

Retroperitoneal hemorrhage – A review of the eponymous cutaneous signs

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Abstract Physical diagnosis by eliciting clinical signs still plays an important role in the management of diseases. In case of retroperitoneal bleeding due to any cause, there are five important eponymous cutaneous signs mentioned in literature. These include Cullen's sign, Turner's sign, Fox's sign, Bryant's sign and Stabler's sign. These signs are briefly reviewed in this article.

Key words

Retroperitoneal hemorrhage, Cullen's sign, Turner's sign, Fox's sign, Bryant's sign, Stabler's sign.

Introduction

In recent years, there have been revolutionary advances in imaging and diagnostic facilities. But in spite of these changes, there are certain time tested objective physical findings that retain their relevance and importance in eliciting diagnosis or in narrowing the differential diagnosis. The eponymous cutaneous signs of retroperitoneal hemorrhage are such clinical signs which aid in diagnosis and management of patients besides highlighting the rich history of dermatology. These eponyms are based on the physician who first described the clinical findings. The present article aims to briefly review the five such cardinal signs which include Cullen's sign, Turner's sign, Fox's sign, Bryant's sign and Stabler's sign.

Methods

The original articles, reviews, case series and case reports dealing with the skin signs of retroperitoneal hemorrhage were searched in PubMed, HINARI, Scopus, Google Scholar,

Web of Science, Semantic Scholar and ResearchGate after search on keywords: retroperitoneal hemorrhage, skin sign, eponymous sign and diagnostic sign. The search was extended across to the cross references. Only the articles published in English were included and no time limits were set.

Clinical presentation

1. **Cullen's sign (Figure 1A)** denotes ecchymosis around the umbilical area as seen after retroperitoneal hemorrhage. This sign is accredited to Thomas Stephen Cullen (1868-1953), a professor of gynecology and obstetrics at John Hopkins Hospital Baltimore USA, who first described it in case of ruptured ectopic pregnancy in 1918.¹⁻³

2. **Grey-Turner's sign (Figure 1B)** denotes refers to induration and bruising seen over the flanks secondary to the spread of blood from the anterior pararenal space. The sign is accredited to the English surgeon George Grey Turner (1877-1951), a British surgeon who described it in a case of acute pancreatitis in 1920⁴ as two large discolored areas in the loins, about the size of the palm of the hand, slightly raised above the surface, and of a dirty-greenish color.

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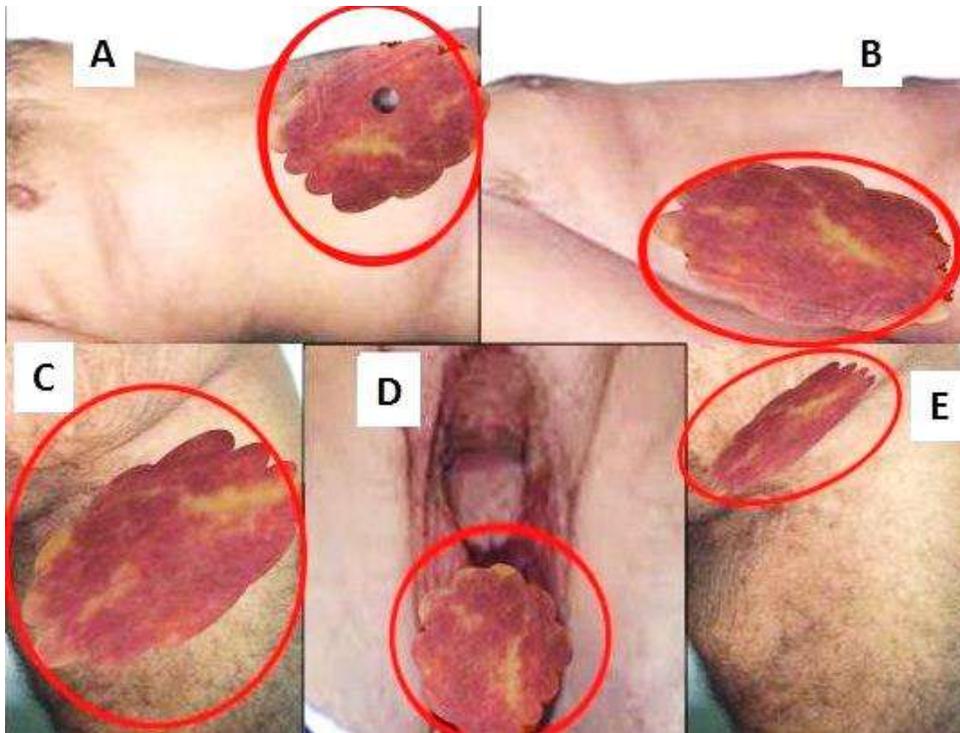


Figure 1 Schematic diagram of eponymous cutaneous signs of retroperitoneal hemorrhage (A) Cullen's sign (B) Turner's sign (C) Fox's sign (D) Bryant's sign (E) Stabler's sign

3. **Fox's sign (Figure 1C)** denotes superficial bruising of the superolateral aspect of the patient's thigh.⁵ The area has a sharply demarcated superior border parallel but inferior to the inguinal ligament. This sign is named after London surgeon John Adrian Fox after he reported two fatal cases of non-traumatic ecchymosis (ruptured abdominal aortic aneurysm and acute pancreatitis) in the upper outer aspect of the thigh as a diagnostic sign of retroperitoneal hemorrhage.⁵ This sign is in occasional accounts incorrectly eponymously attributed to the American dermatologist George Henry Fox (1846-1937).

4. **Bryant's Sign (Figure 1D)** denotes superficial bruising of scrotum or alternatively a ring like ecchymosis in perianal area.⁶ It is also called Bryant's blue sign or blue scrotum sign of Bryant and is named after John Henry Bryant (1867-1906), a British physician who first explained it in a case of retroperitoneal hemorrhage.⁷ Paladugu *et al.* in 1997 presented

an apparent feminine version of this sign by reporting a case of ecchymosis of vulva in acute pancreatitis.⁸

5. **Stabler's Sign (Figure 1E)** denotes superficial bruising in the pubic and inguinal area.⁹⁻¹⁰ It is named after Frank Stabler, a renowned British surgeon and obstetrician who explained this sign in 1930s and also contributed to understanding of Cullen's sign by showing that the skin discoloration is due to blood in the subcutaneous tissues.¹⁰⁻¹¹

Pathogenesis

Cullen's sign is understood to arise from the spread of retroperitoneal blood into the falciform ligament. The blood subsequently spreads to the subcutaneous umbilical tissues through the connective tissue covering of the round ligament.¹² Similarly, Turner's sign arises by the spread of the hemorrhagic fluid from the anterior pararenal space between the two leaves of the

posterior renal fascia and subsequently to the lateral edge of the quadratus lumborum muscle and thereafter to the subcutaneous tissues through defects in the fascia of the flank.¹² Fox's sign arises by tracking of free blood can track extraperitoneally along the fascia of the psoas and iliac muscles to end up in subcutaneous planes in the upper and lateral thigh. The sharp superior border is believed to result from blockage of further blood movement at the junction of Scarpa's fascia with the fascia lata.

Stabler's sign arises by tracking of blood from retroperitoneal to inguinal subcutaneous planes.¹⁰ This sign is rare and is most commonly identified in neonates secondary to adrenal hemorrhage caused by obstetric injury, perinatal hypoxia, and sepsis.¹⁵⁻¹⁶ Very rarely, the sign may arise due to ruptured neuroblastoma, in which case prompt search for underlying adrenal malignancy should be undertaken.¹⁰

Sugimoto *et al.* in 2005 demonstrated the anatomical pathways of the extravasated pancreatic enzymes leading to Grey-Turner's and Cullen's signs, as well as the effects of the enzymes on the ecchymoses by multiplanar reformation images obtained by helical computed tomography in a patient with severe acute pancreatitis.¹⁷

The retroperitoneal blood leading to appearance of cutaneous signs may arise from varied pathologies. The commonly mentioned causes include acute necrotizing pancreatitis,¹⁸⁻²⁴ ruptured aneurysm,⁶⁻⁷ trauma and ruptured ectopic gestation.^{1,3,26}

However there are reports published in literature associating these cutaneous signs uncommonly with a wide range of conditions like metastatic malignancies of kidney,¹⁰ esophagus²⁵ and thyroid,²⁷ amoebic abscess,²⁸ abdominal

lymphoma,²⁹ splenic rupture due to diseases like infectious mononucleosis,³⁰⁻³¹ and even hypothyroidism. Chung *et al.* reported a case of splenic rupture secondary to infectious mononucleosis in a middle-aged patient whose presenting complaint was the presence of Cullen's sign, secondary to the hemoperitoneum. The splenic rupture was managed conservatively, and the Cullen's sign resolved within two weeks of presentation.³⁰ Warwick *et al.* reported Cullen's sign in similar situation of ruptured spleen in infectious mononucleosis in a 22 years old male patient.³¹ Guthrie reported Cullen's sign and Grey-Turner's signs as presenting complaints in rectus sheath hematoma.³² Evan³³ and McKelvie *et al.*³⁴ reported Cullen's sign in perforated duodenal ulcer whereas Sayers and Porter reported it a new association with central dislocation of the hip joint.³⁵

Fan and Zhang reported a patient who developed pain with appearance of Grey Turner's and Cullen's as a result of coughing leading to contrast-enhanced CT proven spontaneous hemorrhage of the abdominal wall.³⁶ Rao *et al.* reported a rare case of desmoid tumor of rectus abdominis that presented with Grey-Turner's and Cullen's Sign.³⁷

These signs have been reported in literature to have appeared after diagnostic and therapeutic procedures. Capron *et al.* found Cullen's sign after percutaneous liver biopsy³⁸ whereas Bentov *et al.* discovered it in female following ultrasound-guided transvaginal oocyte retrieval.³⁹

Significance

The appearance of these signs in a patient indicates internal hemorrhage and warrants very careful history taking and investigations, including coagulation profile studies, serum

lipase/ amylase, and imaging. These signs take 24-72 hours to appear and may appear alone or in conjunction. Cullen and Grey Turner signs appear in conjunction in 3% of cases of acute pancreatitis and signal severe disease and worse prognosis, with a mortality rate of around 37%.⁴⁰ Even when alone, these signs have proven to be an important aid in diagnosis of lethal conditions like ruptured aortic aneurysm⁶⁻⁷ in spite of latest imaging techniques. The presence of Grey Turner sign in patients with acute pancreatitis was found to be associated with a mortality of nearly 40% by Dickson and Imrie.⁴¹ If these signs appear in setting of metastatic malignancies (like esophagus, thyroid), the prognosis is very dismal and usually patient is in terminal stage of the disease.

Avolio *et al.*¹⁵ stressed upon the useful aspect of appearance of these signs and concluded that awareness and correct knowledge about these signs can lead to timely diagnosis in neonatal adrenal hemorrhage manifesting as acute scrotum and thereby prevent unnecessary surgery.

The discoloration may be greenish, yellowish, or purplish depending on the degree of red blood cell (RBC) breakdown in the abdominal wall tissues. Birnaruberl *et al.* conducted a study to evaluate if, and how often, skin signs were noted in autopsy-confirmed cases of necrotizing pancreatitis and in that study extensively reviewed the literature and retrospectively analyzed the reports of 16,000 autopsies performed at the Institutes of Legal Medicine in Frankfurt am Main and Giessen, Germany. They found that in their evaluated medicolegal autopsy pool, skin signs in necrotizing pancreatitis to be a rare occurrence but suggested that, in cases of unexpected death, particularly of individuals with a history of alcohol abuse, necrotizing pancreatitis should be considered in the differential diagnosis of skin

discoloration, otherwise attributed to trauma.⁴²

Differential diagnosis

There are many conditions which can mimic the cutaneous signs of retroperitoneal hemorrhage but careful examination and evaluation can usually lead to diagnosis⁴³. These conditions include:

1. Cellulitis typically causes blanching erythema that is warm to the touch.
2. Subcutaneous administration of heparin or overdose of oral anticoagulants may result in abdominal wall ecchymoses.
3. Blunt trauma to abdominal wall/ may injure cutaneous vessels and cause ecchymoses.
4. In patients of scaling diseases like psoriasis, Darier's disease and actinic keratoses. , there may be erythema with a silvery scale that bleeds on removal (Auspitz sign).
5. Retroperitoneal bile leak , due to rupture of the biliary tree or a duodenal perforation can following natural pathways in the abdominal cavity like blood , reaching the skin and then inducing the development of yellowish discoloration and mimicking the signs of retroperitoneal bleed.

Certain conditions may specifically mimic Cullen's sign. These include:

- a) Metastatic spread of an intra-abdominal malignancy to the umbilicus, may present with thickening and erythema /nodule around the umbilicus (Sister Mary Joseph's sign). Rarely less common malignant conditions may involve the umbilicus and cause discoloration including adenocarcinoma of urachal remnants and squamous cell carcinoma.
- b) Endometriosis with umbilical involvement may cause hemorrhage in conjunction with the menstrual cycle and cause periumbilical

ecchymoses.

c) In cirrhosis of liver, ulceration of a recanalized umbilical vein may cause periumbilical skin darkening.

Similarly several conditions have been described to produce flank discoloration, thereby mimicking Grey Turner's sign. These include bacterial peritonitis due to *Pseudomonas aeruginosa* and retroperitoneal necrotizing fasciitis.

Conclusion

In spite of recent advances in imaging technologies, the eponymous cutaneous signs retain their relevance and should alert the clinician to the possibility of significant intra-abdominal bleeding or pathology with a stormy course and poor prognosis and hence expedite further investigation and management. These cutaneous signs, if they are looked for, are immediately apparent on physical examination and require no sophisticated tests or gadgets for detection.

Acknowledgement/ Disclaimer The author thanks the simulated patient for allowing the usage and editing of his images for academic reasons. Further, it is acknowledged that the figures are schematic diagrams to simplify the explanation of the subject and have been made by modification of images on Paint software. The author does not claim to have managed any case with all the signs explained in the text.

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