome typically present with short stature, webbed neck, distinctive facial features (such as hypertelorism, ptosis, and low-set ears), congenital heart defects, developmental delays, and varying degrees of learning disabilities. Based on patient's clinical features, genetic testing is indicated in the suspected patients for confirmation. Genetic testing mentions the various tests including single gene testing that majorly focuses on the mutated genes such as PTPN11, SOS1, and RAF1, panel testing confirms the multiple genes associated with Noonan syndrome, whole exome sequencing analyses the coding regions of genes to identify novel mutations or the mutations that are very rarely found. Majorly genes associated with noonan syndrome includes the PTPN11, RAF1, KRAS, RIT1, NRAS, MAP2K1, etc. The occurrence of CVG in Noonan syndrome is exceptionally rare. When present, CVG adds a complex dermatological feature to the syndrome's phenotype. This association requires heightened awareness and careful differential diagnosis to manage both the cutaneous and systemic aspects of the syndrome effectively [4,6]. Turner syndrome results from the complete or partial absence of one X chromosome (45, X karyotype), affecting females exclusively. Turner syndrome is characterized by short stature, lymphedema (especially noticeable at birth), a webbed neck, widely spaced nipples, and various congenital heart defects such as a bicuspid aortic valve and coarctation of the aorta. Additionally, patients may experience gonadal dysgenesis leading to primary amenorrhea and infertility. Although extremely uncommon, CVG can occur in patients with Turner syndrome. The presence of CVG in Turner syndrome introduces a unique diagnostic challenge due to its rarity and the overlapping clinical features with other conditions [7].

2. Case presentation

A 38 years old patient was presented with chief complaints of receding hairline, dropping eyelids, cerebral deformations with deep furrows and thickened dermis. Patient's vital signs were normal. Patient had medical history of noonan and turner syndrome which was diagnosed 6 months ago. Later after 6 months patient had a complaint of deep, painful folds on the scalp and forehead. On the basis of patient's complaints noonan or turner syndrome was considered as possible diagnosis but after some detailed diagnostic procedures such as histology, MRI, Skin biopsy patient was finally diagnosed with CVG. Detailed MRI showed development of deep furrows and histology reports showed oedema and hyperplasia showed in (Fig. 1 and Fig. 2) through which CVG was finally confirmed.

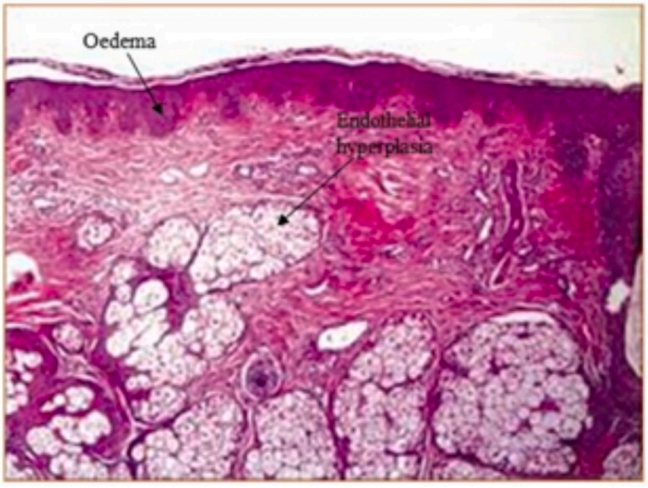

Fig. 1. Showing histology report of patient.

3. Discussion

Initially the Noonan and Turner syndrome were thought to be potential diagnoses because of the patient's complaints and history. Prior to the MRI and histology results, it was thought that the patient had Noonan and Turner syndrome because of the receding hairline, brain deformations with deep furrows, and thickened dermis [8,9]. However, the patient actually has CVG. Also it is seen that CVG is more common in men than women. It is still unclear what causes CVG pathogenesis. The creation of connective tissue septa between the epidermis and the galea is proposed as the structural cause of the folds [10]. The skin would otherwise sag into folds, but these septa stop that from happening. Since the predominant type of the disease typically affects boys in their postpubertal years, an endocrine origin has been proposed. Following the procedure, the primary CVG histology reveals normal skin [11]. Additionally, thicker connective tissue associated with adnexal structural hypertrophy or hyperplasia has been reported. Variable histology in secondary CVG indicates the underlying ailment. CVG patients may receive symptomatic or surgical therapy but it is not proven to be effective till now. Instruction on maintaining proper local hygiene is required to prevent the buildup of secretions that smell bad. The purpose of surgical treatment may be to improve the clinical aspect because an unsightly feature may lower quality of life. Surgical options include partial removal of an abundant region of the lesion, insertion of a tissue expander in healthy skin and subsequent grafting, and total resection of the lesion and grafting. It is stated that the recurrence cannot be stopped by any treatment [12,13]. For the Confirmation of CVG there was presence of pronounced folds and deep furrows on the scalp, particularly in the vertex and occipital regions, with thickened and firm skin texture

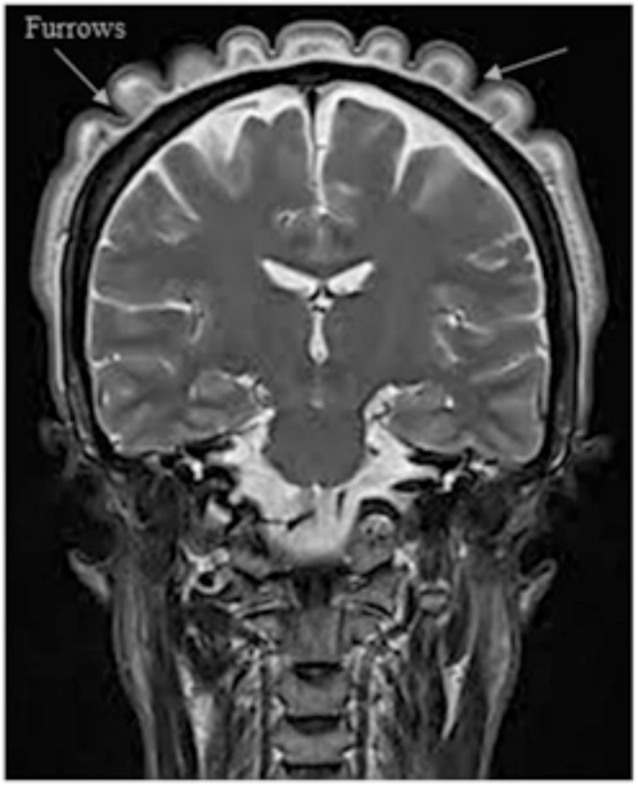

Fig. 2. Showing MRI report of the patient with development of deep cutaneous furrows.

[14]. In this case exclusion of Noonan Syndrome was done through Genetic testing that revealed no pathogenic mutations in genes associated with Noonan syndrome (e.g., PTPN11, SOS1, RAF1, KRAS), ruling out Noonan syndrome as the underlying cause. Also exclusion of Turner Syndrome was done through Karyotype analysis showed a normal female chromosome complement (46, XX), excluding Turner syndrome.

4. Conclusion

This report presents a case of patient with Noonan and turner syndrome exhibit clinical signs and symptoms that are strikingly similar to those of CVG, suggesting that this presents a significant diagnostic problem. Based on the clinical presentation, absence of genetic mutations associated with Noonan syndrome, and a normal female karyotype ruling out Turner syndrome, the diagnosis of CVG is confirmed in this patient. Noonan and Turner syndromes have been effectively excluded as underlying causes of the observed scalp abnormalities. This comprehensive assessment ensures accurate diagnosis and guides appropriate management strategies for the patient's condition. The diagnosis of CVG in patients with Noonan and turner syndrome remains difficult since all of these clinical disorders present with nonspecific symptoms in this particular case. An unfavorable outcome could arise from delayed or incorrect diagnosis. Because of this, it is recommended that healthcare fraternities should include uncommon illnesses like CVG as differential diagnosis to avoid long term treatments, patient's unnecessary exposure with different treatment procedures.

Author contributions

M.K. prepared the manuscript; R.K. and C.P. analysed and interpret the data; P.K. did final review and editing; R.S. designed and supervised the study; V.S. formally analysed the study; S.F.A. provided funding support. All authors reviewed the manuscript.

Ethical approval

This case report has been reported in line with the SCARE criteria.

Consent

Written informed consent was obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Declaration of competing interest

The authors declare that they have no financial conflict of interest with regard to the content of this report.

Data availability

No data was used for the research described in the article.

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