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CASE REPORT

Polythelia Associated with Hypogonadotropic Hypogonadism in Young Male: A Rare Abnormality

Khaled M Hadhoud[1], Abdelmonem Awad Hegazy[2,3*], Mustafa Abdelmonem Hegazy[4]

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Abstract

Polythelia is a congenital anomaly in which there is a third or more nipples. Although it is a relatively rare condition, it is frequently associated with other congenital malformations including the cardiovascular, urogenital, and skeletal systems. It may occur sporadically or with a familial tendency with some genetic factors. We report an association of polythelia with congenital hypogonadotropic hypogonadism (CHH) in a young male. The patient was complaining of delayed puberty. He was short in stature and had hypogonadism. On physical examination, a third nipple was found below the normally located nipple along the left mammary line. The case was carefully evaluated to exclude other disorders. It has been suggested that every newborn can be checked for the presence of accessory nipples which could indicate another internal problem in its body.

Key Words: *Accessory nipple; Congenital anomalies; Hypogonadism; Delayed puberty*

Introduction

Polythelia is a condition of supernumerary nipples in which there are one or more nipples in addition to the two normal nipples. The accessory nipple occurs along the mammary line which is an ectoderm thickening that appears one on each side of the ventral side of the fetus in the early stages of intrauterine life [1]. The onset of the mammary line occurs around the gestational age of 4 to 6 weeks when mammary-specific progenitor cells can be observed. Then, discrete areas of epithelial thickening appear by the 7th week that extend in a ridge called mammary or milk line extending from the fetal axilla to the inguinal region. Most of the line disappears except for the part corresponding to the fourth intercostal space that forms the primary buds or cords [2]. The remaining part of mammary line form 15-20 solid buds that proliferate forming the nipple and breast. They canalize forming the ducts and acini. The ducts

[1]Internal Medicine Department, Faculty of Medicine, Zagazig University, Zagazig City 44519, Egypt

[2]Medical Biotechnology Department, College of Biotechnology, Misr University for Science and Technology, 6th October City 12566, Egypt

[3]Anatomy and Embryology Department, Faculty of Medicine, Zagazig University, Zagazig City 44519, Egypt

[4]Cardiology Department, Faculty of Medicine, Zagazig University, Zagazig City 44519, Egypt

**Corresponding author: Abdelmonem Awad Hegazy, Faculty of Medicine, Anatomy and Embryology Department, Zagazig University, Zagazig City 44519, Egypt, Tel: +201110504321; E-mail: dr.abdelmonemhegazy@yahoo.com*

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open separately in a surface depression formed by cavitation of the original thickened part. Thereafter, the depressed pit becomes everted by proliferation of the underlying mesenchyme to form nipple (Figure 1). At puberty, the breast enlarges in females under the influence of estrogen but remains rudimentary in males [1].

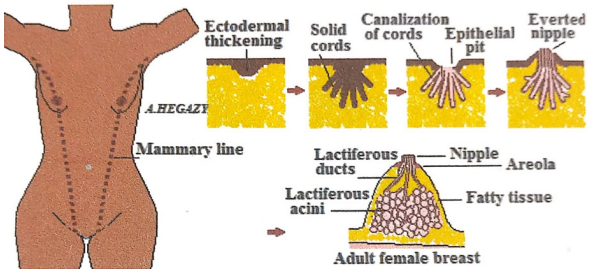

Figure 1) *Development of mammary lines and female breasts [1].*

The incidence of polythelia is very rare, representing less than 1% of the American population and affecting approximately 200,000 Americans; and is more common in males than females. While the third nipple is the most common case in such abnormalities, the polythelia may be up to 8 nipples [3]. Other authors stated that the prevalence of polythelia in females is greater than in males at 5.19% to 1.68%, respectively [4].

On the other hand, supernumerary breasts are called polymastia. Both polythelia and polymastia develop as congenital anomalies due to failure of apoptotic process that cause regression of the mammary ridges during fetal life. The most common location for accessory nipple is just under the breast while the accessory breast mostly occurs in the axilla [5]. Other authors have hypothesized that nipple dichotomy in fetal life might occur and cause an accessory nipple located in close proximity to another normally located nipple [6]. In this article, we report a case of accessory nipple in male.

Case Report

The index case was an 18-year-old male with uneventful medical past history. There was no family history of a similar case. His complaint was delayed puberty. He was short in stature, with a body length of 158cm. On clinical investigation, polythelia was observed. There was a small nipple surrounded by areola along the left mammary line located at a lower level from the navel (Figure 2). The patient did not complain of any pain. Furthermore, he did not encounter any tenderness upon palpation. Hypogonadism and testicular retraction were observed on pelvic examination. Clinical investigation and ultrasound examinations showed the health of the heart, lungs, and digestive and genitourinary systems without any complaints from the patient. Electrocardiogram (ECG) was performed to detect any heart problems not manifested in other investigations. ECG was of normal pattern without showing cardiac abnormalities.

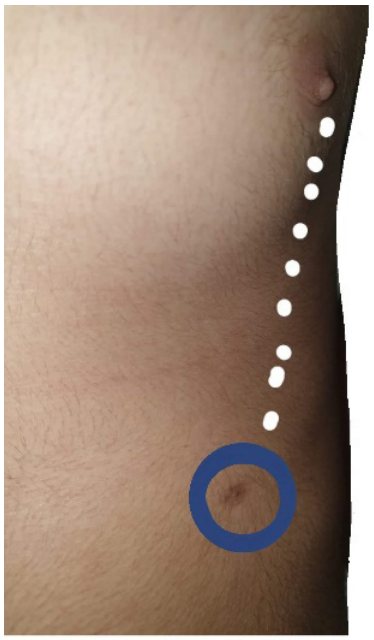

Figure 2) *Photograph showing a small accessory nipple surrounded by pigmented areola (marked by blue circle) found along the left mammary line (dotted white line).*

Laboratory investigation of the case showed luteinizing hormone (LH) of 1.4 IU/L (normal reference level "N": 1.42-15), follicle stimulating hormone (FSH) of 0.3 IH/L (N: 0.3-10 IH/L) and total testosterone 250 ng/dL (N: 270-1070 ng/dL). Growth hormone (GH) level was 0.3 ng/mL (N: 0.4-10 ng/mL). Post-stimulus

levels were after 60, 90 and 120 minutes were 1,4 and 5 ng/mL, respectively. Stimulation test was performed using oral catapres (clonidine) "0.10 mg/m2"to stimulate GH secretion from pituitary gland [7]. Furthermore, X-ray hand showed delayed bone age.

The case was diagnosed as CHH. Treatment was replacement therapy using testosterone (cidoteston) replacement to help growth of bones and genital organs for at least one year. Later on, LH and FSH replacement was advised after marriage to improve fertility through intramuscular injection of merional (75 IU) 3 times weekly.

Discussion

Polythelia or supernumerary nipples are a case of rare congenital anomalies. Presence of an inborn anomaly is an indication for thorough investigation of all parts of body for detection of others not manifested [1]. Therefore, we investigated all organs and systems of body. No other congenital anomalies are detected except presence of hypopituitarism associated with hypogonadism and delayed puberty.

The accessory nipple was noticed by the patient and thought it was a birth nevus, so it was not mentioned in his complaint. It is frequently passing asymptomatic; but it is sometimes be associated with urogenital malformations [8-10]. Although the urinary malformations seen in the general population range from 1 to 2%, the incidence associated with congenital polythelia increases to 14.5% [11]. The case of polythelia has been reported to be associated with other congenital anomalies including familial agenesis of some teeth [12]. Some authors suggested association between congenital cutaneous and cardiovascular disorders [13,14]. Although the reason for this association is unclear, it has been suggested that routine screening for cardiovascular disorders is necessary in the presence of supernumerary nipples [14]. Other authors reported congenital defects of vertebrae associated with polythelia [15]. Polythelia might follow various forms of genetic disorders [12,16,17]. The genetic factor appears to be dominant but with incomplete penetrance [16]. This genetic factor is autosomal, although a dominant X-linked chromosome could also be present. The latter is especially evident in Simpson-Golabi-Behmel syndrome [18]. In this syndrome, supernumerary nipples are associated with macrosomia, intellectual disability, and chrematistic cranial features. Other authors described a hereditary syndrome affecting the first pharyngeal arch and the mammary ridge noticed in four generations of one family [19]. They reported preauricular appendages and epibulbar lipodermoids in addition to polythelia. However, other authors stated that the majority of the polythelia cases are sporadic in origin [20]. This matches our findings in our case which showed no family history.

The accessory nipple may be found along the mammary line as in our patient. However, it could be located as ectopic lesion beyond such line overlying scapula [21].

Surgical excision of the accessory nipples is mostly performed for cosmetic purposes. Some authors added its removal could be conducted to avoid its potential malignancy [10]. Previous reports indicated association of supernumerary nipples with various benign and malignant changes especially in kidneys [6,22]. Therefore, it is advisable to be managed conservatively unless changes in color or size occur and if they do not affect the patient's body. Otherwise, surgical interference is indicated if there are aesthetic and/or psychological disorders [23].

Our case associated with hormonal disturbances represented by delayed puberty and growth is

a rare condition. To our knowledge, no similar reported case of congenital polythelia associated with CHH has been previously published. CHH is a rare congenital disorder. It could be associated with other manifestations including loss of smell, a condition called Kallmann syndrome [24]. Reawakening of the hypothalamic-pituitary-gonadal (HPG) axis occurs after a relative childhood quiescence in order to initiate puberty [25]. This axis is active in mid-gestation but is quiescent toward term [26]. This restriction is removed after birth, resulting in reactivation of the axis and increased levels of gonadotropin. CHH results from failure of normal episodic gonadotropin-releasing hormone (GnRH) secretion from GnRH neurons in hypothalamus. This negatively affects the release of FSH and LH from adenohypophysis and thus leads to delayed puberty and infertility [24]. To promote the growth of the body and reproductive organs, we gave the patient a testosterone replacement therapy. This can be widely offered in order to enhance sexual function as well as manifestations of masculinity [27].

Conclusion

Polythelia is an uncommon anomaly frequently associated with other anomalies. In our case, it is associated with CHH. On a routine clinical investigation of newborns, it may be suggested to look for presence of accessory nipples because of the potential for association with other malformations. Furthermore, future studies are recommended to elucidate the existence of any potential mechanisms by which polythelia may result from or be associated with CHH.

Conflicts of interest: The authors have no conflicts of interest.

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References

1. Hegazy A. Clinical embryology for medical students and postgraduate doctors. Lap Lambert Academic Publishing; 2014.

2. Javed A, Lteif A. Development of the human breast. Semin Plast Surg. 2013;27:5-12.

3. https://www.healthline.com/health/third-nipple.

4. Johnson CA, Felson B, Jolles H. Polythelia (supernumerary nipple): an update. South Med J. 1986;79:1106-8.

5. Miranda EP. Chapter130-Congenital Defects of the Skin and Hands. Pediatric Surgery (7thedn). Elsevier Inc. 2012; pp.1711-24.

6. Lewis EJ, Crutchfield CE, Ebertz MJ, et al. Report of a nipple nevus and an overview of accessory mammary tissue. Cutis. 1998;62:243-6.

7. Borges M, Teixeira FC, Feltrin AK, et al. Clonidine-stimulated growth hormone concentrations (cut-off values) measured by immunochemiluminescent assay (ICMA) in children and adolescents with short stature. Clinics (Sao Paulo). 2016;71:226-31.

8. Cellini A, Offidani A. Familial supernumerary nipples and breasts. Dermatology. 1992;185:56-8.

9. Ferrara P, Giorgio V, Vitelli O, et al. Polythelia: still a marker of urinary tract anomalies in children? Scand J Urol Nephrol. 2009;43:47-50.

10. Köse R, Ozgoönül A, Bingöl I. Intraareolar polythelia: a rare anomaly. J Pak Med Assoc. 2012;62:499-500.

11. Brown J, Schwartz RA. Supernumerary nipples: an overview. Cutis. 2003;71:344-6.

12. Fonseca GM, Cantin M. Familial polythelia associated with dental anomalies: a case report. Colomb Med (Cali). 2014;45:45-7.

13. Abdelmalek NF, Gerber TL, Menter A. Cardiocutaneous syndromes and associations. J Am Acad Dermatol. 2002;46:161-83.

14. Urbani CE. Supernumerary nipple and cardiocutaneous associations. J Am Acad Dermatol. 2004;50:e9

15. Akin L, Akin MA, Sarici D, et al. The association of polythelia with segmentation defects of the vertebrae. Clin Dysmorphol. 2012;21:181-2.

16. Schmidt H. Supernumerary nipples: prevalence, size, sex and side predilection - a prospective clinical study. Eur J Pediatr. 1998;157:821-3.

17. McLaughlin MR, O'Connor NR, Ham P. Newborn skin: Part II. Birthmarks. Am Fam Physician. 2008;77: 56-60.

18. Sajorda BJ, Gonzalez-Gandolfi CX, Hathaway ER, et al. Simpson-Golabi-Behmel Syndrome Type 1. 2006.

19. Goldschmidt E, Jacobsen N. Epibulbar lipodermoids, preauricular appendages and polythelia in four generations: a new hereditary syndrome? Ophthalmic Genet. 2010;31:81-3.

20. Mansel RE, Webster DJ. Hughes, Mansel & Webster's benign disorders and diseases of the breast. (3rdedn), Elsevier Ltd., 2009.

21. Mohammed AA. Accessory nipple over the right scapula of a 14-year-old boy: An extremely rare and unreported location, case report. Int J Surg Case Rep. 2019;55:35-6.

22. Urbani CE, Betti R. Aberrant mammary tissue and nephrourinary malignancy. Cancer Genet Cytogenet. 1996;87:88-9.

23. Somma F, Calzoni C, Arleo S, et al. Polythelia and supernumerary breast. Personal experience and review of the literature. Ann Ital Chir. 2012;83:109-12.

24. Young J, Xu C, Papadakis GE, et al. Clinical management of congenital hypogonadotropic hypogonadism. Endocr Rev. 2019;40:669-710.

25. Plant TM. Neuroendocrine control of the onset of puberty. Front Neuroendocrinol. 2015;38:73-88.

26. Kuiri-Hänninen T, Sankilampi U, Dunkel L. Activation of the hypothalamic-pituitary-gonadal axis in infancy: minipuberty. Horm Res Paediatr. 2014;82:73-80.

27. Millar AC, Faghfoury H, Bieniek JM. Genetics of hypogonadotropic hypogonadism. Transl Androl Urol. 2021;10:1401-9.