Institutional Protocol to Manage Consanguinity Detected by Genetic Testing in Pregnancy in a Minor

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Dr Chen drafted the initial manuscript; Dr Beck conceptualized the manuscript and reviewed and revised the manuscript; Dr Tsuchiya, Ms Chow, Dr Mirzaa, and Dr Wiester reviewed and revised the manuscript; Dr Feldman conceptualized the manuscript and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

www.pediatrics.org/cgi/doi/10.1542/peds.2014-2593

DOI: 10.1542/peds.2014-2593

Accepted for publication Dec 8, 2014

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

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FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: Anita Beck is supported by a grant from the National Institutes of Health (NIH)/National Institute of Child Health and Human Development (5K23HD057331). Funded by the National Institutes of Health (NIH).

POTENTIAL CONFLICT OF INTEREST: Drs Feldman and Wiester evaluate and provide legal consultation for child abuse concerns; the other authors have indicated they have no potential conflicts of interest to disclose.

abstract

Single-nucleotide polymorphism arrays and other types of genetic tests have the potential to detect first-degree consanguinity and uncover parental rape in cases of minor teenage pregnancy. We present 2 cases in which genetic testing identified parental rape of a minor teenager. In case 1, single-nucleotide polymorphism array in a patient with multiple developmental abnormalities demonstrated multiple long stretches of homozygosity, revealing parental rape of a teenage mother. In case 2, a vague maternal sexual assault history and diagnosis of Pompe disease by direct gene sequencing identified parental rape of a minor. Given the medical, legal, and ethical implications of such revelations, a protocol was developed at our institution to manage consanguinity identified via genetic testing.

Different genetic tests, including single-nucleotide polymorphism (SNP) microarrays, make intentional or incidental detection of chromosomal deletions, duplications, or long stretches of copy-neutral homozygosity possible. Detection of long stretches of homozygosity may have clinical utility if an autosomal recessive disorder is suspected. Long stretches of homozygosity (>3 Mb¹) on multiple chromosomes reflect regions that originate from a common ancestor and can suggest relatedness between the proband's parents. Thus, clinicians have the ability to identify previously unrecognized chromosomal disorders and, incidentally, consanguineous parental relationships.² Genetic testing may suggest not only consanguinity between consenting adults, but can also suggest parental rape and child sexual abuse.³ Clinicians have a duty to report cases of suspected or confirmed sexual abuse. Although general guidelines exist for the documentation and reporting of suspected consanguinity and for abuse detected by genomic

testing, each institution should develop its own protocol based on its existing infrastructure and state laws for handling potential child abuse.

We describe 2 cases of teenage pregnancy in which genetic testing incidentally detected first-degree consanguinity, leading to the discovery of parental rape. When our laboratory introduced SNP testing, the possibility of detection of consanguinity was anticipated, leading to development of a protocol for managing our legal obligations.

CASE REPORT 1

A 14-year-old primipara gave birth to a term infant girl, birth weight 2.4 kg (5th percentile), length 42.5 cm, and head circumference 30.5 cm (both less than fifth percentile). The infant had multiple dysmorphic facial features and severe hypotonia. She had early feeding problems leading to Nissen fundoplication and gastrostomy tube placement. She subsequently had a complicated course with multiple

infections (meningitis and preseptal cellulitis), hearing loss, neurologic problems, and developmental delay. Given her complex medical picture, genetics consultation was sought. During her initial hospitalization at our hospital when the child was 3 months old, her mother denied consanguinity, reporting that the child's father was a foreigner. The child's mother resided with her parents and her 2 healthy siblings. A chromosomal oligonucleotide array that lacked SNP coverage did not identify any copy number abnormalities.

The child was lost to genetic follow-up until age 3 years, when she was hospitalized for respiratory complications after tonsillectomy and adenoidectomy for obstructive sleep apnea. During that hospitalization, a repeat chromosomal microarray that included SNP coverage revealed multiple long stretches of homozygosity (~26.8% of the autosomal genome) involving most chromosomes, strongly suggesting a high degree of parental relatedness on the order of first-degree relatedness. Our protocol for positive SNP results was activated, and our Children's Protection Program (CPP) made a referral to the police and Child Protective Services. On initial police interview, the child's mother denied consanguinity. However, when informed that police protocol would require placement of all children in the home in alternative care unless the child's father was identified, she admitted her father was father of her child. The child's underlying genetic cause for neurodevelopmental problems is still being pursued.

CASE REPORT 2

A term, 3.3-kg infant girl was born by caesarian delivery to an 11-year-old gravida 1 mother. She reported that 3 young men had sexually assaulted her at her parents' migrant labor camp. She indicated the assailants had fled the country, but her description was

vague. The newborn had persistent respiratory insufficiency, hypotonia, stridor, and feeding difficulties. Creatinine kinase was elevated (827 IU/L); she was weak and areflexic. Congenital myopathy was suspected. Possible seizures were noted, but electroencephalogram was normal. She had grade II intraventricular hemorrhage, but a normally formed brain on brain MRI. She developed supraventricular tachycardia and subsequently had premature atrial and ventricular contractions. Echocardiogram demonstrated hypertrophic cardiomyopathy.

Ophthalmology examination did not reveal cataracts or corneal clouding.

Because of clinical suspicion for Pompe disease, blood-spot acid α -glucosidase was obtained at 11 picomole/hr/spot, below normal range of 24 to 94, but indeterminate. Subsequent direct gene sequencing detected a homozygous mutation (c. 2104C>T, p. Arg702Cys) in the GAA gene that causes Pompe disease.

Because of young maternal age, the birth hospital made a referral to Child Protective Services and the police. Due to the presence of a homozygous

Identification of Suspected Consanguinity by SNP Array:

When and How to Involve the Seattle Children's Protection SCAN Team

SCH lab identifies long continuous stretches of homozygosity (LCSH) >12 % by the SNP array test, suggestive of a **first-** or **second-**degree relationship between the individual's parents (eg, mother/son, father/daughter, brother/sister, grandparent/grandchild, uncle/niece, aunt/nephew, half-siblings, but does not include first cousins)

Cytogenetics director finalizes the SNP array report to include information about the degree of genetic similarity identified and significance of this finding: *example*
"The long stretches of homozygosity comprise 664 Mb (~23%) of this individual's genome. This result suggests some degree of relatedness between the individual's parents and indicates an increased risk of recessive disorders in this individual."

Lab genetic counselor researches potential relationship between parents and age of parents at time of conception (chart review, conversation with ordering provider)

Age of mother at time conception?

Mother was <18 years at time of conception

Mother was ≥18 years at time of conception

1. Lab genetic counselor informs ordering provider of results and process to involve Seattle Children's Protection SCAN Team
2. Lab genetic counselor recommends that ordering provider refer patient to medical geneticist and/or genetic counselor to discuss results in more detail
3. Lab genetic counselor notifies Seattle Children's Protection SCAN Team and provides case details, including parents ages at time of conception

Lab genetic counselor informs ordering provider of results and recommends referral to medical geneticist and/or genetic counselor to discuss results in more detail

FIGURE 1

Seattle Children's Hospital (SCH) protocol when SNP array results identify suspected consanguinity. SCAN, Suggested Child Abuse and Neglect.

mutation, our CPP encouraged police to perform paternity testing on mother's male relatives. Further investigation revealed her father was the father of her child. The infant's mother was placed in foster care, and she subsequently confirmed incest.

Three months after the initial hospitalization, the infant was discharged and later adopted by the same foster parents as her mother. The infant has made steady improvements on enzyme therapy.

DISCUSSION

The lifetime prevalence of female child sexual abuse and assault by an adult family perpetrator is 5.5%.⁴ Given this high prevalence, general pediatricians should consider intrafamilial sexual abuse in minor teenage pregnancy. Genetic testing has the potential to detect first-degree consanguinity and ultimately uncover parental rape in child sexual abuse. An "incidental finding" is defined as genetic variants that may have medical or social implications not related to primary indications for testing.^{5,6} Recent guidelines published regarding incidental findings of consanguinity by genomic testing note suspicion for child sexual abuse should be high when the proband's mother is a minor.¹ In our cases, incidental findings of genetic homozygosity led to discovery that teenage pregnancy resulted from incest. In case 2, the sexual assault history provided by the teenage mother was vague, leading providers to involve the CPP early in the infant's clinical course. Genetic testing to confirm Pompe disease led to the detection of a homozygous mutation, which ultimately led to discovery via paternity testing of the newborn's grandfather as perpetrator.

SNP microarrays can detect long, uninterrupted regions of homozygosity, which may suggest first-degree consanguinity, either a father-daughter or brother-sister

relationship.^{1,7} Incidental detection of parental consanguinity by SNP array in children with developmental or congenital anomalies has been demonstrated in the literature.^{2,8} In case 1, SNP array was performed for multiple congenital anomalies. Unexpected detection of multiple long homozygosity stretches led to the discovery of paternal child sexual abuse. Previous authors have noted the potential legal and psychosocial implications in cases of child sexual abuse along with the scarcity of published literature on case management.^{3,9}

Given anticipated ethical and legal implications, our hospital's genetics program, CPP, and hospital attorneys developed a protocol for management of consanguinity and, secondarily, child sexual abuse uncovered by SNP array (Fig 1). We expected most requests for SNP arrays would come through our clinical genetics service, which routinely provides pretest

counseling about the possibility of detecting consanguinity. However, as a "listed" laboratory test, some samples could come directly from providers who may not provide full pretest counseling. By protocol, our laboratory reports suspected consanguinity by using wording similar to that suggested in American College of Medical Genetics guidelines.¹ It is important to note that the laboratory typically does not have enough clinical information to determine if consanguinity is due to abuse; therefore, we planned that the laboratory would notify the ordering provider when the level of homozygosity suggests close parental relatedness (first- or second-degree relationship between an individual's parents). The results would also be forwarded to our genetic counselors, who could explore family structure and parental age at conception. If the child's mother was found to be <18 years old, the protocol dictated that genetic counselors would notify

TABLE 1 Intercourse With a Minor Laws in the State of Washington

Victim's (V) Age, y	Perpetrator's Age Difference			
	2 y older	3 y older	4 y older	5 y older
V ≥18	Not a crime based solely on age of victim and perpetrator			
16 ≤ V <18				
				Sexual misconduct with a minor in the first (intercourse) or second (contact) degree, RCW 9A.44.093 or .096 (Class C felony or gross misdemeanor), but only for school employees, foster parents, and limited others
14 ≤ V <16			Rape of a child in the third degree, RCW 9A.44.079 (Class C felony)	
12 ≤ V <14		Rape of a child in the second degree, RCW 9A.44.076 (Class A felony)		
V <12	Rape of a child in the first degree RCW 9A.44.073 (Class A felony)			

When the victim's age and the perpetrator's age difference fall within 1 of the categories on the chart, then the designated crime has occurred. If the victim and the perpetrator are closer in age than 1 of the categories on the chart, no statutory rape has occurred.

the ordering provider and our CPP so appropriate evaluation for abuse can occur and reporting statutes could follow.

In addition, our protocol specified scheduling a genetics clinic visit to discuss genetic implications. In practice, this created a dilemma; the police officer for case 1 requested we provide limited discussion of test implications until investigators had a chance to interview family members. A genetics clinic visit was scheduled, and our CPP social worker was enlisted to provide support and information about abuse referral, investigation, and victim services. However, when the visit occurred, police had already obtained a disclosure from the child's mother of both consensual peer intercourse and several intercourse events with her father. Her father was arrested. She may have initially declined to name the child's biological father not only because of emotional conflicts, but also because she was not certain which sexual partner was the father.

In the United States, incestuous relationships and child rape are illegal in all states, including Washington.^{10,11} However, child-abuse reporting statutes are state-specific. In Washington, child-abuse reporting statutes only require reporting to police or protective services if victims are aged ≤ 18 years.¹² Specifically, rape of a child <12 years old is a first-degree felony¹¹ and of a 12- to 14-year-old, a second-degree felony¹³ (Table 1). Younger children are considered legally unable to consent to sexual acts. As the victim's age increases from <12 years to 16 to 18 years, the necessary age difference between perpetrator and victim for the sexual act to be considered criminal increases (Table 1). All states have mandatory child-abuse reporting statutes.¹⁴ Police reporting rules for

consanguineous adults' consenting relationships will vary, but reports are usually optional and based on the mother's preferences. Because specifics of state laws vary, clinicians should be aware of statutes in their practice's state.

CONCLUSIONS

When a minor parent has an infant with a suspected genetic condition, genetic testing has the potential to incidentally detect consanguinity and consequently uncover parental rape. A pediatrician caring for a minor parent or that parent's child can play a key role in recognizing the potential for parental rape in cases of recessively inherited diseases and understanding potential implications of genetic testing. Developing an institutional protocol to manage consanguinity detected by genetic testing in cases of minor teenage pregnancy can standardize the care provided.

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