Cyclic Bleeding Over Eyes Associated with Cyclic Epistaxis and Bleeding from Ears in Pubertal Females. Suggested Lacrimal Endometriosis

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Abstract

Introduction and Objective: Bilateral bleeding found over healthy eyes, in healthy pubertal females, that is cyclic and concomitant with menses, is a very rare event. Rarer is its association with cyclic epistaxis and cyclic bleeding from ears and skin bleeding.

We present a series of such cases and a trial to diagnose and manage them. Those cases remained undiagnosed for years. We also present literature review about different diagnosis and about similar cases.

Cases Report: We report a case series of 6 eyes of 3 patients, with history of cyclic bleeding over eyes. It was associated with epistaxis in two patients, with bleeding from ears in one and skin bleeding in one patient. Ages of these girls at presentation to us were as follow: 12, 13 and 20 years old. All of them reported its incidence at 12-13 years age (onset of their puberty). Bleeding was cyclic and took place around the menses time. No systemic or local disorders were found to explain this bleeding. Bilateral dacryocystography, blood and clotting profiles and CT scan for skull and sinuses, all were unremarkable. Cases were followed up as follows. Case 1 for 7 years, Case 2 for 7 years and Case 3 for 1 year.

Photographs for all cases are available. As a therapeutic test, all cases received an intramuscular injection of Triptorelin acetate (Decapeptyl CR®, Ipsen) at the first day of their menstrual cycle. Bleeding stopped in all subjects from all sites.

Discussion: This report shows 3 cases with multiple site cyclic bleeding concomitant with menstrual cycle. Bleeding occurred over eyes, from nose, from ear and skin.

After gynecological consultation and injecting Decapeptyl as a therapeutic test, bleeding stopped in all cases. This gives a clue about suggested lacrimal endometriosis. Some reports about similar cases are included. Decapeptyl is a gonadorelin (synthetic luteinizing hormone releasing hormone (LHRH) analogue. It acts on the pituitary gland in the brain and lowers estrogen levels in the blood.

Conclusion: In view of the cyclic occurrence of bleeding over eyes that was associated with epistaxis and bleeding from ears, and its association with each menstrual cycle and the disappearance from all these sites after Triptoreline (Decapeptyl CR®) injection, the diagnosis of lacrimal endometriosis could be the most likely one.

Key Words: Bleeding from eyes – Bloody tears – Cyclic ocular bleeding – Eye bleeding associated with epistaxis – Triptoreline (Decapeptyl) – Eye bleeding associated with ear bleeding – Distant endometriosis-lacrimal endometriosis.

Introduction and Purpose

In this paper, we present a case series that have the following characteristics: patients are females, around and after puberty. They had spontaneous intermittent bleeding over eyes, starting most of the time during sleep, and concomitant with menstrual cycle. The bleeding sometimes was bilateral, and when it was washed, eyes looked completely normal. It was sometimes associated with bleeding from nose and from ears and sometimes from skin. No systemic problems were present in these females and no positive history of drug intake or trauma or hospital admissions. Those cases remained undiagnosed for years and patients consulted many physicians of different specialties (Eye doctors, ENT doctors, Gynecologists, Internists, Radiologists and Lab physicians). After every visit to all physicians, they were told that they are clinically free. We present a differential diagnosis and literature review of related conditions.
Bleeding over eyes or bloody tears is an unusual clinical entity that concerns patients and can perplex physicians. It could be idiopathic and of unknown cause and occurs in both sex. Four cases were reported [1] that had recurrent unilateral bloody tears. They were one boy and 3 girls, ranging in age from 6 to 14 years, reported spontaneous bloody tearing. Workup included probing and irrigation of the nasolacrimal system, blood and coagulation profiles, blood typing, serum hormone levels, conjunctival biopsy, and imaging. All findings were normal and failed to suggest a cause in any of the cases. In all patients, bloody tearing eventually resolved without further sequela. No recurrence has been reported over a follow-up period of 9 months to 11 years. These idiopathic cases typically resolved without treatment [1].

Bloody tears and spontaneous bleeding over eyes could also be produced by systemic or local disorders like Reactive lymphoid hyperplasia of the nasolacrimal duct presenting as bloody epiphora [2], localized orbital amyloidosis involving the lacrimal sac and nasolacrimal duct [3], congenital factor VII deficiency [4] and hereditary hemorrhagic telangiectasia or Rendu-Osler-Weber disease [5,6]. In this last disorder [5], one patient was a 45-year-old woman who had recurrent episodes of hematic epiphora, repeated epistaxis for which no cause was found and a family history of gastric hemorrhage. One of her daughters also suffered from spontaneous hemorrhages.

The occurrence of bloody tears occurring spontaneously in a patient with epistaxis or gastric hemorrhage should lead to suspicion of hereditary hemorrhagic telangiectasia or Rendu-Osler-Weber disease [5].

Hereditary hemorrhagic telangiectasia [6] (Osler-Weber-Rendu disease) remains a challenge for all clinicians, as in about 80% of cases nasal bleeding is the first manifestation of this disease, which is characterized by a clinical triad of multiple telangiectasias, recurrent hemorrhages and familial occurrence. A cure for this rarely life-threatening but often burdening and handicapping disease is still not possible [6].

An important differential diagnosis for bleeding over eyes or bloody tears is subconjunctival hemorrhages. According to an epidemiological study [7], it was found to be 58 (0.8%) of 6843 consulting patients examined between 1999-2004 in Congo. It was found to be spontaneous in 28 patients (48.3%) or traumatic in 30 patients (51.7%). It was unilateral in 90% of eyes. In spontaneous cases, no apparent associated condition was found in 64.3%. Hypertension (14.3%) was the most frequent associated condition. Other associated conditions were rare and included vomiting, sneezing, malaria, hypoglycaemia, sickle cell disease and delivery.

Other studies [8] showed that the incidence of subconjunctival hemorrhage is 2.9%, and that most common cause was local trauma, systemic hypertension and acute conjunctivitis.

Bilateral subconjunctival hemorrhage was reported after acetylsalicylic acid overdose [9] and after Warfarin therapy [10].

Another possibility and cause for bloody tears or spontaneous bleeding over eyes is presumed distant lacrimal endometriosis.

Endometriosis [11] (from endo, "inside", and metra, "womb") is a medical condition in women in which endometrial cells are deposited in areas outside the uterine cavity. This tissue, possessing the same steroid receptors as normal endometrium, is capable of responding to the normal cyclic hormonal milieu. Microscopic internal bleeding, with the subsequent inflammatory response, neovascularization, and fibrosis formation, is responsible for the clinical consequences of this disease. In the typical patient, the ectopic implants are located in the pelvis and manifest as severe dysmenorrhea, chronic pelvic pain, or infertility. More unusual systemic implantation sites can be responsible for bizarre symptoms such as cyclic hemoptysis and catamenial seizures. The hormonal responsiveness of the implants can be exploited and provides the rationale for current methods of medical therapy [11].

It has many digital names [12]. In the International Classification of Diseases number 9 (ICD-9), it has this digital name: 617.0. In the ICD-10, it is named: N80. In Online Mendelian inheritance in man (OMIM), it has this name: 131200. In diseases data bases it is named: 4269. In Medline Plus it is named: 000915. In eMedicine it is named: med/ 3419, ped/677 and emerg/165. The different systemic loci for endometrial implants, according to the ICD-9 [13], are shown in Table (1).

It is remarkable that this international classification did not report any cases of bleeding from eyes or nose or ears.
### Table 1: Locations of endometriosis in the ICD-9, the latest international classification of diseases, 2008.

<table>
<thead>
<tr>
<th>Disease (site of endometriosis)</th>
<th>Code</th>
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<th>Code</th>
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<tbody>
<tr>
<td>Appendix</td>
<td>617.5</td>
<td>Cul-de-sac (Douglas')</td>
<td>617.3</td>
</tr>
<tr>
<td>Bladder</td>
<td>617.8</td>
<td>Exocervix</td>
<td>617.0</td>
</tr>
<tr>
<td>Bowel</td>
<td>617.5</td>
<td>Fallopian tube</td>
<td>617.2</td>
</tr>
<tr>
<td>Broad ligament</td>
<td>617.3</td>
<td>Female genital organ NEC</td>
<td>617.8</td>
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<tr>
<td>Cervix</td>
<td>617.0</td>
<td>Gallbladder</td>
<td>617.8</td>
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<tr>
<td>Colon</td>
<td>617.5</td>
<td>In scar of skin</td>
<td>617.6</td>
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<tr>
<td>Intestine</td>
<td>617.5</td>
<td>Rectovaginal septum</td>
<td>617.4</td>
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<tr>
<td>Lung</td>
<td>617.8</td>
<td>Rectum</td>
<td>617.5</td>
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<tr>
<td>Myometrium</td>
<td>617.0</td>
<td>Round ligament</td>
<td>617.3</td>
</tr>
<tr>
<td>Ovary</td>
<td>617.1</td>
<td>Skin</td>
<td>617.6</td>
</tr>
<tr>
<td>Parametrium</td>
<td>617.3</td>
<td>Specified site NEC</td>
<td>617.8</td>
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<tr>
<td>Pelvic peritoneum</td>
<td>617.3</td>
<td>Stromal (M8931/1)</td>
<td>236.0</td>
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<tr>
<td>Peritoneal (pelvic)</td>
<td>617.3</td>
<td>Umbilicus</td>
<td>617.8</td>
</tr>
<tr>
<td>Uterus (internal)</td>
<td>617.0</td>
<td>Vagina</td>
<td>617.4</td>
</tr>
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</table>

The prevalence of endometriosis in the general population is estimated to be 10 percent. It is as high as 45 percent in women of reproductive age. A much higher prevalence of up to 82 percent occurs in women with pelvic pain, and in women undergoing investigation for infertility the prevalence is 21 percent [14].

Several theories have been suggested to explain the pathogenesis of endometriosis. The most widely held theory involves the retrograde reflux of menstrual tissue from the fallopian tubes during menstruation. Two other possibilities are the celomic metaplasia and embryonic rests theories. Celomic metaplasia hypothesizes that the mesothelium covering the ovaries invaginates into the ovaries, then undergoes metaplasia into endometrial tissue. The embryonic rests theory hypothesizes that Müllerian remnants in the rectovaginal region differentiate into endometrial tissue [14,15].

### Theories for distant endometriosis:

Uterine contractions quiet possibly force endometrial cells into the lymph channels and blood vessels that are in and around the uterus and then ship the cells the endometrial cells up into the pelvis or other far-off places, such as the lungs or brain. This theory makes somesense because the uterus is rich in lymphatics and blood vessels [16].

### Other international reports about similar cases:

After intensive search of literature, three international reports about three cases were found, one [17] about a case 17 years, from Egypt at 1971, PRESENTED WITH bilateral bleeding from both eyes concomitant with menses and there were no stemic or local reasons to explain after thorough examinations and investigations (and the diagnosis was called vicarious menstruation). Another one [18] about a patient 13 years old at 2006, from Turkey (the diagnosis was named nasolacrimal endometriosis) and a third report [19] about a case at 2008 also from turkey (also the diagnosis was named presumed nasolacrimal endometriosis).

### Cases report

Before presenting to us at year 2002, this clinical disorder stayed unexplained for few years and patients consulted many doctors of different specialties to find a cure, but without any success. All physicians (Ophthalmologists, ENT specialists, and gynecologists, radiologists and lab doctors) concluded that they are normal and found no explanation for the bleeding. The girls used to have this bleeding over eyes mostly at night (when lying down and no effect of gravity is present), at the morning they wash their faces and go to doctors. Desperately, they have been thinking about solutions in alternative medicine or going to the non medical, non-scientific, so called (al Zar dancing mixed with religious beliefs and rituals practiced by low class non-educated people). All the patients had anxiety and depression and lost their trust in medical profession, since no body could help them stopping this cyclic shameful bleeding over their eyes and nose.

### Cases descriptions:

#### Case 1:

This case was fully studied and showed compliance with our instructions.

Condition started with onset of her puberty, when she was 12 years old. She presented to us 3 years later. Bleeding over her face and eyes, occurred around the period time (few days before, during or after). Fig. (1), shows the patient. She was intelligent and made a table that describes accurately the timing of menses, timing of the bleeding and its sites. She reported pain around
the eyes and the nose perimenstrual, then bleeding occurred. It occurred over her left eye most of the time, sometimes over her right eye, sometimes from her nose and sometimes she got skin bleeding (skin bleeding was not photographed, but indicated in the table she presented to us in Arabic language). She had psychic upsets and depression. All her family were anxious about her and wondered if this would affect marriage, fertility and her social life and future. On frequent physician consultations. they examine her, nothing abnormal is seen. She stayed like that for 3 years. Physicians prescribed systemic medicines to reduce bleeding and strengthen capillaries, like cyclokapron, konakion, and iron therapy.

**Description of bleeding:**
- Timing: anytime during period, occurred mostly during sleep.
- Site of exit: puncti of both eyes- nose- skin.
- Colour: dark or fresh red.
- Odour: no odour.
- Pain: sometimes present at the brows, forehead, occiput especially during the bleeding attack.
- Association: hard scales or fragments like chips of finger nails (Fig. 1).
- The scales were repeated several times.

**Relation to menses:**
- Onset: 3-7 months after menarche. Stay: one day up to 6 consecutive days.
- Concomitant with menstrual flow. Duration of menses: ranged between 4-6 days.

**Ocular examination:** External eye and fundus examinations revealed no abnormalities in both sides.

**Investigations done:**

Pelvic ultrasonography: Normal uterus and left ovary. The right ovary: prolapsed in the Douglas pouch. Lt. ovarian endometriosis 20X22 mm seen with ground glass appearance.

CT Scan (brain and sinuses): Examination of the paranasal sinuses and orbits with standard brain cuts: mild deviation of the bony nasal septum to the left side. Otherwise, normal study.

Tc 99m Dacryocystography (DCG): Showed normal tear flow kinetics in the lacrimal pathways of both sides.

**Pathologic examination of the associated hard scales (Tissue Fragments):**

Sections reveal epithelial tissue composed of acanthotic hyperkeratotic squamous cells. There is underlying sever infiltration of neutrophils with many vascular spaces, no malignant changes.

**Blood picture, coagulation studies:** Coagulation profile was normal in all cases with good prothrombin time.

**Therapeutic test:**
- Triptoreline (Decapeptyl CR) injection was given intramuscular (IM) in the 1st day of the cycle. One week later red tears recurred for one day then disappeared.
- Another injection of Decapeptyl CR was given after one month.

**Recurrence:** 1 year ago (during 2007), she contacted telling about recurrence of one bleeding attack. She was advised to have the injection again.

**Case 2:**

This case presented to us also, at year 2002. She was 13 years old. She showed her photos (Fig. 2). They show bilateral bleeding from both eyes, coming from the inner canthal areas (where puncti are there) and associated with ear bleeding. We asked her to make some investigations and told her about the injection, but she did not comply with our instructions and disappeared for 7 years. She presented again showing her photos in (Fig. 3), with frank bleeding, from both eyes, coming from inner angles of eyes. This time, being 20 years old, she asked for the injection. Once she got Decapeptyl IM injection, bleeding stopped. She gave similar description of bleeding periodicity and relation to menses. Like patient in case 1.

**Case 3:**

This patient presented to us the last year. She was 20 years old. We asked her to bring photographs showing the bleeding (Fig. 4). Bleeding is seen over both eyes bilaterally and is seen coming from the inner angles where puncti are present. Bleeding is shown also coming from her nose. The eye itself appears normal. Blood investigations and pelvis ultrasonography were also normal.

She stayed for years complaining of this bleeding, without any help from physicians. Once she got intramuscular Decapeptyl, bleeding stopped.
Fig. (1): Case 1 patient with bleeding over eyes, as she reports coming from the inner angles (places of lacrimal puncti). Photos on the left side when she was 12 years old. That on the right top when was 15 years old. Right bottom shows scales found in the blood clots.

Fig. (2): Case 2 patient with bleeding from both eyes and associated with ear bleeding.
Fig. (3): Case 2 patient, presented when she was 20 years old. She made this image by camera of her mobile. Bilateral bleeding coming from inner canthi area.

Fig. (4): Case 3 patient with bleeding over both eyes, coming from the inner angles and associated with epistaxis. The eye itself looks normal.

Discussion

In this article, we reported 6 eyes of three patients who had bilateral bleeding over eyes, in pubertal females. This bleeding was cyclic and concomittent with their menses. It was sometimes associated with epistaxis and from the ear. Skin bleeding was reported also from case number 1.

It is noted that bleeding at these sites was not yet included in the international classification ICD 9.
In this paper, we had made an overview of the available literature about possible causes of bloody tears or subconjunctival hemorrhage. Also an overview of of endometriosis and its theories is provided.

The cyclicity of the bleeding and its association with menstrual flow as well as the disappearance when Decapeptyl CR was given, gave the possibility of lacrimal endometriosis.

Decapeptyl SR injection contains the active ingredient triptorelin acetate, which is a synthetic type of medicine known as a gonadorelin (LHRH) analogue. It acts on the pituitary gland in the brain. The pituitary gland produces and stores various hormones, including the sex hormones, luteinising hormone (LH) and follicle-stimulating hormone (FSH). In women, FSH and LH cause the production of oestrogen by the ovaries and help control the menstrual cycle. The amount of LH and FSH released from the pituitary gland is controlled by another hormone, called gonadorelin (LHRH).

Gonadorelin acts on LHRH receptors in the pituitary gland, causing the release of LH and FSH and hence the subsequent production of testosterone in men and oestrogen in women.

Initially, triptorelin causes an increase in the amount of FSH and LH released from the pituitary gland, with resulting increase in testosterone production in men, and oestrogen production in women. However, chronic administration of triptorelin desensitises the pituitary gland. This means that it produces less and less FSH and LH, which in turn stops the production of oestrogens in women and testosterone in men. This reduction in the levels of sex hormones caused by triptorelin is used to treat disorders that are linked to levels of oestrogen or testosterone. In women, endometriosis and uterine fibroids are treated with triptorelin. The growth of the endometrium is stimulated by oestrogen, so decreasing oestrogen levels with triptorelin will stop the growth of this tissue, thereby relieving symptoms. Triptorelin is given as a monthly or three-monthly injection for six months to treat endometriosis, starting in the first five days of the menstrual cycle.

Unfortunately biopsy from the interior of the lacrimal sac, the suggested place for endometrial implants, needs technical instruments that are not available.

Other causes of bloody tears were considered and were excluded from our patients like Hemangioma, Fibroma, Hereditary hemorrhagic telangiectasia, Inflammatory granuloma, Malignant melanoma, Orbital and conjunctival amyloidosis, Metastatic carcinoid tumour, Sever conjunctivitis with hyperemia. Also all causes of subconjunctival hemorrhage mentioned in the introduction, were excluded from subjects of this report.

Also other causes of epistaxis had to be excluded like: Idiopathic, Rhinoscleroma (early stages), Nasopharyngeal angiofibroma, Sarcoidosis of the nose, Trauma.

Lacrimal endometriosis with the occurrence of cyclic red tears and epistaxis may be a window to predict pelvic endometriosis which could occur in these three cases.

Unfortunately biopsy from the lacrimal sac needs technical instruments that are not available.

Summary:
The cyclicity of the bleeding and its association with menstrual flow as well as the disappearance when Decapeptyl CR was given, gave the possibility of lacrimal endometriosis.

Conclusion and recommendations:
In view of the cyclic occurrence of bleeding and epistaxis with each menstrual flow and the disappearance after Decapeptyl CR injection, the diagnosis of lacrimal endometriosis could be the most likely one.

Lacrimal endometriosis with the occurrence of cyclic red tears and epistaxis may be a window to predict pelvic endometriosis which could occur in these three cases.

References
Cyclic Bleeding Over Eyes Associated with Cyclic


