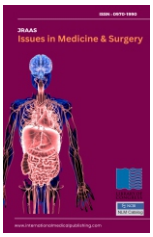
JRAAS
Special Issue in Medicine & Surgery
www.internationalmedicalpublishing.com



Research Article

Section: Surgery

Giant Fibroadenoma with TP53 Pro/Pro Variant in a 19-Year-Old: Case Report & Implications for Early Risk Stratification

Chinmay Gaidhankar[1*], Anjani Jalaj[1], Himanshu Chandel[1] & Ankita Mishra[1]

[1]Department of General Surgery, Gajra Raja Medical College, Gwalior, Madhya Pradesh, India

HIGHLIGHTS

- Giant fibroadenoma with TP53
- Rare benign genetic association
- Codon 72 Pro genotype
- Low penetrance cancer risk
- Early biomarker potential

Key Words:
Giant fibroadenoma
TP53 polymorphism
Arg72Pro
Benign breast lesion
Cancer risk
p53

ABSTRACT

Introduction: Fibroadenomas are common benign breast tumors, particularly in young women, while giant fibroadenomas, defined as those exceeding 5 cm, are rare. TP53 mutations are generally associated with malignancies and are seldom observed in benign breast lesions. The Arg72Pro polymorphism of TP53 is a low-penetrance variant that may modulate cancer susceptibility. **Aim & Objectives:** This report presents a rare case of a giant fibroadenoma harboring a TP53 codon 72 Pro/Pro polymorphism and explores its potential relevance in early cancer risk stratification. **Material & Methods:** A 19-year-old female presented with a palpable breast lump. Surgical excision was performed, and histopathology confirmed a giant fibroadenoma. Immunohistochemistry for p53 protein was carried out to assess protein expression. Genomic DNA from peripheral blood was analyzed for TP53 mutations, focusing on codon 72 polymorphism. A literature review was conducted to contextualize TP53 variants in benign breast disease. **Results:** The excised tumor measured 7.5 cm and displayed benign histology without atypia or malignancy. p53 immunohistochemistry was negative, indicating no protein accumulation. Genetic analysis revealed a homozygous Pro/Pro genotype at codon 72, with no pathogenic high-penetrance TP53 mutations detected. Previous studies suggest that this variant may modestly increase cancer susceptibility in specific populations. **Conclusion:** This case demonstrates a rare coexistence of a TP53 Pro/Pro polymorphism in a benign giant fibroadenoma. While the lesion itself was benign, the presence of a low-penetrance TP53 variant may provide insight into subtle cancer predisposition. These findings underscore the potential role of such polymorphisms as early biomarkers for risk assessment and highlight the need for further research into their prognostic and preventive implications.

*** Corresponding Author:** Chinmay Gaidhankar, e-mail: drchinmaygaidhankar37@gmail.com
Article History: Received 26 February 2026; Received in Revised form 01 April 2026; Accepted 08 April 2026
How To Cite: Chinmay Gaidhankar, Anjani Jalaj, Himanshu Chandel & Ankita Mishra. Giant Fibroadenoma with TP53 Pro/Pro Variant in a 19-Year-Old: Case Report & Implications for Early Risk Stratification. *JRAAS : Special Issue in Medicine & Surgery.* 2026;41(1):1-10. DOI: https://doi.org/10.71393/95gxfr51
This publication is licensed under CC-BY 4.0. Copyright © 2026 The Authors. Published by International Medical Publishing Group.

INTRODUCTION

Fibroadenomas are the most common benign breast tumors in adolescent and young adult females [1]. They are typically well-circumscribed, hormonally responsive lesions that do not confer a significant long-term cancer risk [2]. Giant fibroadenomas defined as those exceeding 5 cm in diameter, weighing over 500 g, or replacing at least 80% of breast volume are uncommon, accounting for only about 0.5–2% of all fibroadenomas [3]. These giant variants often present in teenage patients and can grow rapidly, raising clinical concern for phyllodes tumors or malignancy. Nevertheless, giant fibroadenomas remain histolo-gically benign, and malignant transformation or coexistence of carcinoma is exceedingly rare (<0.2%) [4]. The TP53 tumor suppressor gene (encoding p53 protein) plays a pivotal role in cell cycle control, DNA repair, and apoptosis [5]. TP53 is one of the most frequently mutated genes in human cancers, including breast carcinoma [6]. In contrast, TP53 mutations are virtually never observed in typical benign breast lesions. For instance, studies of benign breast disease (BBD) lesions have shown no p53 mutations (exons 5–9) in fibroadenomas, aside from rare germline polymorphisms [7]. Similarly, other benign breast changes like fibrocystic disease rarely show TP53 mutations, whereas malignant phyllodes tumors and breast carcinomas often do [8]. This contrast underscores that p53 pathway alterations are generally associated with malignancy & are highly unusual in benign conditions.

We describe a case of a 19-year-old woman with a giant fibroadenoma in which genetic testing revealed a homozygous TP53 Pro/Pro variant (codon 72 polymorphism) [9]. The codon 72 Arg>Pro single nucleotide polymorphism (SNP) in TP53 results in a proline variant of p53 with distinct biochemical activity. The p53^{72}Pro allele is considered a less potent tumor suppressor; the arginine variant induces apoptosis and cell-cycle arrest more effectively, making the proline variant functionally weaker [10]. Epidemiological studies and meta-analyses have linked the Pro allele with a modestly increased risk of several cancers, including breast cancer [11]. The co-occurrence of a TP53 variant with a benign tumor in this young patient provides a unique opportunity to explore the role of genetic profiling in benign breast disease as an early indicator of cancer susceptibility. It also highlights the implications of identifying low-penetrance cancer susceptibility alleles for preventive oncology strategies. Patients with such findings may benefit from enhanced surveillance and prophylactic measures, including selective estrogen receptor modulators (SERMs) and lifestyle modifications. This case suggests a paradigm where benign diagnoses, when combined with specific genetic markers, may guide early risk stratification and preventive interventions [12]. A giant fibroadenoma prompts genetic testing, leading to identification of the TP53 codon 72 Pro/Pro polymorphism. This low-penetrance variant enables risk stratification and guides subsequent management through enhanced surveillance and preventive strategies, including chemoprevention and lifestyle modification (**Figure 1**).

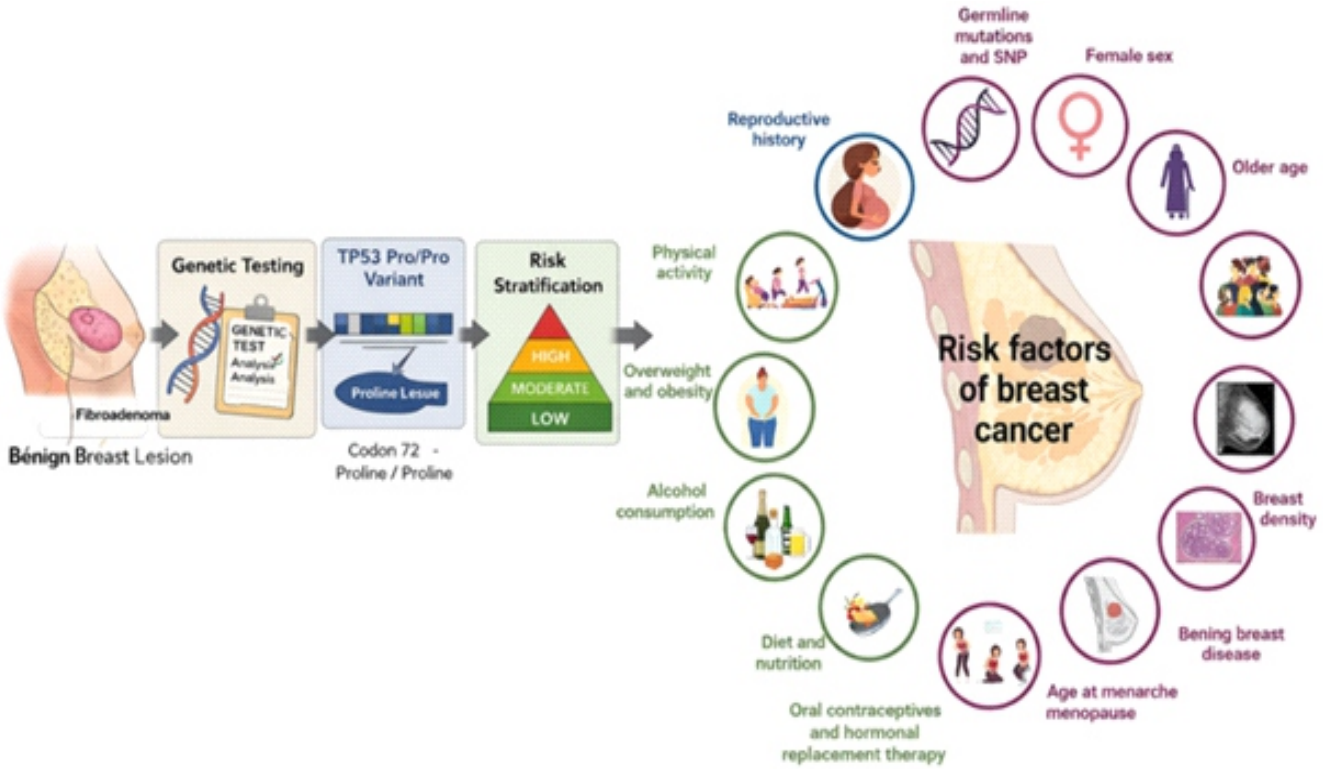


Figure 1: Proposed model illustrating the relationship between benign breast disease and genetic risk assessment. Adopted from [24].

Case Presentation

Patient Profile: A 19-year-old female with no significant medical history presented with a rapidly enlarging mass in her right breast. She first noticed a small lump 8 months prior, which grew markedly during the last 3 months. There was no known family history of breast or ovarian cancer, and no personal history of chest radiation or other predisposing factors. She was otherwise healthy, nulliparous, and had regular menstrual cycles.

Clinical Examination: On examination, the right breast was markedly enlarged and asymmetric. A palpable, non-tender, firm mass occupied almost the entire upper outer quadrant and extended to the central breast. The mass was well-defined but caused stretching of the overlying skin. No skin ulceration, nipple retraction, or peau d'orange was observed. There were dilated veins over the stretched skin due to the mass effect. Axillary lymph nodes were not enlarged on palpation. The contralateral breast was normal.

Imaging Studies: Breast ultrasound revealed a large, oval, heterogeneous but predominantly solid lesion measuring approximately 7.5 × 6 cm. It had well-circumscribed lobulated margins and was wider-than-tall on the sonographic view, features suggestive of a benign fibroadenoma. There was internal vascularity on Doppler consistent with a highly cellular fibroadenoma. No suspicious axillary lymph nodes were seen. Given the patient's age and ultrasound findings, a mammogram was deferred to avoid unnecessary radiation (especially in context of potential TP53 mutation carrier status, where radiation can be risky). MRI was considered, but surgical excision was deemed both diagnostic and therapeutic due to the tumor's size.

Biopsy & Surgical Management: A core needle biopsy was performed initially, which showed benign fibroepithelial lesion consistent with a fibroadenoma (no malignancy on cores). The patient subsequently underwent a lumpectomy /excisional biopsy to remove the mass for definitive diagnosis and to alleviate symptoms. An encapsulated tumor weighing 580 grams and measuring 7.5 cm in its largest diameter was excised; grossly it was lobulated with a whorled cut surface, typical of fibroadenoma.

Pathology: Histological examination confirmed a juvenile (cellular) fibroadenoma, characterized by an overgrowth of both glandular and stromal elements without atypia. The stroma was moderately cellular but lacked leaf-like fronds or mitotic activity that would suggest a phyllodes tumor. Ductal epithelial components were benign, with no hyperplasia, atypia, or carcinoma in situ identified. Margins were clear. Special staining and immunohistochemistry for p53 protein showed no abnormal accumulation of p53 in the lesional cells, consistent with the expected wild-type TP53 status in a benign tumor (mutant p53 proteins, when present, often accumulate to detectable levels due to prolonged half-life). These pathology findings confirmed that the mass was a benign giant fibroadenoma with no malignant features.

Genetic Findings: Given the patient's young age and the unusual presentation of a very large tumor, genetic counseling was provided and germline genetic testing was offered. After informed consent, a peripheral blood sample was taken for DNA analysis. Targeted sequencing of the TP53 gene was performed (covering all coding exons and splice sites). No pathogenic TP53 mutations (such as those classically seen in Li-Fraumeni syndrome) were found. However, the patient's genotype at the TP53 codon 72 polymorphism was Pro/Pro (homozygous proline). This result was notable as this SNP (rs1042522) leads to a proline variant of p53 protein. The finding of a TP53 Pro/Pro genotype in a 19-year-old with a giant fibroadenoma - in the absence of a high-penetrance TP53 mutation - suggests a possible low-penetrance genetic predisposition. Other genes commonly associated with hereditary breast tumors (BRCA1, BRCA2, etc.) were also screened via a multigene panel; no pathogenic variants were detected in those genes.

The patient recovered well post-surgery. At three-month follow-up, the surgical site was healing and there was no evidence of recurrence. She was counseled on the significance of the genetic finding and enrolled in a high-risk breast clinic for close observation. The case was discussed in a multidisciplinary tumor board and surgical oncology conference, given its unique features and implications for prevention.

Methods & Methods

Clinical Data Collection: Detailed clinical information was gathered from patient interviews, physical examinations, and medical records. This included demographic data, family cancer history, risk factors, and the timeline of tumor development. The patient provided consent for her case to be reported (with identifying details anonymized) due to its educational value.

Imaging and Diagnostic Workup: Standard breast imaging protocols were utilized (ultrasound as first-line in this young patient, with consideration of MRI). Radiologic findings were correlated with pathology after excision.

Pathologic Analysis: The excised tumor was fixed in formalin and embedded in paraffin. Multiple histological sections were stained with Hematoxylin and Eosin (H&E) and examined by breast pathologists. Key assessments included tumor subtype (fibroadenoma vs. phyllodes), cellularity, presence of mitoses, atypia, or malignant transformation. Given the interest in TP53 status, immunohistochemistry (IHC) for p53 was performed on representative sections using a monoclonal anti-p53 antibody. The proportion of tumor cell nuclei showing p53 immunoreactivity was recorded. In benign lesions without Tp53 mutati-

on, one expects either completely negative or only scattered weak nuclear staining (reflecting normal p53 dynamics), whereas a strong diffuse nuclear positivity would suggest a TP53 missense mutation leading to protein stabilization.

Genetic Testing: Genomic DNA was extracted from the patient's blood leukocytes using standard phenol-chloroform or column-based methods. We performed targeted sequencing of TP53 exons 2–11 (which cover the DNA-binding domain and common mutation hotspots) using PCR amplification followed by Sanger sequencing. Attention was given to identifying any single nucleotide variants corresponding to known pathogenic mutations. In addition, the polymorphism at codon 72 (exon 4, CGC→CCC, Arg→Pro) was specifically analyzed, as this was of research interest. The genotype was ascertained by sequencing electropherograms and confirmed by restriction fragment analysis (using BstUI enzyme which differentially cuts the codon 72 alleles, a method commonly used in research of this SNP). To provide a broader genetic context, we also employed a next-generation sequencing hereditary cancer gene panel (covering ~30 genes including BRCA1/2, TP53, PTEN, etc.) to ensure no other actionable variants were present.

Literature Review: A comprehensive review of medical literature was conducted to contextualize the case findings. This involved searching PubMed, Google Scholar, and conference proceedings for keywords such as "fibroadenoma TP53 mutation," "benign breast p53 polymorphism," "Arg72Pro breast cancer risk," and "chemoprevention tamoxifen high-risk benign." Priority was given to studies examining p53 in benign breast disease, the functional differences of p53 codon 72 variants, epidemiologic data on cancer risk associated with TP53 low-penetrance alleles, and clinical guidelines on prophylactic measures (SERMs, lifestyle) for high-risk individuals. Notable publications were used to support the discussion, and all sources are cited in References.

Data Analysis: Given that this is a single-case report, data analysis was descriptive. The pathological and genetic findings in this patient were compared against established data (for example, how frequently fibroadenomas show p53 alterations, and how this particular TP53 polymorphism might influence cancer risk). We interpreted the significance of the Pro/Pro genotype using published risk estimates and biochemical studies. No statistical comparisons were applicable beyond referencing those in the literature.

This methodology ensures that the case is examined from clinical, pathological, and genetic perspectives, and that interpretations are anchored in the current scientific understanding. By combining a case report with a focused literature analysis, we aimed to draw meaningful insights about early detection and prevention in the context of benign breast disease with underlying genetic susceptibility.

RESULTS

Clinical and Pathologic Findings: The patient's tumor was confirmed to be a benign giant fibroadenoma, consistent with her age and clinical presentation. Grossly and microscopically, it showed the characteristic features of a fibroadenoma (lobulated architecture, fibrous stroma, and ductal elements without malignancy). The absence of any in situ or invasive carcinoma within the lesion was an important finding, affirming that this young patient's large tumor was purely benign. The p53 IHC was entirely negative in tumor cell nuclei, indicating no abnormal accumulation of p53 protein. This aligns with expectation, as typical fibroadenomas do not harbor TP53 mutations that lead to protein stabilization. In contrast, in the malignant counterpart (breast cancers), one-third to one-half of cases show strong p53 staining due to mutations; our patient's negative p53 stain corroborated the benign nature of the lesion.

Genetic Results: Sequencing of TP53 revealed no pathogenic mutations in exons 5–8 (the hotspots frequently mutated in cancers), nor in exons 4, 9, 10, or 11. Instead, the notable finding was the single nucleotide polymorphism at codon 72, where this patient's DNA encodes proline on both alleles (Pro/Pro genotype). This variant (rs1042522) is not a mutation acquired in the tumor; it is a germline genetic variant present in all cells (confirmed by its presence in normal tissue and blood DNA). The significance of this result is twofold:

1. ***Rarity in Benign Context:*** It is exceptionally unusual to identify any TP53-related alteration in a purely benign breast lesion. While this codon 72 Pro/Pro is technically a polymorphism present in a portion of the general population, its occurrence in our patient's context draws interest because fibroadenomas almost uniformly lack TP53 changes. Prior studies have occasionally reported TP53 point mutations in benign breast lesions, but those were often silent (not altering the amino acid) or were very infrequent. Our patient's fibroadenoma did not have a somatic mutation, but the discovery of a germline variant with known functional impact is a novel aspect. It suggests that even in a benign lesion, underlying genetic makeup (in this case, a less active form of p53 protein) could be a contributing factor to tumor development or an indicator of future risk.
2. ***Potential Risk Implication*****:** The TP53 Arg72Pro polymorphism has been extensively studied for its effect on cancer biology. The Pro/Pro genotype has been associated with a modest increase in cancer risk and differences in tumor behavior. Our literature review found that individuals carrying the Pro allele (either Pro/Pro or Arg/Pro) can have higher susceptibility to breast cancer in certain ethnic groups. In functional assays, the proline variant of p53 is less efficient at triggering apoptosis and cell cycle arrest compared to the arginine variant.

Specifically, Pruckner et al. (2012) demonstrated that the p53^72Arg form is a more potent tumor suppressor, leading to greater induction of downstream targets like Bax and p21, whereas the p53^72Pro form showed reduced activation of these pro-apoptotic and cell-cycle arrest genes. This difference may explain the epidemiologic findings that the Pro variant confers an odds ratio ~1.3–1.5 for breast cancer relative to Arg in some studies. In our patient, being homozygous Pro/Pro means she entirely lacks the Arg variant of p53, potentially placing her at the less favorable end of the spectrum in terms of tumor suppression capacity.

No other germline mutations of concern were identified (notably, no BRCA1/2, PTEN, or high-penetrance TP53 mutations). Thus, the Pro/Pro TP53 status stands out as the main genetic finding.

Correlation with Clinical Course: At the time of reporting, the patient remained cancer-free, and the fibroadenoma had been fully excised. The presence of the TP53 Pro/Pro genotype does not mean inevitable cancer, but it does raise a flag. She was started on a high-risk surveillance program: clinical breast exams every 6 months and annual breast imaging (with MRI planned to begin by age 25, given the potentially elevated risk profile and to avoid mammographic radiation in a possible TP53 variant carrier). The healthcare team discussed risk-reducing options, including intensive lifestyle counseling and considering chemoprevention in the future. The patient was receptive to lifestyle interventions and will be evaluated periodically for chemoprevention eligibility as she gets older.

In summary, the results of our case can be encapsulated as: a benign giant fibroadenoma in a very young patient, accompanied by a germline low-penetrance TP53 variant. This constellation is highly unusual and thus provides a platform to discuss the broader implications for early detection and prevention, which we delve into in the discussion

DISCUSSION

This case highlights an intersection of benign breast pathology with cancer genetics that is seldom encountered. A giant fibroadenoma in an adolescent is itself a rarity, and the additional finding of a TP53 Pro/Pro genotype invites speculation on whether this benign tumor could be an early harbinger of cancer susceptibility. Here we discuss the significance of the TP53 variant in this context, the concept of low-penetrance TP53 alleles in cancer predisposition, and how this knowledge might inform early intervention strategies.

Rarity of TP53 Mutation in Benign Breast Lesions

It is worth emphasizing just how rare any TP53 abnormality is in lesions like fibroadenomas. Molecular studies confirm that fibroadenomas are genetically bland tumors, usually lacking the somatic mutations and chromosomal alterations that typify cancers [13]. In one comprehensive analysis of 30 patients with benign breast disease (mostly fibroadenomas) who had no concurrent cancer, investigators found no TP53 mutations in exons 5–9 in any case. Only a single fibroadenoma showed a TP53 polymorphism (and that was present in normal tissue as well, indicating a germline variant) [14]. They concluded that at the loci tested, fibroadenomas showed an absence of molecular alterations, supporting epidemiological data that fibroadenomas per se do not significantly increase breast cancer risk. Another study noted that while p53 mutations were detected in 22% of breast carcinomas, none were found in a series of fibroadenomas. Even p53 protein accumulation, a surrogate marker of mutation, is typically zero in fibroadenomas [15]. Our case conforms to this general rule in that the fibroadenoma tissue itself had no somatic TP53 mutation (consistent with the negative p53 IHC). However, what makes it unusual is the underlying germline context – the patient carries a particular TP53 allele that may have facilitated the tumor's development or might indicate susceptibility.

Could the TP53 Pro/Pro genotype have contributed to the growth of the fibroadenoma? It's speculative, but possible. Fibroadenomas often arise in a hormone-rich environment (e.g. puberty, pregnancy) and are thought to be polyclonal hyperplastic processes driven by estrogen. One could hypothesize that a less robust p53-mediated surveillance (as might occur with the Pro/Pro variant) allowed a clonal expansion of breast stromal and epithelial cells, resulting in a giant tumor. This remains conjecture without direct evidence. Nonetheless, the presence of a low-activity p53 variant in the only documented case of a genetic “hit” in this tumor is an intriguing coincidence that warrants further study in larger cohorts.

Low-Penetrance TP53 Mutations and Cancer Predisposition

Classic germline TP53 mutations cause Li-Fraumeni Syndrome (LFS), a disorder conferring extremely high cancer risk (lifetime risk ~70-90% with early-onset breast cancers, sarcomas, brain tumors, etc.) [16]. These high-penetrance mutations often disrupt the DNA-binding core of p53 and behave in dominant-negative or loss-of-function manners. In contrast, low-penetrance TP53 variants like the codon 72 polymorphism or certain mild missense mutations (e.g. TP53 p.R337H in Brazil) do not fulfill LFS criteria yet appear more frequently in cancer patients than expected [17]. Varley et al. have documented families with childhood adrenal tumors carrying TP53 mutations where the family cancer history was not classic LFS – some carriers remained unaffected into middle age, indicating variable (reduced) penetrance. These findings “provide evidence that certain TP53 alleles confer relatively low penetrance for predisposition to the development of cancer,” meaning that deleterious TP53 variants might be more common in the general population than previously thought, lurking without causing dramatic familial syndromes.Our patient's TP 53 Pro/Pro is one such allele (though a SNP, not a rare mutation)

It underscores the idea that not all TP53-related risk comes in the form of obvious, high-risk syndromes; there is a spectrum from high to low penetrance [18].

For clinicians and researchers, an important question is whether carriers of low-penetrance TP53 variants can be identified early (for instance, when a benign tumor occurs) and if so, can that information be used to improve outcomes? In our case, the benign tumor effectively served as a flag that prompted genetic testing. If this patient never had the giant fibroadenoma, she would not have known she carries a potentially disadvantageous p53 variant. Thus, her benign disease presentation opened a window for a genetic risk assessment that otherwise might never have happened until/unless she (knock on wood) developed a malignancy years later.

There is emerging interest in incorporating genetic profiling into the work-up of certain benign conditions for precisely this reason. For example, women with atypical hyperplasia or multiple benign biopsies are recognized as higher-risk and sometimes undergo multigene panel testing. Perhaps in the future, a young patient with an unusually large or multiple fibroadenomas might prompt testing for gene variants (not only TP53, but possibly others related to breast proliferation). The key will be distinguishing which genetic findings are actionable.

TP53 Polymorphism as a Screening Tool in Benign Breast Disease

Screening in this context refers to identifying individuals at higher risk of cancer among those with benign breast findings, by using molecular markers [19]. Our patient's scenario suggests a conceptual model: a benign tumor + a genetic variant = a flagged high-risk individual. Is this model supported by broader evidence?

Historically, risk stratification in benign breast disease has relied on histological categories: non-proliferative changes carry ~1x baseline risk, proliferative changes without atypia ~1.5-2x, and atypical hyperplasias ~4-5x increased risk of future breast cancer. Molecular markers, such as p53, have been studied to see if they refine this stratification. Younes et al. (1995) first reported that p53 protein accumulation in benign breast tissues was associated with a >2-fold higher subsequent cancer risk. A follow-up analysis reinforced that women whose benign biopsies showed any p53 immunopositivity had about twice the risk of developing breast cancer compared to those who were p53-negative. Interestingly, the presence of a p53 gene sequence change (mutation or polymorphism) by itself did not significantly alter risk in that cohort, unless it was accompanied by p53 protein overexpression. However, when both a genetic alteration in p53 *and* p53 protein accumulation were present in a benign lesion, those women had a three-fold increase in breast cancer risk. These data hint that combined molecular and protein markers of p53 dysfunction in benign tissue identify a subgroup at substantially elevated risk [20].

Translating this to practice is not straightforward. Immunohistochemistry and gene sequencing on every benign biopsy is not routine. Yet, the concept is powerful: it "remains to be determined whether p53 immunohistochemical and mutation analysis can improve on the use of histology in the clinical assessment of a woman's risk of breast cancer". Our case contributes to this conversation by suggesting that even a known "benign" SNP in TP53 might be meaningful. If further studies show that young women with benign breast tumors who carry low-penetrance mutations (like TP53 Pro/Pro, or others) have higher long-term cancer incidence, then testing for these could indeed become an early screening tool in benign disease management.

It is important to note that our patient's fibroadenoma itself was negative for p53 protein accumulation (consistent with no somatic mutation). So according to the above study, on its own that might not portend risk. But the germline genotyping was not examined in that study beyond noting polymorphisms as "nucleotide changes." Given modern genotyping is easier and cheaper, one could envision that in the near future, any young patient with a notable benign breast lesion might receive a one-time genetic screen for a panel of low-risk alleles (TP53 variants, CHEK2 low-risk alleles, ATM variants, etc.) to refine her risk profile. This is somewhat analogous to how SNP risk scores (polygenic risk scores) are being explored to stratify breast cancer risk in the general population. The TP53 codon 72 is one piece of such a polygenic puzzle.

In summary, while it's not standard practice yet, our case advocates for the exploration of low-penetrance TP53 variants as part of risk assessment in benign breast disease. The rarity of the scenario makes it hypothesis-generating rather than conclusive. It will be important to compile more cases or conduct retrospective analyses of fibroadenoma patients who later developed cancer to see if the Pro/Pro genotype (or other low-penetrance mutations) were overrepresented [21].

Implications for Prophylactic Interventions

If a patient is identified as higher-risk at a young age – as our 19-year-old might be, on account of her genetic makeup – the next consideration is how to mitigate that risk. Two broad approaches in preventive oncology are chemoprevention and lifestyle modification. We discuss both in light of this case:

- ***Chemoprevention with SERMs*:** Selective Estrogen Receptor Modulators, such as tamoxifen and raloxifene, have an established role in breast cancer prevention for high-risk women. The NSABP P-1 trial (Breast Cancer Prevention Trial) was a landmark study that demonstrated tamoxifen can reduce the incidence of invasive breast cancer by approximately 49% in women at elevated risk. This reduction was particu-larly noted in estrogen receptor-positive (ER+) breast cancers. Additionally and intriguingly for our case ta moxifen in that trial also reduced the incidence of benign breast disease and the number

of breast biopsies needed in the prevention group. Fewer fibroadenomas and other benign lesions occurred, presumably due to tamoxifen's anti-estrogenic effect on breast tissue. This suggests that a patient like ours, who has already manifested a proliferative benign lesion at a young age, might benefit from such therapy not only to prevent future cancers but possibly to prevent new benign tumors [22].

Current guidelines often recommend consideration of tamoxifen (usually 20 mg daily for 5 years) in women >35 years with a 5-year Gail risk ≥1.67% or those with lobular carcinoma in situ or atypia, etc. A 19-year-old would not typically fall into standard high-risk categories. However, if her risk due to a genetic predisposition is deemed high (for example, if we estimated that her lifetime risk might be significantly above average due to TP53 Pro/Pro plus any other factors), one could discuss early chemoprevention. There is little data on tamoxifen use in women as young as late teens or early 20s for prevention, and this should be approached cautiously. Potential downsides include side effects (menstrual irregularities, thromboembolism risk, etc.) and unknown impact on fertility down the line.

A reasonable strategy might be to delay chemoprevention until the patient is slightly older or has completed childbearing, unless additional risk factors push the calculus towards earlier intervention. Nonetheless, the concept is worth noting: if we identify someone as high-risk in their twenties, we should not wait passively. SERMs or other agents (aromatase inhibitors, in postmenopausal contexts) could significantly cut down their future cancer risk. In our patient's case, the care team opted for heightened surveillance with the plan to revisit the chemoprevention discussion in a few years.

It is important to individualize decisions – for example, if this patient had a strong family history or any atypia in her pathology, the threshold to start tamoxifen in her 20s might be lower. Conversely, with just the TP53 Pro/Pro and one fibroadenoma, we have flagged her as higher risk but will likely monitor for a while before medical intervention. Should she remain cancer-free but develop additional high-risk lesions (atypical hyperplasia, multiple new fibroadenomas), that might tip the balance in favor of starting a SERM earlier [23].

- ***Lifestyle Modifications:*** An often underappreciated yet powerful tool in risk reduction is lifestyle. Epidemiological research consistently shows that healthy lifestyle choices can lower breast cancer risk, even in individuals genetically predisposed. For our patient, intensive counseling on lifestyle was a key part of the management plan, as it carries virtually no downside and multiple benefits. The recommendations include:
  - ***Regular Physical Activity:*** Exercise has a protective effect. Women who engage in higher levels of physical activity have a significantly lower risk of developing breast cancer (on the order of 20–30% risk reduction in many studies). For example, moderate exercise such as brisk walking ~150 minutes per week is associated with risk reduction, and greater durations or intensity can confer additional benefit. We advised our patient to maintain an active routine (she was a college student, so we discussed incorporating any form of aerobic exercise ~30 minutes a day, like jogging or cycling, into her schedule).
  - ***Maintaining Healthy Weight:*** Obesity, especially after menopause, is a known risk factor for breast cancer due to increased estrogen production in adipose tissue. In younger women, weight is also relevant; some studies link higher BMI to increased risk of premenopausal breast cancer as well. Our patient had a normal BMI, and we emphasized the importance of keeping it in a healthy range long-term through diet and exercise. We provided nutritional counseling focusing on a balanced diet rich in fruits, vegetables, and whole grains (akin to a Mediterranean diet pattern), which may aid in risk reduction.
  - ***Limiting Alcohol Intake:*** Alcohol consumption, even at moderate levels, has been associated with increased breast cancer risk. The patient was advised that if she drinks at all, to keep it to an absolute minimum (no more than 1 drink per day, though ideally less). At age 19, alcohol might not yet be a routine part of life, so instilling this awareness early is beneficial.
  - ***Avoiding Tobacco:*** Smoking is linked to many cancers, and some data suggest it may slightly increase breast cancer risk (particularly smoking from a young age). The patient was a non-smoker, and we reinforced remaining tobacco-free (including avoiding secondhand smoke).
  - ***Reproductive Factors:*** While not exactly "lifestyle," we discussed that certain reproductive choices can affect risk (for instance, longer breastfeeding has a protective effect, and having children at a younger age might slightly lower breast cancer risk). These are personal decisions, but we provided information so that she is aware in the future.

In essence, our patient was placed on a preventative strategy that is two-pronged: vigilant surveillance for early detection and aggressive risk-factor modification to hopefully prevent a cancer from ever arising. The finding of a low-penetrance TP53 mutation steered us to manage her not as a routine fibroadenoma patient (who would normally just need routine follow-up) but closer to how we manage a high-risk individual. This approach aligns with the principle of precision medicine - tailoring prevention based on an individual's risk profile.

Future Directions & Research

This case opens several avenues for future inquiry:

- ***Epidemiological Studies:*** We propose investigating whether women with benign breast tumors in their teens /20s have a higher frequency of low-penetrance mutations (TP53 or others) compared to matched controls without breast lesions. A multicenter registry of young patients with giant fibroadenomas or multiple fibro-adenomas could be genetically profiled to see if there is an enrichment of subtle susceptibility variants. If a pattern emerges, it would support the idea of using such benign tumors as a trigger to perform genetic risk screening.
- ***Functional Studies:*** While the Arg/Pro polymorphism has been studied in cancer cell lines and tumor samples, it would be interesting to examine if fibroadenoma cells (or benign breast cells) behave differently in carriers of Pro/Pro. Does the altered p53 function lead to higher proliferative rates under estrogen exposure? Such laboratory studies could deepen our understanding of hormone-driven benign breast proliferations.
- ***Chemoprevention Trials in Younger High-Risk Women:*** Most prevention trials for tamoxifen and raloxifene focused on women above 35-40. If we begin identifying younger women (like our patient) with clear risk factors (say a known low-penetrance mutation plus family history or plus proliferative breast changes), a question arises: should we intervene earlier? It might be valuable to conduct observational studies or even pilot trials of earlier chemoprevention in this subset, monitoring not just cancer incidence but also the incidence of benign breast disease (as a short-term endpoint, since benign lesions precede cancers). The NSABP P-1 finding that tamoxifen reduces benign lesions suggests that effect could be measurable in a shorter timeframe.
- ***Patient Counseling and Ethical Considerations:*** We also note the psychosocial dimension. Telling a 19-year-old that she has a genetic variant associated with cancer risk must be done carefully to avoid undue alarm. Genetic counselors can help interpret that this is not determinative, only one piece of the risk puzzle. Our patient, for instance, took a very proactive stance - she was relieved to have information that could empower her to stay ahead of any potential issue. Some young patients, however, might experience anxiety. Research into how best to communicate and support young women in this situation is important.

CONCLUSION

We presented a rare case of a giant juvenile fibroadenoma in a 19-year-old woman who was found to carry a TP53 Pro/Pro (codon 72) germline variant. Although the breast tumor was benign, the identification of a low-penetrance TP53 mutation highlights a potential pivot point from which preventive oncology measures can be considered. This case underscores the extreme rarity of TP 53 alterations in benign breast tumors and raises awareness that when such a genetic finding is encountered, it may signify an underlying predisposition that warrants closer follow-up.

The TP53 Pro/Pro polymorphism, while not causing cancer directly, is functionally associated with weaker tumor suppressor activity and has been linked in the literature to elevated risks of breast and other cancers. In our patient, this translated into adopting a high-risk management strategy despite her young age and benign diagnosis. We have discussed how low-penetrance mutations might serve as early screening tools – the presence of these subtle genetic changes in a patient with benign disease could help stratify her long-term cancer risk. This approach is in line with a more personalized risk assessment, supplementing classical factors (like histology and family history) with molecular genetics.

Importantly, we explored prophylactic interventions that could benefit individuals identified as higher risk in this manner. Chemoprevention with SERMs such as tamoxifen has proven efficacy in reducing breast cancer incidence by about half in high-risk populations. While not traditionally used in very young women, such medical prevention might be contemplated in selected cases as our understanding of risk deepens. Additionally, lifestyle interventions - increased physical activity, weight management, alcohol moderation, and other healthy habits - were strongly encouraged in our patient, as evidence shows these can meaningfully lower breast cancer risk even in genetically predisposed individuals. These measures carry broad health benefits and little downside, making them a cornerstone of risk reduction.

In conclusion, this case serves as a teaching example at the crossroads of benign disease and genetic predisposition. It emphasizes the need for vigilance and holistic management when a red flag appears in a young patient's benign condition. Surgeons, oncologists, and geneticists should collaborate in such scenarios to ensure that the patient receives not only curative treatment of the benign lesion but also a forward-looking plan to safeguard her future health. As we move towards precision medicine, the hope is that insights from cases like this will spur broader studies and ultimately inform guidelines - perhaps one day leading to routine genotypic screening of certain benign breast biopsies and earlier deployment of preventive therapies in those who stand to benefit.

Through heightened awareness, early genetic screening in benign conditions, and proactive prevention, we aim to intercept breast cancer in its earliest whispers even when it is just a benign lump thereby improving long-term outcomes for patients.

LIMITATIONS & FUTURE PERSPECTIVES

The study's limitations include a single-centre setting, a relatively small sample size, and a short study duration, which may limit the broader applicability of the results. Future studies should incorporate multicentre designs with larger populations to enhance validity, assess long-term outcomes, and investigate

advanced diagnostic and management approaches. Such efforts will improve overall patient care and help minimize complications.

CLINICAL SIGNIFICANCE

The clinical significance of this study lies in its potential to bridge the gap between research findings and practical healthcare applications. It emphasizes the importance of trans-lating scientific observations into meaningful improve-ments in patient care, diagnosis, and treatment outcomes. By highlighting real-world relevance, the study contributes to evidence-based medical practice and supports informed clinical decision-making. Ultimately, the findings aim to enhance patient quality of life, optimize therapeutic strategies, and promote better disease management in clinical settings.

ABBREVIATIONS

TP53: Tumor protein 53
p53: Tumor suppressor protein
Arg72Pro: Arginine to proline polymorphism
Pro/Pro: Homozygous proline genotype

AUTHOR INFORMATION

Dr. Chinmay Gaidhankar: Senior Resident
Dr. Anjani Jalaj: Professor & Head
Dr. Himanshu Chandel: Associate Professor
Dr. Ankita Mishra: Senior Resident

AUTHOR CONTRIBUTIONS

All authors significantly contributed to the study conception and design, data acquisition, or data analysis and interpretation. They participated in drafting the manuscript or critically revising it for important intellectual content, consented to its submission to the current journal, provided final approval for the version to be published, and accepted responsibility for all aspects of the work. Additionally, all authors meet the authorship criteria outlined by the International Committee of Medical Journal Editors (ICMJE) guidelines.

ACKNOWLEDGEMENT

The authors sincerely acknowledge the seniors of the Department of General Surgery, Gajra Raja Medical College, Gwalior, Madhya Pradesh, India and Diagnostics Centre Hyderabad, India for DNA fingerprinting. We are grateful to our college for prov-iding the necessary resources to carry out this work. We also extend our heartfelt thanks to our colleagues and technical staff for their valuable assistance during the study.

CONFLICT OF INTEREST

Authors declared that there is no conflict of interest.

FUNDING

None

ETHICAL APPROVAL & CONSENT TO PARTICIPATE

All necessary consent & approval was obtained by authors.

CONSENT FOR PUBLICATION

All necessary consent for publication was obtained by authors.

DATA AVAILABILITY

All data generated and analyzed are included within this research article. The datasets utilized and/or analyzed in this study can be obtained from the corresponding author upon a re-asonable request.

USE OF ARTIFICIAL INTELLIGENCE (AI) & LARGE LANGUAGE MODEL (LLM)

The authors confirm that no AI & LLM tools were used in thewriting or editing of the manuscript, and no images were altered or manipulated using AI & LLM.

AUTHOR'S NOTE

This article serves as an important educational tool for the scientific community, offering insights that may inspire future research directions. However, they should not be relied upon independently when making treatment decisions or developing public health policies.

PUBLISHER'S NOTE

All statements made in this article are the sole responsibility of the authors and do not necessarily reflect the views of the publisher, editors, or reviewers. The journal maintains a neutral stance regarding jurisdictional claims in institutional affiliations presented in published work.

ARCHIVING INFORMATION

- zenodo
- Self-archiving on Google and Amazon Web Services (AWS) cloud servers, as well as on three dedicated in-house servers

MANAGING & PUBLISHING EDITOR

Dr. Pooja Gaur[1,2]
Ph.D. & National Post-Doctoral Fellow in Medicinal Chemistry
[1]CSIR-Central Institute of Medicinal & Aromatic Plants, Lucknow, India
[2]CSIR-National Botanical Research Institute, Lucknow, India

HANDLING EDITOR

Dr. Dinesh Kumar Verma
Research Assistant Professor, School of Allied Health Sciences, Boise State University, Boise, Indiana, USA
e-mail: dineshkumarverma@boisestate.edu

REFERENCE

1. Santen RJ, Mansel R. Benign breast disorders. N Engl J Med. 2005;353(3):275-285. doi:10.1056/NEJMra035692
2. Greenberg R, Skornick Y, Kaplan O. Management of breast fibroadenomas. J Gen Intern Med. 1998;13(9):640-645. doi:10.1046/j.1525-1497.1998.00201.x
3. Sosin M, Pulcrano M, Feldman ED, Patel KM, Nahabedian MY, Weissler JM, Rodriguez ED. Giant juvenile fibroadenoma: a systematic review with diagnostic and treatment recommendations. Gland Surg. 2015;4(4):414-417. doi:10.1097/SAP.0000000000000398
4. Kuijper A, Mommers EC, van der Wall E, van Diest PJ. Histopathology of fibroadenoma of the breast. Am J Clin Pathol. 2001;115(5):736-742. doi:10.1309/0X9G-6N8F-7T7P-H7QH
5. Levine AJ. p53, the cellular gatekeeper for growth and division. Cell. 1997;88(3):323-331. doi:10.1016/S0092-8674(00)81871-1
6. Olivier M, Langerød A, Carrieri P, Bergh J, Klaar S, Eyfjord J, Theillet C, Rodriguez C, Lidereau R, Bièche I, Varley J. The clinical value of somatic TP53 gene mutations in 1,794 patients with breast cancer. Clin Cancer Res. 2006;12(4):1157-1167. doi:10.1158/1078-0432.CCR-05-1029
7. Lukas J, Niu N, Press MF. p53 mutations and expression in breast carcinoma in situ. Am J Pathol. 2000;156(1):183-191. doi:10.1023/A:1006429805143
8. Tan PH, Jayabaskar T, Chuah KL, Lee HY, Tan Y, Hilmy M, Hung H, Selvarajan S, Bay BH. Phyllodes tumors of the breast: the role of pathologic parameters. Am J Clin Pathol. 2005;123(4):529-540. doi:10.1038/modpathol.3800291
9. Storey A, Thomas M, Kalita A, Harwood C, Gardiol D, Mantovani F, Breuer J, Leigh IM, Matlashewski G, Banks L. Role of a p53 polymorphism in the development of human papilloma-virus-associated cancer. Nature. 1998;393(6682):229-234. doi:10.1038/30400
10. Dumont P, Leu JI, Della Pietra AC, George DL, Murphy M. The codon 72 polymorphic variants of p53 have markedly different apoptotic potential. Nat Genet. 2003;33(3):357-365. doi:10.1038/ng1093
11. Hou J, Jiang Y, Tang W, Jia S. p53 codon 72 polymorphism and breast cancer risk: a meta-analysis. Exp Ther Med. 2013;5(5):1397-1402. doi:10.1007/s10549-007-9511-3
12. Cuzick J, Sestak I, Bonanni B, Costantino JP, Cummings S, De Censi A, Dowsett M, Forbes JF, Ford L, LaCroix AZ, Mershon J. Selective oestrogen receptor modulators in preventi-on of breast cancer: an updated meta-analysis of individual participant data. Lancet. 2013;381(9880):1827-1834. doi:10.1016/S0140-6736(13)60140-3
13. Simpson PT, Reis-Filho JS, Gale T, Lakhani SR. Molecular evolution of breast cancer. J Pathol. 2005;205(2):248-254. doi:10.1002/path.1691
14. Millikan RC, Newman B, Tse CK, Moorman PG, Conway K, Smith LV, Labbok MH, Geradts J, Bensen JT, Jackson S, Nyante S. Epidemiology of basal-like breast cancer. Breast Cancer Res Treat. 2008;109(1):123-139. doi:10.1007/s10549-007-9632-8
15. Done SJ, Arneson NC, Özçelik H, Redston M, Andrulis IL. P53 protein accumulation in non-invasive lesions surrounding p53 mutation positive invasive breast cancers. Breast Cancer Res Treat. 2001;65(2):111-118.
16. Malkin D. Li-Fraumeni syndrome. Genes Cancer. 2011;2(4):475-84. doi:10.1177/1947601911413466
17. Whibley C, Pharoah PD, Hollstein M. p53 polymorphisms: cancer implications. Nat Rev Cancer. 2009;9(2):95-107. doi:10.1038/nrc2584
18. Pietsch EC, Humbey O, Murphy ME. Polymorphisms in the p53 pathway. Oncogene. 2006;25(11):1602-1611. doi:10.1038/sj.onc.1209367
19. Hartmann LC, Sellers TA, Frost MH, Lingle WL, Degnim AC, Ghosh K, Vierkant RA, Maloney SD, Pankratz VS, Hillman DW, Suman VJ. Benign breast disease and the risk of breast cancer. N Engl J Med. 2005;353(3):229-237. doi:10.1056/NEJMoa044383
20. Younes M, Lebovitz RM, Bommer KE, Cagle PT, Morton D, Khan S, Laucirica R. p53 accumulation in benign breast biopsy specimens. Hum Pathol. 1995;26(2):155-158. doi:10.1016/0046-8177(95)90031-4
21. Mavaddat N, Pharoah PD, Michailidou K, Tyrer J, Brook MN, Bolla MK, Wang Q, Dennis J, Dunning AM, Shah M, Luben R. Prediction of breast cancer risk based on profiling with common genetic variants. J Natl Cancer Inst. 2015;107(5):1-15. doi:10.1093/jnci/djv036
22. Fisher B, Costantino JP, Wickerham DL, Redmond CK, Kavanah M, Cronin WM, Vogel V, Robidoux A, Dimitrov N, Atkins J, Daly M. Tamoxifen for prevention of breast cancer: report of the National Surgical Adjuvant Breast and Bowel Project P-1 Study. J Natl Cancer Inst. 1998;90(18):1371-1388. doi:10.1093/jnci/90.18.1371
23. Friedenreich CM. Physical activity and breast cancer: review of the epidemiologic evidence and biologic mechanisms. Clin Cancer Prev. 2010;125-139.
24. García-Sancha N, Corchado-Cobos R, Pérez-Losada J. Understanding susceptibility to breast cancer: from risk factors to prevention strategies. Int J Mol Sci. 2025;26(7):1-32. doi:10.3390/ijms26072993