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REVIEW ARTICLE

Main clinical manifestations of a bleeding diathesis: an often disregarded aspect of medical and surgical history taking

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Summary. A suitable clinical evaluation of a bleeding diathesis is often forgone. The young doctor is often unprepared to describe in an accurate way the different types of bleeding. An adequate classification and adequate clinical information about a bleeding diathesis are instead of paramount importance. Bleeding may be cutaneous, mucous, articular, muscular, parenchymal, intracavitary, orificial. Each of these sites and forms may have diagnostic implications. An accurate description of the several forms of cutaneous bleeding (petechiae, purpuric spots, ecchymosis, haematomas, etc.) is needed for referrals and for controls. The correct evaluation of cutaneous bleeding manifestations of children (battered child syndrome) is absolutely important for clinical and medico-legal purposes. The same is true for the battering syndrome seen in women abused by their spouses. The grading of haemarthrosis in haemophilia patients is important for the follow-up. A proper description of haematuria is essential in suggesting the probable site of bleeding (kidney or bladder or urethra). A proper evaluation of bleeding may give also useful information on the general health status of the patients (presence of anaemia, poor nutrition, renal insufficiency, etc.). The combination of bleeding and thrombosis in the same patient is also a clinical challenge. The relationship between haemorrhage and thrombosis may be sequential or concomitant. Sequential thrombosis may occur in a patient confined in bed for a brain haemorrhage. Concomitant thrombosis and bleeding occur in DIC and in patients with thrombosis being treated with anticoagulants. Finally, it should be kept in mind that a proper evaluation of the bleeding diathesis of a given patient may help the caring doctor in ordering appropriate laboratory tests (e.g. a platelet count for petechiae, a PTT for a patient with haemarthrosis, etc.).

Keywords: bleeding, clinical picture, diathesis, signs and symptoms

Introduction

The clinical approach to the bleeding patients has received lesser and lesser attention over the last two decades. Due to the widespread and increasing use of laboratory facilities there is today the tendency among internists, haematologists and even coagulation experts to disregard the clinical approach to the patients. Often, even in Physical Diagnosis or Semiology major textbooks the subject is treated in a cursory way [1–5]. Even internal medicine and most haematology textbooks seem often deficient in this regard [6–9]. Some information may be gathered only from books dealing exclusively with coagulation-related problems or diseases [10–16]. Even the latter are scanty. Few have dealt in a systematic way with the problem [17,18]. Young doctors or medical students barely know, if asked, the different forms of cutaneous bleeding. This is wrong for several reasons, namely:

1 Bleeding patients may present with peculiar patterns which could orient the doctors towards the correct diagnosis.
2 Atypical or complex bleeding manifestations may suggest non-coagulation-related conditions. In fact, excessive bleeding often occurs even in the absence of any systemic alteration of blood coagulation.
3 Bleeding pattern may be repetitive in a given patient. It may be variable and this may also have significance.

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4 The bleeding patient may harbour co-morbid conditions besides the one responsible for the bleeding. These confusing events are relatively rare in haemophilia A or B and in other rare coagulation disorders as their basal condition is usually sufficient to explain the findings.
5 Bleeding in any area or part of the body may have systemic causes (e.g. a congenital or acquired coagulation disorder) or it may have local, non-coagulation-dependent causes.

A correct semiological approach to the bleeding patient should follow the established patterns of a proper clinical evaluation. This consists of (i) a proper medical history, (ii) a careful evaluation of forms and types of bleeding (present illness) and (iii) a general physical examination (Tables 1–4).

A proper medical history for bleeding disorders should be gathered along the following lines [16–18].

Table 1. Correct approach to the bleeding patient.

Family history (more than one patient affected)
Type of bleeding (petechiae, haematomas, GI bleeding, haematuria)
Duration and pattern of bleeding (repetitive, spontaneous)
Age at onset of symptoms
Exclusion of common acquired conditions (cirrhosis, hypertension, anticoagulant drugs)

Table 2. Important clues for a proper evaluation of bleeding.

Acute or chronic bleeding
Type of bleeding (hidden, overt)
Basal Hct level
Clinical alertness of caring doctor
Proper appreciation of initial symptoms by patient

Table 3. Evaluation of severity of acute bleeding.

Mild: no change in Hct
Moderate: 2–5% decrease in Hct
Severe: 5–20% decrease in Hct
Life-threatening: 20–35% decrease in Hct

Family and past history

1 Is there a positive history for a bleeding tendency in the family? If yes, what type and what is the hereditary pattern? Do symptomatic family members show the same intensity of bleeding manifestations or not?
2 Past personal history for undue bleeding. Has the patient had haemostatic challenges (tooth extraction, surgery, tonsillectomy, delivery, etc.)? Has he or she ever been transfused?
3 What type of bleeding was present (cutaneous, haematuria, etc.)?
4 Did bleeding condition change with time?

Forms and types of bleeding (present illness)

1 Recent bleeding manifestation: modality of onset, type, intensity (less or more than usual), difference, if any, from previous patterns.
2 Assumption of medications (ASA, non-steroid anti-inflammatory drugs, ticlopidine, etc.).
3 Recent illness (infections, traumas, etc.).
4 Drugs or other procedures taken or carried out for the present bleeding (antifibrinolytics, vitamin K, nasal tamponade, compression, etc.).
5 Recent transfusions.

Physical examination

A proper physical examination of bleeding patients should include:
1 general status evaluation (pallor, dyspnoea, hypertension, state of consciousness, swelling of the abdomen, etc.).
2 a specific evaluation of bleeding manifestation as previously detailed.

The manifestation of bleeding may be subdivided into:
1 cutaneous,
2 mucosal (respiratory, oral and gastrointestinal, urinary tract, genitourinary tract)
3 muscular,

Conjunctival ecchymosis	Hypertension, thrombocytopenia, anticoagulants
Petechiae (skin or mucosae)	Thrombocytopenia
Papular lesions in legs	Cryoglobulinaemia, SH, other purpuras
Mucosal	Rendu-Osler, VWD, platelet disorders
Haematomas	Single factor congenital deficiency, circulating anticoagulants, traumas
Haemarthrosis	Haemophilia A and B, and less frequently, in FII, FVII or FX deficiency
Easy bruising	Thrombocytopenia, Cushing's disease

Table 4. Diagnostic clues obtainable by means of proper evaluation of type or site of bleeding.

4 articular,
5 intraparenchymal (brain, spleen, liver, etc.),
6 intracavitary (abdomen, pleura, etc.),
7 bleeding in unusual sites,
8 bleeding with thrombosis.

Bleeding in any part and in any form may be due to congenital or acquired conditions [16–19]. The bleeding patient should be properly and extensively evaluated [20–23]. Important clues that may allow one to decide which type of bleeding one is confronted with are featured in Tables 5–8.

Table 5. Clinical clues for an acquired bleeding disorder.

Negative family history
Presence of associated diseases
Variable in time
Variable in aspect and type
Onset usually in middle age or later

Table 6. Clinical clues for congenital bleeding disorders.

More than one patient in the family is affected
Hereditary pattern
Onset at early age
Positive history for blood transfusion
Rather fixed pattern of bleeding

Cutaneous bleeding

These are the most common and most important bleeding manifestations. The general term by which skin bleeding is defined is purpura. In reality skin haemorrhage may and should be subdivided into purpuras, easy bruising, haematomas and massive cutaneous bleeding (Table 9) [24–27].

The most important ones are probably the purpuras (Table 10). Bleeding in the skin is due to an extravasation of red blood cells in perivascular spaces. These skin haemorrhages or purpuras could be, in general terms, divided in non-palpable purpuras and palpable purpuras if they cannot be appreciated by a careful palpation of the area; palpable if they can be appreciated as a skin elevation respectively [23,28,29]. Among the causes of non-palpable purpuras we may list livedo reticularis, coagulation disorders, steroids, cryoglobulinaemia and erythrocyte autosensitization. On the contrary, among the causes of palpable ones we have vasculitis, infections, Schnlein-Henoch and urticarial forms. It has to be remembered that distinction is not always absolute depending on preexisting condition of skin and severity of the form. The main features and/or subtypes of purpuras are: (i) the petechiae, (ii) the purpuric lesions or spots and (iii) ecchymosis.

Table 7. Type of bleeding in main congenital bleeding disorders.

Defect	GI	Joints	Cerebral	Muscular	Skin and mucosae	Urinary tract
Fibrinogen defects	+	+	++	+	+	++
Factor II, VII, X	+	+	++++	++	+	++
Haemophilia A and B	+	++++	++	++	+	++
VWD	+++	+	+ −	+	+++	+

Table 8. Clinical features of bleeding in main acquired conditions.

Condition	GI	Joints	Cerebral	Muscular	Skin and mucosae	Urinary tract
Coumarin-induced	+	+ −	++	++	++	++
Heparin-induced	++	+−	++	+++	+++	++
Liver failure	++++	+ −	+ −	++	+++	+
Thrombocytopenia	++	+ −	+	++	++++	+
Hyperfibrinolysis	++	−	++++	++	++	++

Table 9. Problem of semantics.

Petechia	Discrete, pinhead-like, <2 mm in diameter, which do not coalesce but often cluster in peculiar sites
Purpuric spots or lesions	3–4 mm in diameter, resulting often from confluence of many petechiae in a particular area or spot
Ecchymosis	Irregular, variable, patch-like haemorrhagic skin lesions, larger than 1 cm with tendency to coalesce. No modification of profile of skin
Haematomas	Musculo-cutaneous haemorrhage forming a mass that modifies profile of the skin surface and is also palpable and hot
Haemarthrosis	Bleeding in joints
Easy bruising	Susceptibility to several skin haemorrhagic contusions even after minor traumas

Table 10. Main causes of purpuras.

Coagulation disorders, thrombocytopenia, thrombocytopathy, other coagulation defects
Drugs (steroids, heparin, warfarin)
Vasculitis (livedo reticularis, erythema nodosun, SH, polyarthritis nodosa)
Infections (meningococcal, Rocky mountain fever, scarlet fever)
Dysproteinemias (amyloidosis, Waldestrom, cryoglobulinaemia)
Vascular fragility (Ehlers-Danlos, Scurvy, cortisone therapy)
Embolization (fat emboli, atrial mixoma, endocarditis)
Miscellaneous (erythrocyte autosensitization or psychogenic purpura, trauma, solar purpura, purpura simplex)

Petechiae are small, <2 mm in diameter, pinhead lesions, frequently present in the limbs and in skin folds. Oral mucosal petechiae may be an index of particularly severe thrombocytopenia. The main cause of petechiae is thrombocytopenia of any cause. Petechiae may occur in waves, in accordance with the variation of platelet count. If platelet count improves they may disappear without leaving any trace in 2–3 days. If they persist for several days they may tend to coalesce and give the appearance of ecchymosis. They are often associated with easy bruising.

Purpuric spots are irregular lesions, larger than petechiae (about 3–6 mm in diameter), usually localized in the lower limbs and with a variable tendency to coalescence. The most important causes are Schnlein-Henoch purpura and mixed cryoglobulinaemia. In the latter case they may be associated with rusty coalescing spots of the skin. The sites of the purpuric lesions may vary and this may suggest a specific diagnosis (Table 11).

The large numbers of non-coagulation-related idiopathic purpuras (Schamberg, Gougerot-Blum, etc.) may be included in this group, even though sometimes the skin lesion is larger. The differentiation from ecchymoses is based on the fact that these lesions do not show signs of red blood cells extravasation. Therefore, the lesions do not undergo the typical colour changes due to the in loco transformation of haemoglobin.

Ecchymoses are large, irregular extravasations of blood (diameter is more than 6–7 mm). They often occur in exposed sites (e.g. limbs, hips, etc.). They may coexist with petechiae and purpuric spots. The main causes of ecchymosis are thrombocytopenia, cortisone therapy and erythrocyte autosensibilization or psychogenic purpura (Gardner-Diamond syndrome), several types of purpuras (senile, liver failure, etc.).

Table 11. Differential diagnosis of most frequent purpuras.

Type	Arms	Mucosae	Skin folds	Legs
Senile	++	+	+	+ −
Cortisone-induced	++	+ −	+ −	++
Thrombocytopenia	++	++	++++	++
Cryoglobulinaemic	+ −	+ −	+	++++
Schnlein-Henoch	+ −	+−	+	++++
Scarlet fever (infectious)	++	+	++++	+

'Easy bruising' is a general term that indicates a tendency presented by a given patient to have variable skin lesions, usually ecchymosis or, more rarely haematomas of different size and location, due to even minor traumas.

Skin lesions usually occur in areas prone to minor traumas in everyday life (arms, legs, hips). The patient is often unaware of the cause of the lesion. Main causes are thrombocytopenia by any cause, Cushing's syndrome, senile vessel fragility and coagulation disorders.

A proper evaluation of ecchymotic lesions and of easy bruising has became important in recent times because of the abused or battered child syndrome [30–34]. The condition is apparently, judging from the available literature on the subject, more frequent in the USA and in England. It is of paramount importance in these cases to evaluate the relationship between the haemorrhagic lesion and the purported trauma which, allegedly, are claimed by parents, relatives or baby sitters to be the cause of it. The lack of correlation between the site and entity of lesions and the alleged trauma must raise suspicion. Doctors have to be very alert because, often persons who accompany the child to the ER or office are those responsible for the lesions. They often tend to minimize the nature of the trauma. This could suggest, in the mind of an inexperienced doctor, that the child has an underlying congenital coagulation disorder. This may be the case, but it is uncommon. Usually the entity of the battering was in reality much more important than what claimed and it is the agent responsible for the haemorrhagic lesions. These are usually ecchymotic in nature but may appear also as coalescing haematomas. Strictly related to the battered child syndrome is the 'battering syndrome' seen in women or, more rarely, in men, as a result of abuse by their spouses or other family members (domestic violence) [35–37]. The same may occur in aged people, often confined in nursing homes or in hospitals, but occasionally, even if kept at home, due to abuse by family members or other caring persons. In this form, however, due to the frequent concomitant presence of a senile purpura and multiple organ impairment due to age, ecchymotic lesions may be larger and bone fractures may be present. Diagnosis may be difficult because of denial of caring persons and because of poor cooperation on part of the patient.

Haematomas

Haematomas are conditions resulting from sufficient extravasation of blood, thus producing a pronounced elevation of the skin and a palpable mass. Margins are irregular and the mass is red at first, later shades into a brownish blue, then bluish and finally green-yellowish. In about 10 days they fade out completely without leaving any trace. Haematomas are seen in congenital bleeding disorders such as haemophilia A or B, other factor deficiencies, acquired haemophilia (circulating inhibitors), acquired von Willebrand's disease (VWD), and in erythrocyte autosensibilization. They may be spontaneous or post-traumatic. Sometimes they may be so important and repetitive so to cause the appearance of anaemia.

Cutaneous bleeding (easy bruising, ecchymosis and haematomas) may occasionally be self-inflicted (factitious illness). This may be part of the Munchausen syndrome and is always a diagnostic challenge. The main features that could suggest this diagnosis are personal or family psychiatric traits, localization of bleeding manifestation only in areas that can be reached by the arms of the patient, or lack of any other causal event. It is usually a diagnosis of exclusion. The self-inflicted cutaneous bleeding manifestations may be caused by trauma, subcutaneous injection of several substances, tight strapping, etc. Occasionally indurations or nodes are palpable underneath the ecchymotic area. It could be confused with an erythrocyte autosensibilization or psychogenic purpura [38]. Denial on part of the patient is the rule and psychiatric assistance is indicated. Strictly associated with this condition are the cases of bleeding diathesis caused by surreptitious administration of coumarin drugs to children (Munchausen syndrome by proxy). The child may present with various cutaneous bleeding manifestations which are a diagnostic challenge [39].

Oozing

Oozing indicates the continuous, even though not massive, loss of blood from vein puncture sites or wounds. Therefore, it should be treated among the cutaneous haemorrhagic manifestations. However, oozing may be seen during surgery from any internal surgical procedure. In this latter case it is usually due to lesions of the small vessel (bleeders). As far as the cutaneous form is concerned, it is often due to hypofibrinogenemia and/or thrombocytopenia, by any cause, to FXIII deficiency, and to iatrogenic or spontaneous hyperfibrinolysis. The pathogenetic base is the lack of formation of an adequate haemostatic plug. The frequent bleeding from the umbilical stump seen in infants with afibrinogenemia or FXIII deficiency may be considered a sort of oozing.

Massive cutaneous bleeding is characterized by large ecchymotic area associated or not with large haematomas that may involve up to one-third or two-thirds of the entire skin. Necrotic changes of skin are often present and this may lead to an expholiative pattern. It may be seen in warfarin-treated patients who are deficient in protein C, or protein S, in severe DIC and meningococcal sepsis.

Rare forms of cutaneous bleeding

In patients with severe coagulation disorders, both congenital and acquired, sometimes any rash, macula, papule, nodule, pustule, vescicle, plaque, crusts may assume a haemorrhagic hue or discoloration. This may cause diagnostic difficulties. For example a haemorrhagic Varicella has been described in a patient with severe factor V deficiency [40].

Mucosal bleeding

Mucosae cover several apparati and anatomic structures and it may be useful to subdivide mucosal bleeding according to the system involved, namely: (i) gastrointestinal, (ii) respiratory tract, (iii) urinary tract, (iv) utero-vaginal tract, (v) eyes and (vi) the external auditory canal. It could be termed also 'orificial bleeding'.

It may be spontaneous, as epistaxis, haemoptysis or secondary to local disease (ulcers, tumors, traumas, etc.). It is frequent in three conditions: thrombocytopenias, (together with skin haemorrhages), Rendu-Osler disease and VWD.

Rendu Osler may be suspected on the basis of an autosomal dominant inheritance, by repeated mucosal bleeding and by the presence of small capillary ectasias in the areas of junction between mucosa and skin (perioral area). The association between Rendu-Osler and VWD is not uncommon.

Digestive tract bleeding may be subdivided into oral, gastrointestinal and rectal. Oral bleeding usually is secondary to the presence of petechiae, to gingival bleeding or to rupture of sublingual varicose veins. Main causes are thrombocytopenias, other clotting defects and venous stasis. It may also occur in normal subjects (vigorous tooth brushing).

Swelling and bleeding of gingival may be seen also in lead toxicity, phenytoin therapy, leukaemia, traumas and agranulocytosis. The presence of an underlying coagulation defect aggravates gingival bleeding.

Gastrointestinal bleeding is characterized by haematemesis, melena or haematokezia. These are probably the most frequent, together with skin bleeding and haemorrhage manifestations. Ruptured oesophageal varices, gastric ulcers or cancers and duodenal ulcer are the commonest causes. In these cases bleeding is usually acute and important. Oesophageal hiatus hernias, carcinoma of the right colon, Meckel's diverticulum and haemorrhoids are usually the main causes of chronic anaemia. With the exception of haemorrhoids, diagnosis in these cases may be difficult as the patient may otherwise be asymptomatic or paucisymptomatic. Bloody stools accompanied by cramps and colicky pain may be seen in colon diverticulitis, ameliosis, ulcerative colitis and Crohn's disease.

Respiratory tract bleeding is characterized by haemoptysis. This occurs usually with cough and may consist of pure blood or may result from a variable mixture of phlegm or sputum and blood. Usually the amount of blood loss is limited (initial tbc, bronchial adenomas, pulmonary infarction, etc.) but it may be massive (rupture of an aneurism within a cavitation induced by aspergillosis or advanced tbc) (Table 12).

Haemoptysis should be considered in the context of the presence of other local or systemic symptoms and signs (e.g. fever, cough, mitral valve defect, etc.).

Urinary tract bleeding

Bleeding from the urinary tract is defined as haematuria. This is an important clinical sign and symptom which has widespread significance beyond a bleeding diathesis. It often occurs in non-coagulation-related disorders.

Haematuria may be subdivided into upper urinary tract haematuria and lower urinary tract haematuria. They are important clinical clues for a correct clinical diagnosis.

Upper urinary tract bleeding is usually not accompanied by any other signs or symptoms. It is often sudden in onset. Occasionally there is a lumbar pain and tenderness. It is often massive and in this case urine is uniformly haemorrhagic.

Table 12. Main causes of haemoptysis.

Tbc and other bacterial infections (pneumonias)
Fungal infections (aspergillosis)
Tumours
Mitral valve defect with secondary pulmonary stasis
Congenital or acquired bleeding disorders (Rendu-Osler, thrombocytopenia, etc.)
Vasculitis (Wegener, Goodpasture)
Idiopatic pulmonary haemosiderosis

On the contrary, lower urinary tract bleeding is often accompanied by strangury, dysuria and pollakiuria. In this case, bleeding occurs often at the end of micturation. Urethral bleeding occurs usually at the beginning of micturation. Bleeding due to stones is accompanied by a renal colic and it is usually modest in entity. Other important clinical features of haematuria are upper urinary tract (acute nephritis, renal cancer, coagulation disorders) or lower urinary tract bleeding (cancer of bladder, prostate), sudden appearance with no other signs or symptoms (suspect renal carcinoma), importance of urine analysis (proteinuria, pyuria, etc.) and contraindication of antifibrinolytic drugs.

Uterine and vaginal bleeding

Uterine and/or vaginal bleeding may occur both in non-pregnant or in pregnant women. Obviously the clinical significance is quite different in the two cases. In non-pregnant women, excessive menstrual flow, namely menorrhagia, may be an indication of not only local (endometriosis) and systemic hormonal conditions but also of congenital or acquired coagulation disorders. Thrombocytopenia is a frequent cause of menorrhagia. Women with VWD often present with this symptom and sign [41,42]. Sometimes menomethrorrhagia is also present, with variable blood loss. Minor bleeding may, for example, be caused by 'breakthrough' bleeding due to hormonal imbalance The same may occur in congenital deficiency of clotting factors (factor II, factor V, factor X) [43–45]. Often menomethrorrhagia is so important and persistent causing anaemia. In this case long-term oral contraceptive therapy seems to be effective in controlling bleeding with a consequent decrease in transfusional needs, and improvement of the anaemia [44]. Bleeding occurring in a pregnant woman needs immediate gynaecological assistance as it may lead to fetal loss.

Muscular

Intramuscular bleeding causes deep haematomas. Contrary to what is seen in cutaneous haematomas, overlying skin, at least at first, is variably distended but normal in colour. They may occur spontaneously or after trauma and/or strain in all congenital disorders and every group of muscles may be involved. The most typical form is the haematoma of the ileo-psoas, a frequent and serious manifestation in haemophilia patients. The clinical picture is fairly typical, even though sometimes a differential diagnosis is difficult. There is abdominal pain and

limitations in the extension or lifting of the corresponding leg. The patient is unable to lace his shoes. An abdominal, para umbilical mass that tapers down towards the proximal inguinal canal is palpable. It appears on palpation as a 'sausage-like' mass that is variably tender. Femoral nerve paralysis may ensue due to compression [46]. Anaemia may appear as the fascia enveloping the ileo-psoas muscle may contain a lot of blood and therefore bleeding may be severe [46,47]. The condition occurs also during excessive anticoagulation with heparin or coumarin drugs [46]. Another area frequently involved by deep haematomas is the thigh. This causes swelling and variable limitation of movements. Deep muscle haematomas resolve very slowly and, often, only partially. Repeated haematomas in a given area may give rise to pseudotumours which are masses of degenerated muscles, cyst formation and important fibrotic reactions which often require surgical excision with variable results.

Strictly related to the ileo-psoas muscle hematoma, is the hematoma in the rectus muscles of the abdominal wall. This causes, in some cases and often when intraperiotoneal bleeding is also present, the so called abdominal compartment syndrome. This event may occur after abdominal surgery, trauma, tumors, but, occasionally, may occur also during anticoagulant therapy [48,49]. The condition is of difficult diagnosis on clinical grounds. Abdominal distension, occasional palpable mass in para-umbelical areas, anemia are the main signs and symptoms. Sonography, CT and MRI are diagnostic and should be promply carried out on first clinical suspicions. In severe cases, intrabdominal increased pressure causes encroachment on the bladder, vessels, nerves and diaphragm with secondary respiratory difficulties. The therapy of choice is surgical decompression as in ileo-psoas haematomas. If undetected there is a significant mortality due to multiple organ failure [48].

Articular bleeding

It may be divided into primary or spontaneous, and secondary bleeding in the articular joints, and is a common occurrence in haemophilia A and B [16,47]. It has also been described, occasionally, in severe FII, FVII, FX deficiencies. Synovial tissue is richly supplied with blood so that bleeding is common. Repetitive intrarticular bleeding lead to a series of pathology and clinical changes that may be summarized along the following lines (Table 13).

In congenital conditions, intrarticular bleeding is usually spontaneous but it may occur and even be more severe after traumas. Haemophilic arthropathy is the consequence of repeated intrarticular bleeding. Knees and ankles are most frequently involved but wrists and elbows are also occasionally involved.

Table 13. Evolution of haemarthrosis in haemophilia A or B patients.

Normal joint
First few episodes with *restitutio ad integrum*
First signs and symptoms of chronic (established) arthropathy
Chronic, established arthropathy with occasional worsening
Secondary changes (muscular atrophy, progressive limitation in function, etc.)
Frozen joint

Intraparenchymal bleeding

This is a form of bleeding that occurs usually after a trauma which might have gone undetected. Abdominal traumas may give rise to spleen or liver haematomas. However, traumas may cause renal haematomas which are usually perirenal. Intracerebral haemorrhages are usual spontaneous and have been described in several coagulation disorders. Particularly prone are patients with severe factor II or FVII or FX deficiencies [18,19]. Post-traumatic bleeding is usually characterized by epidural or subdural haematomas. Subarachnoid bleeding is usually secondary to hypertension (coartation of aorta) or to the presence of malformations in the circle of Willis (aneurysms).

Cerebral haemorrhages give clear neurological signs and symptoms. On the contrary, spleen or liver haematomas, if not severe, may be asymptomatic or, occasionally, if important or repetitive, present with vague abdominal tenderness and discomfort together with variable anaemia.

Intracavitary bleeding

This usually refers to the abdomen. Rupture of spleen or rupture of an aneurysm of the aorta are the most common causes of intestinal bleeding. Bleeding in all these cases is massive and the two fundamental signs are abdominal swelling and severe anaemia. In patients with congenital coagulation disorders, abdominal bleeding may occur occasionally during ovulation, extrauterine pregnancies and endometriosis (Table 14). These events represent often medical and surgical emergencies and should be suspected in any female patient known to have a congenital coagulation disorder. Symptoms and signs are often conditioned by the presence of bleeding in the abdominal cavity with consequent peritoneal

Table 14. Main clinical and laboratory findings in intracavitary bleeding.

Pallor, hypotension, dizziness, fatigue
Unexplained drop in Hct and/or Hb levels
Abdominal bleeding (bloating of abdomen, pain, tenderness)
Pleural (dyspnoea and chest dullness on percussion, absent vocal fremitus, etc.)
Pericardial (decreased heart sounds, jugular vein distension, cardiac tamponade)

irritation. The main causes of intrabdominal bleeding are rupture of the spleen or liver, rupture of aortic aneurysm, neoplasias (peritoneal carcinomatosis), ectopic pregnancy, endometriosis and severe portal hypertension.

Intrapleural bleeding is less frequent. The main causes are traumas, pneumonias, pulmonary embolism, mesotheliomas and other carcinomatosis, and pulmonary hypertension. Spontaneous intracavitary bleeding is exceptional in congenital coagulation disorders unless they are due to a trauma.

Bleeding in unusual sites

Bleeding may occur sometimes in unusual sites such as the retina or the external auditory canal. The clinical significance of these forms of bleeding is always very important and clinicians should investigate the possible causes along the lines suggested in Table 15.

Bleeding with thrombosis

Finally one must remember that bleeding may occur in different areas in concomitance or immediately after a thrombotic phenomenon. This peculiar association also has significant clinical relevance (Table 16).

Table 15. Bleeding in unusual sites.

Periorbital and/or conjunctival bleeding. Conjunctival bleeding may occur in hypertension and local inflammation. Orbital and periorbital haematoma is an important clinical sign for thrombosis of orbital cavernous sinus. The impediment to receive blood from facial tissue causes periorbital stasis and extravasation. Needless to say the periorbital haematomas due to external trauma is much more frequent
Retina (diabetes, hypertension, acute leukaemias, thrombosis of retinal veins, etc.)
Bloody discharge from external auditory canals (traumas, skull fractures, infections)
Nail (splinter haemorrhage in endocarditis)
Suprarenal glands (sepsis)
Epidural haematoma due to epidural anaesthesia (back pain and flaccid paralysis of legs)
Intestinal parietal wall bleeding with consequent bowel occlusion (complication of anticoagulant therapy)
Carenal haematoma with consequent dyspnoea (complication of anticoagulant therapy)

Table 16. Thrombo-haemorrhagic conditions.

Patients with venous or arterial thrombosis treated with anticoagulants or fibrinolytic drugs
Venous thrombosis in immobilized patients with haemorrhagic stroke
DIC (wound or puncture sites oozing, haematomas, etc.)
HIT (late bleeding)
Moschovitz, Gasser (little bleeding)

One of the most striking and disturbing events in clinical practice occurs when a doctor is confronted with a patient who has both thrombosis (venous or arterial) and bleeding. Due to the widespread use of anticoagulant therapy, cardiovascular or orthopaedic surgery and the increase of the elderly population, this event is getting common. The most frequent cause (Table 16) is represented by undue anticoagulant therapy (UFH, LMWH, pentasaccharide, coumarin drugs, etc.) in patients with thrombosis.

Another frequent association occurs in patients with a haemorrhagic stroke, kept in bed for several days. Immobilization together with antihaemorrhagic medications (e.g. antifibrinolytic drugs) will often induce a DVT of legs.

Bleeding due to DIC syndrome are also to be included in this group. Bleeding manifestations due to over anticoagulation are varied. Haematomas, haematuria, melena and cerebral haemorrhage are the most frequent. Cerebral haemorrhage seems particularly frequent after treatment with fibrinolytic drugs.

Conclusions

A correct general clinical approach and a suitable evaluation of bleeding manifestations may supply useful clues as to a correct diagnosis of a bleeding condition. They may not be fully diagnostic and should not be intended to be substitutive for laboratory tests, but they may orient the clinician towards an adequate selection of laboratory tests. Appropriate follow-up of patients is also important as the same or different bleeding manifestations may reoccur or appear *ex novo*. In general, fixed or similar bleeding manifestations, often occurring also in other members of a given family (e.g. epistaxis, haemarthrosis), are seen in congenital coagulation disorders. Bleeding due to acquired conditions is often more variable in forms and may vary also in intensity from time to time and be absent in family members.

The proper use of terms is of paramount importance for defining a bleeding condition and for communicating with the referring doctor and with patients. Semantics is not only important in the contacts among doctors, it also plays an important role in the explanation given to patients.

Adequate explanation to the patients of the cause of his or her bleeding manifestations will help him or her to cope with the symptoms. Patients are always more receptive to a clinical description of the disease than to an enumeration of clotting times, percentile figures, activity or antigen levels and amino acid substitutions or mutations.

If this recommended approach is used, only benefits for the patients would stem from it.

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