CASE REPORT

Breast reconstruction in a patient with Noonan syndrome

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SUMMARY

Noonan syndrome (NS) is a relatively common genetic disorder with an autosomal dominant inheritance pattern affecting 1 in 1000–2500 births. Patients with this syndrome present with characteristic facial, musculoskeletal, cardiac and endocrine abnormalities. Lack of postpubertal breast development is a common manifestation of this syndrome and may result in severe hypomastia and a masculine appearance of the female chest. We report the first case of breast reconstruction in a 24-year-old woman with NS who lacked postpubertal breast development. Technical considerations for addressing the existing chest wall deformity, implant pocket selection as well as emphasis on the role of the plastic surgeon are presented.

BACKGROUND

Noonan syndrome (NS) is a relatively common multisystem disorder with variable clinical and genetic characteristics. Up to eight genes have been implicated in the aetiology of this autosomal dominant genetic disorder.¹ Patients with NS present with typical facial features in early childhood such as a large cranial to facial size, tall forehead, narrow bitemporal width, telecanthus or hypertelorism and down-slanting palpebral fissures. Additionally, patients typically have micrognathia and neck webbing.^{1,2} Common cardiac anomalies in NS include pulmonary valve stenosis, atrial septal defects and hypertrophic cardiomyopathy. Associated musculoskeletal deformities include superior pectus carinatum, inferior pectus excavatum, wide-spaced and low-set nipples and rounded shoulders. Patients with NS display variable growth delay consistent with the syndrome's genetic heterogeneity. Short stature is common and growth hormone deficiency is present in up to 45% of patients with NS.^{1,3} Thyroid dysfunction and the presence of thyroid antibodies have been reported.

Puberty is delayed in boys and girls an average of 1–2 years and the pubertal growth spurt is diminished.¹ Oestrogen or testosterone induction of secondary sexual characteristics may be necessary. Subsequently, delay in breast development is a common manifestation in postpubertal female patients. We report the first case of addressing lack of breast development in a 24-year-old woman with NS.

CASE PRESENTATION

A 24-year-old woman with an established diagnosis of NS since childhood presented to the plastic surgery

clinic complaining of lack of postpubertal breast development and severe hypomastia. As a neonate, she underwent repair of patent ductus arteriosus at 12 days of age. This was followed by balloon valvotomy for pulmonary valve stenosis and subsequent pulmonary valvectomy with pericardial patch reconstruction of the pulmonary artery at 3 months of age. She underwent routine follow-up with her cardiologist and had no significant cardiac dysfunction. The patient reported absence of postpubertal breast development, but normal menstrual cycles, however. On presentation, she reported low self-esteem secondary to her masculine chest appearance. On examination, she had the typical general and facial dysmorphic features of NS, including short stature (height 152 cm), webbed neck and Tanner stage I breast development. There was no palpable parenchymal breast tissue bilaterally and the nipples were widely set. Her sternotomy scar was well healed. A midline sternal step off with prominence of the left hemithorax was evident (figure 1). She expressed a desire for a modest enhancement of her breast size. Given her chest wall asymmetry and previous cardiac surgery (figure 2), a subfascial implant pocket was planned rather than a submuscular pocket. Through a 4 cm incision along the inframammary fold, subfascial dissection was performed bilaterally to create a well-defined tight implant pocket. Meticulous haemostasis was achieved with electrocautery and surgical access was facilitated with lighted breast retractors. A 240 mL sizer was inserted in each pocket.

Volume fill adjustments were required to achieve breast symmetry due to a more prominent left chest wall. The pockets were irrigated with double antibiotic solution (vancomycin and gentamicin) and a 240 cc smooth round gel implant with moderate projection (Natrelle, Inspira, SRM, Allergan, Irvine, California, USA) was used on the less prominent right chest and a 175 cc implant was placed on the more prominent left side. The patient had an uneventful postoperative course and achieved the desired breast size augmentation. Furthermore, her chest wall asymmetry was better concealed following the breast reconstruction (figure 3).

OUTCOME AND FOLLOW-UP

The patient was seen for follow-up 6 months following breast reconstruction after an uneventful recovery. The breasts were soft and symmetric. The chest wall asymmetry was improved. She was pleased with her reconstruction (figure 3).

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Figure 1 (A) Preoperative lateral view showing lack of breast development. (B) Anterior view showing Tanner stage I breast development, wide-set nipples, ill-defined inframammary folds and neck webbing. (C) Left lateral view.

DISCUSSION

NS is an autosomal dominant disorder affecting 1 in every 1000–2500 live births globally.⁴ Affected individuals present with growth delay, short stature, delayed puberty, cardiac anomalies and multiple dysmorphic facial features. NS is considered one of RASopathies, a group of related syndromes caused by changes that eventually disrupt the Ras/Mitogen-Activated-Protein Kinase (Ras/MAPK) signalling pathway.^{1,4} Different genetic abnormalities have been shown to lead to a wide range of presentations of NS. Half of reported cases include mutations in the protein tyrosine phosphatase, non-receptor type 11 gene (PTPN11, HGNC:9644), which encodes a protein critical in the development of the heart, blood cells, bone and other tissues. Other mutations in son of sevenless homolog 1 (SOS1), rapidly accelerated fibrosarcoma 11 (RAF11), and RIT1 genes also cause this syndrome.^{1,4} Despite the genetic variability, patients with NS share similar features to other disorders such as LEOPARD syndrome (Lentignos, Electrocardiographic conduction defects, Ocular hypertelorism, Pulmonary stenosis, Abnormalities of the genitalia, Retarded growth, and Deafness), cardiofaciocutaneous syndrome, neurofibromatosis type 1 and Turner syndrome. Due to the genetic heterogeneity of this syndrome, however, clinical diagnosis as well as genetic testing are often required.

Multidisciplinary care of patients with NS is recommended, which, depending on the syndrome's manifestations, may include paediatrics, cardiology, endocrinology, genetics, nephrology, haematology and neurology specialists. Our patient had many typical features of NS including short stature (height: 152cm), hypertelorism, neck webbing, and cardiac anomalies requiring early life interventions. In addition, she had hypothyroidism and lacked postpubertal breast development. The latter, combined with anterior chest wall deformity exacerbated her

Figure 2 Intraoperative view showing the chest wall asymmetry. Note the prominence of the left medial sternal border.

Figure 3 (A) Postoperative superior view 6 months following breast reconstruction. (B) Anterior view showing improved chest asymmetry and breast appearance. (C) Lateral view.

concerns regarding chest appearance and low self-esteem. To our knowledge at the time of preparing this manuscript, this is the first report addressing breast reconstruction in NS. The existent anterior chest wall asymmetry with prominence of the left hemithorax required asymmetric breast augmentation (65 cc difference in final implant volume). A subfascial pocket was chosen instead of a submuscular pocket or dual-plane dissection in order to improve breast aesthetics given existing chest wall asymmetry, as the left pectoralis major muscle sternocostal insertion was more prominent than the right side. In addition, the relatively small volume breast enhancement desired by the patient made a subfascial implant position more feasible without a noticeable implant boundary. Lastly, given the patient's cardiac surgical history, the pectoralis major muscles were not dissected and preserved as possible future flapoptions should she require reopening the sternotomy scar. A subfascial pocket offers the advantage of reduced muscle dissection, less postoperative pain, avoids the animation deformity associated with submuscular placement and overcomes the limitations of pectoralis muscle asymmetry. With regard to risk of capsular contracture and subglandular pocket selection, we agree with Lista *et al* regarding the lack of current evidence on such association.⁵

A full haematological workup was not necessary in this patient as she had no bleeding history, but may be necessary for patients with NS and suspected bleeding diatheses.¹ While the reconstruction of other congenital breast deformities such as in Poland syndrome are usually covered by health insurance companies, we encountered initial difficulty in having this procedure covered by our patient's health insurance company. Communicating the patient's congenital diagnosis, lack of postpubertal breast development and physical examination findings of the breast to the insurance company was necessary to obtain coverage.

In conclusion, patients with NS often present with growth delay and lack of normal pubertal growth and secondary sexual characteristics. Lack of breast development and existing chest wall deformities in female patients are common and may require

Learning points

- ▶ Female patients affected with Noonan syndrome (NS) may lack postpubertal breast development, which results in severe hypomastia in adulthood.
- ▶ Chest wall deformities are common in patients with NS and should be considered in preoperative planning of pocket location and implant type.
- ▶ Achieving symmetric breast reconstruction outcome in patients with NS may be challenging due to existing chest wall abnormalities.
- ▶ Careful surgical planning and proper implant selection will help improve outcomes in breast reconstruction of patients with NS.

special considerations to achieve symmetric breast appearance. Plastic surgeons may be involved in the management of various breast deformities in patients with NS and should advocate for insurance coverage of the correction of this congenital deformity.

While the correction of other congenital breast deformities such as in Poland syndrome is usually covered by health insurance companies, we hope that further reporting of NS congenital breast deformities and successful reconstruction will help add novel and valuable knowledge to the surgical literature. Proper planning, considerations of the chest wall deformity and implant size selection are necessary to achieve a satisfactory outcome.

Contributors MDS performed the literature review, S-GR prepared the case report and BS critically edited the manuscript.

Competing interests None declared.

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