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## **Bloody Nipple Discharge in Infants: Case Series**

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### **Author's contribution**

*This work was carried out in collaboration between all authors. Authors ESM and AG wrote the first draft and the final draft of the manuscript. Authors AG, ESM, LB and GB managed the literature searches. Authors AG, DC and RG collected our cases. All authors read and approved the final manuscript.*

**Case Study**

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### **ABSTRACT**

Bloody nipple discharge very rarely occurs in infants and often is associated with benign mammary duct ectasia.

Just because it is a rare symptom and frequently associated with adults' mammary cancer, it is inadequately managed: inappropriate diagnostic tools are used, consequently inappropriate treatments are given.

We here describe four cases of bloody nipple discharge, which resolved spontaneously within a few weeks of diagnosis and we present a review of the literature.

In conclusion, a "wait and see" approach is enough and avoids unnecessary invasive diagnostic procedures.

*Keywords: Infant; blood; discharge; nipples; mammary duct ectasia.*

## **1. INTRODUCTION**

Bloody nipple discharge (BND) very rarely occurs in infants [1-9] and is a rather distressing finding for both parents and consulting pediatricians [10-12]. Although this symptom can be associated with breast cancer in adults, in most reported cases of infants it has been associated with mammary duct ectasia and found to be idiopathic in nature. Knowledge regarding the management protocol of this rare entity is not well defined and hence is mandatory, in order to avoid unnecessary invasive intervention [6,13].

We here report 4 cases of infants of and under 6 months of age, presenting with unilateral bloody nipple discharge, which spontaneously resolved within a few weeks and discuss the management of this entity besides presenting a review of the literature.

## **2. CASES**

### **2.1 Case 1**

In 2002, a healthy 2 month old boy presented with unilateral left bloody nipple discharge. On physical examination, both breasts appeared normal. Bacterial culture and cytologic evaluation of nipple discharge were negative; routine laboratory chemistries were normal, and hormonal studies (such as prolactin, estradiol, progesterone, alfafetoprotein) were within appropriate age-reference ranges; breast ultrasound imaging showed left mammary ductal ectasia. The bloody discharge persisted 15 days, then disappeared spontaneously and didn't appear again during a year's follow-up.

### **2.2 Case 2**

In 2004, a healthy 6 month old girl presented with unilateral left bloody nipple discharge. On physical examination, both breasts appeared normal. Bacterial culture and cytologic evaluation of nipple discharge were negative; routine laboratory chemistries were normal, and hormonal studies (such as prolactin, estradiol, progesterone, alfafetoprotein) were within appropriate age-reference ranges; breast ultrasound findings were non-significant. Spontaneous bloody discharge continued for 5 weeks, subsequently persisted, yet only when squeezing the nipple, until the child was a year old and then resolved spontaneously. During the following year of follow-up, bloody nipple discharge didn't appear again.

### **2.3 Case 3**

In 2007, a healthy 6 month old girl presented with unilateral right bloody nipple discharge. On physical examination, both breasts appeared normal. Bacterial culture and cytologic evaluation of nipple discharge were negative; routine laboratory chemistries were normal, whereas hormonal studies (such as prolactin, estradiol, progesterone, alfafetoprotein) showed increased borderline prolactin and alfafetoprotein; breast ultrasound imaging showed right mammary ductal ectasia. BrainCT was normal. The bloody discharge thereafter disappeared spontaneously, while prolactin and alfafetoprotein blood levels dropped down to normal ranges within 8 weeks. Thereafter no other hormonal studies were performed, because subsequent clinical 2 year follow-up was normal.

## **2.4 Case 4**

In 2011, a healthy 6 month old girl presented with unilateral left bloody nipple discharge. Breast ultrasound findings were non-significant. The bloody discharge occasionally occurred for a month and never appeared again during a year's follow-up. No routine laboratory chemistries were done. Spontaneous bloody discharge continued for 4 weeks and then resolved spontaneously. Subsequent year follow-up was normal.

## **3. DISCUSSION**

Bloody nipple discharge (BND) is rarely described in literature, whereas milky nipple discharge associated with breast enlargement is not an unusual finding in neonates [14] and infants. BND is thought to be linked to both the transplacental passage of maternal hormones and the infant's hormonal adaption process in the first few months of life.

In the last 30 years many cases of BND have been reported in literature, in children of both sexes under 5 years of age; reported cases clearly described of infants under a year of age, amount to 27 (Table 1). Other cases have certainly been described, but with not enough useful details. Imamoglu et al. [15] for example, present 11 cases of BND, ranging from 3 months to 12 years of age, but not individually and extensively described.

In 1983 Berkowitz et al. described bloody nipple discharge in two infants, a boy and a girl (both 6 weeks old): both patients presented with unilateral bloody nipple discharge and mammary enlargement, without signs of local infection. At that time, no diagnostic testing, or surgical procedure was performed. The bloody discharge disappeared spontaneously over a period of a few weeks and hence the author associated the clinical findings with ductal hyperplasia caused by hormonal stimulation, i.e. both maternal hormones (estrogen and prolactin) and fetal prolactin.

In later reports on the phenomenon, physicians recounted performing invasive procedures, such as biopsies and subcutaneous mastectomies (Stringel et al.; Miller et al.; Olcay et al.; Bober et Al-Arfai et al.): thereafter specimen histology suggested that mammary duct ectasia might be the underlying cause. Subsequently researchers performed breast ultrasonography, which showed either mammary ectasia or nonspecific findings [28]. Yet in 2011 McHoney reported three pediatric cases of bloody nipple discharge, all of which underwent surgical excision of an underlying cyst. One of these cases was a six month old boy who presented with persistent bleeding for more than ten weeks and a palpable mass. Hence he underwent surgical excision of this mass. Histological examination revealed a cyst, with several dilated and fibrous ducts, which contained blood.

One major concern about bloody nipple discharge is the underlying fear of breast cancer. Researches have reported on exceptional manifestations of breast cancer in children, such as juvenile secretory or phyllodes tumors, of ages ranging from 20 months to 17 years [3], [16,13] or breast carcinomas in patients between 3 and 18 years of age [7,17]. These rare tumors are not inherited and often present as unilateral masses that slowly progress and bloody nipple discharge can occur due to spontaneous infarction of the tumor.

**Table 1. Clinical characteristics, ultrasonographic findings and outcome of reported cases of bloody nipple discharge, in infants under nine months**

Case no	Reference	Year	Age	Gender	Side	Physical findings (besides BND)	US findings	Duration of symptoms	Outcome
1	Berkowitz et al. [21]	1983	6 weeks	female	unilateral	breast enlargement	-	<9 mo	SR
2	Berkowitz et al. [21]	1983	6 weeks	male	unilateral	breast enlargement	-	1 mo	SR
3	Fenster et al. [5]	1984	8 mo	male	unilateral	non specified	-	2 mo	SR
4	Sigalas et al. [28]	1986	7 mo	male	unilateral	non specified	-	5 mo	SR
5	Stringel et al. [24]	1986	5 mo	female	n.s.	small lump	-	3 mo	SR
6	Gershin et al. [20]	1992	3 mo	female	Unilateral	breast enlargement	-	6 mo	SR
7	West et al. [33]	1995	4 mo	female	n.s.	mammary mass	-	15 days	SR
8	Phan et al. [8]	1996	2 mo	female	n.s.	breast enlargement	-	15 days	SR
9	Weimann et al. [12]	2003	8 mo	male	bilateral	normal	MDE	6 mo	SR
10	George et al. [14]	2006	3 mo	female	bilateral	normal	MDE	7 mo	SR
11	Kelly et al. [7]	2006	4 mo	male	bilateral	normal	-	5 mo	SR
12	De Praeter et al. [10]	2008	2 mo	male	unilateral	normal	MDE	15 days	SR
13	Bayrak et al. [3]	2008	3 mo	male	bilateral	soft mass	MDE, cysts	1 mo	SR
14	Gupta et al. [6]	2009	7 mo	male	unilateral	normal	normal	3 mo	SR
15	Ujiie et al. [9]	2009	4 mo	female	unilateral	normal	MDE	non specified	SR
16	JiYeon et al.	2010	4 mo	female	bilateral	normal	MDE	6 wks	SR
17	Harmsen et al. [30]	2010	9 mo	male	unilateral	normal	non specific	6 mo	SR
18	Harmsen et al. [30]	2010	8 mo	female	bilateral	normal	non specific	3 mo	SR
19	Ahmed et al.	2011	7 mo	male	unilateral	normal	non specific	1 mo	SR
20	McHoney et al. [25]	2011	6 mo	male	unilateral	normal-then palpable small mass	non specific-then cyst	non specified	surgical excision
21	Pampal et al. [11]	2012	5 mo	female	unilateral	normal	non specific	2 weeks	SR
22	Pampal et al. [11]	2012	3 mo	female	unilateral	normal	non specific	2 weeks	SR
23	Djilas et al. [4]	2012	3 mo	male	bilateral	small bilateral palpable masses	bilateral MDE	non specified	SR
24	Plesa et al. [34]	2013	5 mo	male	unilateral	normal	normal	4 weeks	SR
25	Aydin et al. [2]	2013	20 d.	male	bilateral	bilateral hypertrophy	bilateral MDE	15 days	SR
26	Affranchino et al. [1]	2013	4 mo	male	bilateral	hypertrophy	hypertrophy	6 weeks	SR
27	Affranchino et al. [1]	2013	5 mo	male	unilateral	normal	MDE	4 weeks	SR
28	Our case	2014	2 mo	male	unilateral	normal	MDE	15 days	SR
29	Our case	2014	6 mo	female	unilateral	normal	normal	5 weeks	SR
30	Our case	2014	6 mo	female	unilateral	normal	MDE	8 weeks	SR
31	Our case	2014	6 mo	female	unilateral	normal	normal	4weeks	SR

*BND: bloody nipple discharge; MDE: mammary duct ectasia; SR: spontaneously resolved*

Bacterial infections causing bloody nipple discharge, are part of the differential diagnosis [1,18,13], yet mastitis commonly presents with breast pain and erythema and usually presents before 6 weeks of age, but rarely includes bloody nipple discharge [1,4,7].

Finally pituitary adenomas often present with nipple discharge, but it usually is milky and bilateral and patients normally range between 7 and 17 years of age [19,7].

Benign discharge is in general bilateral and not spontaneous, and it occurs with breast manipulation or stimulation; whereas pathologic discharge is usually unilateral, spontaneous and persistent [13].

Typical clinical presentation of benign bloody nipple discharge is characterized by the presence of intermittent clear or serous discharge, which gradually becomes pink or bloody in the absence of any inflammatory features [20,6,7].

As mentioned above, case reports most commonly attribute bloody nipple discharge in infancy to infantile mammary ductal ectasia [21-24]: a process involving dilation of the mammary ducts, cystic lesions, periductal inflammation and fibrosis and hemosiderin laden macrophages [25], the exact aetiopathogenesis of which is not clearly understood [7].

Maternal hormones including oestrogen, progesterone and prolactin and fetal hormones such as prolactin appear to influence the ductal hyperplasia and secretion [21,24,26], however, it has been suggested that the early development of the breast is more influenced by the infant's than the mother's endocrine activity [27,26], while some authors [28], had suggested that temporary elevated progesterone level might be responsible for the bloody nipple discharge.

There are no studies in literature concerning the type of feeding in relation to bloody nipple discharge; however Kelly et al. [7] reported spontaneous resolution of the discharge after interrupting breastfeeding. Nevertheless, this state was documented in both breast-and formula-fed infants, which downgrades the role of breastfeeding in this condition [4,29].

In literature reviews, almost all patients who received only a watchful follow-up, without surgical treatment, had outcomes within 9 months suggesting that bloody nipple discharge was a self-limited condition. [13], just as our four cases prove.

Diagnostic approach and managing of nipple discharge have been discussed by quite a number of authors in the last three years. Suggestions, according to updated literature, are as follows.

Initial workup includes thorough clinical examination to assess the nature of the discharge, signs of inflammation and presence of hypertrophy or of any lump in the breast [6].

Laboratory evaluation includes: microbial examination of the discharge in the form of gram staining, microscopic examination and culture; biochemistry studies such as blood cell count, C reactive protein, coagulation, followed by hormonal analysis in the form of serum prolactin, progesterone, oestrogen and thyrotropin levels [4,30,13].

Ultrasonographic evaluation [2,6,7,13,26] and also doppler imaging are ideal and recommended for studying the pediatric subareolar region [31,30,32].

The presence of infection on microbial analysis requires treatment of mastitis and the infant should be managed consulting an endocrinologist if hormonal levels are abnormal [6,7].

Treatment of infantile bloody nipple discharge is mainly conservative: reassurance and parental counselling remains the mainstay of treatment, which results in spontaneous resolution after 3-6 months [6]. Close monitoring of infants with BND is advisable to avoid unnecessary invasive investigations [33,26].

Only if ultrasonography reveals a mass or an abnormality other than mammary duct ectasia, or if the discharge persists for more than 9 months, should further investigation, including invasive intervention, be considered [2,7].

Indeed invasive intervention including biopsy should be avoided, especially in girls, because even minimal operative injury to the breast bud may produce severe tissue damage, resulting in functional disability and persistent disfigurement [2].

Due to our experience, we suggest a "wait and see" approach from the very beginning, once clinical diagnosis has been hypothesized and performing breast ultrasounds only if spontaneous resolution hasn't occurred within expected timing or if imaging documentation is personally desired to complete first diagnostic approach. For our four cases, we applied a year clinical follow-up.

In agreement with Plesa et al. [34], we finally offer a few suggestions for the management of bloody nipple discharge in the first year of life:

- Diagnosis should be based mainly on clinical approach; ultrasound examination can be useful if resolution does not occur within expected timing or for initial diagnostic approach when personally considered.
- This condition resolves spontaneously.
- There is no relation with breast feeding.
- Manipulation of the nipple can prolong bleeding.
- Further diagnostic tests should be performed only when initial suspicion is different.
- Antibiotics should be given only in the presence of clear clinical and cytological signs of infection.
- Parent reassurance is a fundamental part of infantile bloody nipple discharge.

#### **4. CONCLUSION**

Bloody nipple discharge (BND) very rarely occurs in infants and is a rather distressing finding for both parents and consulting pediatricians. Careful review of the literature has shown that the underlying cause is mammary duct ectasia, a benign condition that resolves spontaneously.

We therefore suggest a "wait and see" approach from the very beginning, once clinical diagnosis has been hypothesized and performing ultrasound only if spontaneous resolution hasn't occurred within expected timing, or if imaging documentation is personally desired to complete first diagnostic approach.

#### **CONSENT**

Not applicable.

## **ETHICAL APPROVAL**

Not applicable.

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## **COMPETING INTERESTS**

Authors have declared that no competing interests exist.

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