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Barber-Say Syndrome and Ablepharon-Macrostomia Syndrome: A Patient's View

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Keywords

Ablepharon-macrostomia syndrome · Barber-Say syndrome · Body satisfaction · Patient perception · Psychosocial functioning · Quality of life · Questionnaire study

Abstract

Barber-Say syndrome (BSS) and ablepharon-macrostomia syndrome (AMS) are infrequently reported congenital malformation disorders caused by mutations in the *TWIST2* gene. Both are characterized by abnormalities in ectoderm-derived structures and cause a very unusual morphology of mainly the face in individuals with otherwise normal cognition and normal physical functioning. We studied the impact that the presence of BSS and AMS has on psychosocial functioning of affected individuals and their families, using their point of view to start with. We tabulated frequently asked questions from affected individuals and families, and a parent of an affected child and an affected adult woman offered personal testimonies. We focused on perception of illness, body satisfaction, and the consequences for an otherwise normal individual who has a disorder that interferes with

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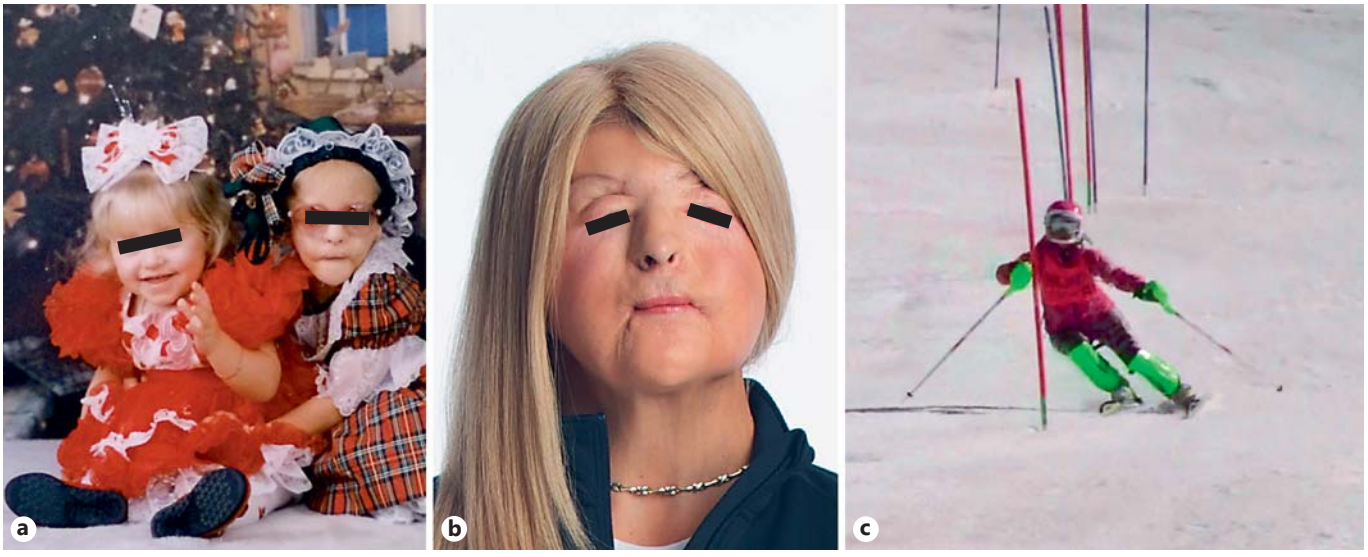

Fig. 1. A female with ablepharon-macrostomia syndrome at the age of 5 years with her younger sister (**a**), as an adult at the age of 23 years (**b**), and performing her favorite sport: skiing (**c**).

body image. The importance of paying particular attention to the management of both the physical appearance and the consequences of these entities on the quality of life is stressed by the affected individuals themselves.

Barber-Say syndrome (BSS) and ablepharon-macrostomia syndrome (AMS) are infrequently described congenital malformation syndromes which both include a remarkably abnormal morphology, especially of the face, with limited internal organ anomalies, and normal cognition. We recently analyzed literature and found 16 individuals with BSS and 16 with AMS which were reliably diagnosed [De Maria et al., 2016].

Here, we focus on the influence that BSS and AMS have on the psychosocial well-being of affected individuals, in order to gain insight into their perception of illness, body satisfaction, and issues of personal and social functioning for an otherwise normal individual, who has a disorder that disturbs facial morphology.

Methods

Study Design

We developed a tailored questionnaire for the present study which could use for both syndromes. The questionnaire consisted of 3 sections: (1) medical history, (2) psychomotor development and growth, and (3) specific characteristics of BSS and AMS, combining questions on both the nature of the signs and symptoms in an affected individual and the influence they had on their life. There was an open question at the end allowing additional comments if desired. The questionnaires were forwarded to all authors of publications describing individuals with BSS or AMS. The authors of 13 publications responded. Three BSS individuals [Barber et al., 1982; Dinulos and Pagon, 1999; Tenea and Jacyk, 2006] and 1 AMS individual [Stevens and Sargent, 2002] were lost to follow-up, so we gathered questionnaires from 10 BSS individuals and 2 AMS individuals [David et al., 1991; Mazzanti et al., 1998; Stevens and Sargent, 2002; Brancati et al., 2004; Haensel et al., 2009; Martins et al., 2010; Roche et al., 2010; Marchegiani et al., 2015; Singh et al., 2016]. The questionnaire was written in English, and in case a participant was unable to read and write English, local persons acted as interpreters.

In addition, patients, families, or caregivers were invited to participate in a semi-structured interview; Skype was used to overcome geographical distances (for online suppl. material, see www.karger.com/doi/10.1159/000472408). The interviews explored the age and the way they were informed about the diagnosis, body image and their satisfaction with their body, previous and current physical and psychosocial well-being, satisfaction with respect to the management they received, and the quality of relationships within their family, with friends, schoolmates, or working colleagues. Four affected individuals were interviewed. Answers from both the interviews and the questionnaires with the same meaning were combined and organized in such a way that they offered answers and opinions about questions frequently asked by patients and their families.

Finally, 2 personal testimonies are enclosed: one by a mother of a 5-year-old child with BSS, and one from a 25-year-old woman with AMS.

Table 1. Frequently asked questions by affected individuals and their relatives regarding Barber-Say syndrome and ablepharon-macrostomia syndrome

Question	Answer
Can plastic surgery be done on the eyes?	This is often done in the first months of life, depending on the severity of exposure of the eyes to the air. Until now, it has invariably been successful.
Can cosmetic surgery be done for nose/mouth/chin? At what age?	Surgical procedures have included nasal reconstruction with rib cartilage grafts, orthognathic surgery, cheiloplasty, local skin flaps, and botox injections. Procedures are often deferred until adolescence or early adulthood, when craniofacial growth is completed.
Can cosmetic surgery be done because of the small breasts? At what age?	This has been done several times with good success. It can be done at the end of puberty but also at any age thereafter.
Will an affected woman be able to breast feed?	There is no adult known to have breastfed her child. In general, it will depend on the amount of breast tissue that is present and not on the size of the nipples. It is difficult to be sure about this in advance, and there is no study that can reliably predict this.
Is therapy for the hirsutism and regional alopecia possible? At what age?	Laser therapy for hirsutism has been used successfully in several individuals at different ages. Infrequently hair implants have been used for alopecia in adults, and they were successful.
Will cognition be normal? How will the child develop?	Almost all children have a normal cognition. Their motor and speech development will be normal. There have been exceptions in the literature, but the abnormal cognition in them may have been unrelated to the syndrome.
Will it be possible for a child with BSS/AMS to attend normal school? What level of education could the child reach?	All children except 3 have been/are attending normal schools. Of these 3, one was at a special school, however, only temporarily. Four children earned a high school diploma and went on with academic studies.
Will it be possible for affected adults to find a job?	All 8 adults about whom we have data are employed.
At what age and how do affected families discuss the condition with the child?	Children become aware of their different appearance from very early stages on. Early and honest communication, adapted to the level of the child, has been performed, sometimes by treating physicians, sometimes by parents.
What kind of support do children and adults like to receive?	Acceptance by family and peers is absolutely essential. Psychological support is useful at various ages. All stated that surgical treatments had improved their self-confidence and quality of life markedly.
Will it be possible for a child to make friends?	All reported to be really satisfied with their social lives and had several close friends. They stated rejection due to their appearance occurs only rarely and almost exclusively before surgery was performed.
Would it be possible for an adult to find a partner?	Two adult females had a partner and were pleased with this. One adult stated he/she had not yet found the right person.
Will an affected person be able to have children?	All with mosaicism had children (ascertainment bias!). No non-mosaic adults are known to have had children, but this may have been voluntary as prenatal studies would have been impossible in the past. There is no evidence that fertility is decreased. The recurrence risk for a child of a non-mosaic affected person will likely be 50%, although it cannot be excluded that some affected embryos will lead to early miscarriage, resulting in a lower recurrence risk for live-born offspring.
What is known about life expectancy?	The eldest known adult with AMS is 58 years and with BSS 47 years of age. Others may be older but were lost to follow-up. There is no reason to assume life expectancy is reduced.

AMS, ablepharon-macrostomia syndrome; BSS, Barber-Say syndrome.

Table 2. Selected quotes about personal experiences from individuals with Barber-Say syndrome/ablepharon-macrostomia syndrome and their relatives

Person	Quote
Mother	"We do not believe that there is a direct correlation between the specific syndrome itself and how an individual would react to it."
Mother	"My daughter's condition does not define her as person nor us as a family."
Sister	"The quality that separates my sister from everyone I know is not her appearance, nor is it her ability to assimilate no matter the difficult changes. But it is her ability to go from someone I used to feel the need to protect, to someone I completely idolize, and one day hopefully I can accomplish half of the amazing things she has accomplished." *
Affected woman	"Before interventions, I felt terribly bad. I wondered Why? Why? I never looked in the mirror. After the [surgical] intervention, I have become more vain. I spend much more time in front of the mirror."
Affected woman	"To be treated with great humanity as well as professionality helped me to not be afraid in the path to take."
Affected woman	"I think that quality of life is basically based on your personality and how you are. At the same time, I absolutely think my surgery helped a lot."
Affected woman	"Everyone has something, so for me this is my something."
Affected woman	"You are a normal person like everyone else and if they have questions – and they are respectful about – then answer their questions. It is part of who you are."
Affected woman	"Just know who your friends are and find those people you can trust, but also don't be afraid of who you are."
Affected adolescent girl	"At that time, I underwent [surgical] intervention it was bad, it hurt, I suffered. But now I realize that I will advise other people to do surgery. I would have more issue if I didn't submit to surgery. I am much more self-confident."
Affected adolescent girl	"Attending church meetings has been a very important support psychologically speaking."

* From the manuscript *Through My Sister's Eyes* by Jamie Sarubbi, currently awaiting publication.

Results

The combined results of the questionnaires and interviews are summarized in Table 1. Some remarkable quotes about personal experiences are listed in Table 2. An AMS patient in her ordinary circumstances is shown in Figure 1, and the phenotypic changes over time after multiple cosmetic procedures in a BBS patient are demonstrated in Figure 2.

Personal Testimony of a Mother

"Born with a Visible Difference"

"Becoming parents for the very first time is a very daunting, almost nerve-wrecking experience. But this goes a few steps further when your child is born with something that nowadays is classified as a visible difference. And yes, I would like to stop for a few moments at the last two words of the previous sentence. Barber-Say syndrome is only a visible difference; it does not change or define the being of that little person who arrived in the world.

Our daughter was born with a mutation in one of her genes. In that very moment of complete and utter confusion from both our side as parents, but also the medical staff looking after our daughter, a very dark picture was painted. She was kept in NICU (neonatal intensive care unit) because nobody knew to what extent she was affected; numerous tests and scans were done on her whole body. In hindsight, our little girl was probably one of the strongest, healthiest babies in the hospital at that time, who only happens to look a bit different. We were told she might not be able to see or hear, she might have intellectual disabilities, and various other scenarios were presented which would only be determined as time goes by. None of these scenarios played out over the past few years. In fact, other than the original diagnosis, we have only received good news since.

We do believe in the evolution of medical science to assist with some of the visible differences. Think about it – 20 years ago, something as simple as hair removal treatment was not an option; today it's a fairly common procedure.

We do not live under any disillusions; many challenges have been, are and will be faced in our family's future. We know we also live in the world of cyber bullying, but this can happen to any person, regardless of their genetic

Fig. 2. An adult female with Barber-Say syndrome before (**a**) and after (**b**) multiple maxillofacial and facial plastic surgery interventions. The patient underwent an orthognathic surgery procedure based on maxillomandibular advancement and genioplasty according to the concept of "facial expansion"; in a second step, she underwent malar implants and rhinoplasty. Cheiloplasty was performed twice to obtain a better vermilion exposure together with upper lip shortening, blepharoplasty, and correction of the eyelid position.

make-up. *But* we also live in a world, which is becoming more and more accepting of differences, embracing them, and cheering for people to succeed no matter what their circumstances are.

Our daughter's arrival indeed was a nerve-wrecking experience, but her life is a blessing not only to us, but also to everybody who has the privilege of meeting her."

Testimony of an Affected Adult Woman

"Yes We Can"

"Many may think that having AMS is a life debilitating curse that you cannot overcome. Don't get me wrong, it certainly can be hard at times. I have had over sixty reconstructive surgeries beginning when I was just three days old. I am also visually impaired, which brings with it its own set of daily challenges. However, for me, it has also been a blessing in its own way. I have been fortunate enough to have parents that had the opportunity and desire to give me the best care possible in order to improve my quality of life from a very early age. More importantly, they never treated me any differently because of my syndrome. I believe this is very important for any child with any type of disability.

Children with disabilities face unique hardships that their able-bodied peers may not go through. These hardships have taught me a lot about finding the strength within myself. They have taught me to overcome adversity and to never stop fighting for your dreams and goals. This drive that I have to achieve and live life to the fullest is what gave me the ability to graduate from Harvard University. It was this same drive that allowed me to compete at the 2010 Paralympic Games as an alpine ski racer. Finally, it is this drive, and my gratitude towards my own doctors, that propels me forward in my dream of becoming a doctor myself.

At times it may be challenging, but this is who I am, and I am proud of and happy with who I am. People strive to be the best they can be. Everyone has something that makes them unique and great. Everyone has something that challenges them and makes them work harder in life. For me, having AMS does both. For young children with this syndrome, it won't be the easiest road, but have confidence in who you are and never stop believing in your dreams."

Discussion

We reviewed pertinent literature and collected additional information to provide an overview of both BSS and AMS with the aim to delineate all physical features that characterize the entities [De Maria et al., 2016]. During this study, we directly came in contact with caregivers and also with several patients. We were impressed by the influence each of these disorders had on the patients' lives, both positively and negatively. We realized this aspect of the syndromes needed specific attention which urged us to perform the present study, in which we aimed at participation of affected individuals and their families. Indeed, we decided to focus on the psychological and social consequences of BSS and AMS from an affected individual's perspective. The present information is reported in such a way that other affected individuals may benefit.

We realize the present information is based on only a very limited number of affected individuals. However, this is inherent to ultrarare disorders [Hennekam, 2011]. Individuals with these disorders often face virtually complete absence of information, also information regarding the (very) limited number of individuals affected by the same entity. This is of extraordinary importance to them and should not be easily discarded.

From an affected individual's point of view, there are several major questions (Table 1) which were derived from queries patients, or their families, asked us when they learned about our studies. These questions differ substantially from the strictly medical aspects and demonstrate that an affected individual is typically focused on the impact on quality of life as well as on practical issues for optimal management. The literature does not provide answers to such questions, and physicians are left without useful information to respond. Individuals with ultrarare disorders often experience their situation in a lonely, personal way. Providing information, even based on very limited numbers, will be extremely helpful to them.

The interviews we report yielded 2 major issues: the positive influence of corrective surgery and the importance of building adequate self-esteem. Surgery in many cases works best if the surgeon has experience with the disorder involved. Similarly, in ultrarare disorders such as BSS or AMS, surgical procedures should be performed in centers specialized in treating these specific conditions. Communication and exchange of information regarding procedures and results between sites are essential [Hennekam, 2011]. For adequate self-esteem, especially parents and other relatives play a very important role. Affected individuals even considered the acceptance of a disorder by the family as being of paramount importance. Today, there are many effective ways to improve self-esteem of individuals with conditions such as facial disfigurement, and this knowledge and experience should start in early childhood with the help of social scientists [von Soest et al., 2009; Bradbury, 2012; Versnel et al., 2012].

The personal testimonies presented in this study show a common, positive attitude toward the disorder, particularly regarding the visible difference from other children and adults. Both mention the challenge this poses, but at the same time, both state that the condition should not be an impediment for fulfilling one's personal and professional goals in life. The importance of the familial and social context for a natural integration in society is also evident.

Although physicians invariably aim to offer optimal care to their patients, the impact of having a disfiguring syndrome on the psychological dynamics of the family and the individual him/herself is often undervalued. Physicians tend to assign a higher priority level to the physical consequences of disorders rather than to the psychosocial aspects. In this study, individuals with BSS and AMS teach us that there should be a balance between the 2, and true care means addressing both the physical and psychosocial consequences of these disorders, gaining a more holistic view.

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