CASE REPORT

Blue rubber bleb naevus syndrome: a rare cause of iron deficiency anaemia

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SUMMARY

We report a case in an adolescent male patient with a history of chronic fatigue, headache and unexplained iron deficiency anaemia since 2007. Numerous bluish-black lesions were found over his body surface. A surgical scar from a previous lumpectomy with a small lump were noted at the left submandibular region and another smaller lesion on the left lobe of the thyroid was also palpated. His most recent blood indices displayed the presence of moderately severe iron deficiency anaemia. Endoscopic evaluation exhibited multiple vascular lesions throughout the gastrointestinal tract. MRI of the brain revealed an irregular intracranial vascular lesion at the cerebellopontine angle. Further work-up with abdominal CT demonstrated the absence of similar lesions in the extraintestinal abdominal organs. Putting these together with histological findings, the diagnosis of blue rubber bleb naevus syndrome was confirmed. The patient was treated conservatively at this point and future management planning was discussed with him.

BACKGROUND

Blue rubber bleb naevus syndrome (BRBNS) is a rare condition characterised by the presence of multiple bluish, soft or rubbery textured subcutaneous lesions of different sizes as a result of venous malformation.^{1 2} In addition, patients commonly develop chronic iron deficiency anaemia. This is attributed to the presence of similar vascular lesions in the gut wall.³ The cutaneous lesions are usually present earlier in life than the gut lesions.³ Other body organs such as the liver, pancreas, spleen, brain, thyroid, parotid, etc, are rarely involved.⁴ Bone deformity and joint problems have also been recorded.⁴ The disease is transmitted in an autosomal dominant inheritance pattern but it could occur sporadically.^{5 6} Treatment of this condition may be challenging due to its vascular nature and tendency for recurrence.^{7 8}

CASE PRESENTATION AND INVESTIGATION

A 25-year-old male patient presented with a history of chronic fatigue, recurrent unilateral left-sided headache and increasing pallor of 7-year duration, which worsened during the 2 months prior to his current presentation. Review of his medical and surgical history was relevant for the presence of numerous cutaneous naevi since early childhood, and repeated hospitalisation for blood transfusion during the past few years. In addition, the patient had a history of removal of a lump at the neck. He had never been on non-steroidal anti-inflammatory drugs. He denied any history of haematemesis,

melaena or peptic ulcer disease. There was no history of a similar condition in his family. On clinical examination, signs of anaemia were evident. There were numerous blackish-to-bluish rubbery and/or soft textured, and to some extent compressible, painless elevated (sub) cutaneous lesions of different sizes (of a few millimetres–centimetres) distributed throughout the body surface especially over feet and hands (figure 1). Head and neck examination revealed the presence of a lump at the left submandibular and parotid region with a surgical scar at the same site. A single small lesion was also palpated on the left lobe of the thyroid. No obvious skeletal abnormalities were found. Systemic examination of the heart, chest, abdomen and central nervous system (CNS) were unremarkable.

The patient was submitted to thorough haematological and biochemical laboratory tests. The values of his most recent blood tests prior to the blood transfusion in reference to the normal range (NR) of our laboratory were: haemoglobin 7.5 g/dL (NR 12–17), serum iron 55 µg/dL (NR 60–170), serum ferritin 19.2 ng/mL (NR 30–400), total iron binding capacity 493 µg/dL (NR 250–370) and transferrin saturation percentage 14 (NR 15–50%). The blood film showed hypochromic/microcytic red blood cells with mean corpuscular volume 72 fL, while platelet count, white cell count and prothrombin time were normal. Other serum biochemical tests were within NR. Screening for HIV, hepatitis B and hepatitis C viruses was negative.

The diagnosis of iron deficiency anaemia was established according to the patient's blood indices.

As the underlying cause of anaemia was unclear at this point, the patient underwent a second endoscopic evaluation in February 2014. Prior to endoscopic examination he was resuscitated with two units of matched blood in addition to an iron supplement, which he had already received. His current upper and lower gastrointestinal tract endoscopy displayed the presence of numerous, different sized (0.5–3.0 cm) purplish-to-bluish sessile vascular lesions at the gastro-oesophageal junction, gastric fundus, second part of the duodenum, and sigmoid and descending colon (figures 2 and 3). No other lesions were found proximally in the colon or oesophagus. The endoscopy report described the lesions as 'haemangiomas'. There was no obvious bleeding from lesions but faecal occult blood test results were positive on several occasions. A review of endoscopic reports from 2007 was surprisingly unremarkable.

Imaging evaluations initially started with chest X-ray, abdominopelvic sonography and skull X-ray

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Figure 1 Bluish-black cutaneous lesions on the flexure surface of the left wrist, the dorsum of the left foot and the inner side of the right foot near the sole.

were normal. Sonography of the neck revealed the presence of small lesions in the left parotid gland and in the left lobe of the thyroid gland, while MRI examination confirmed the vascular nature of these lesions. MRI of the brain demonstrated the presence of an irregular intracranial vascular lesion at the left cerebellopontine angle with extension to the surrounding areas (figure 4). The subsequent imaging included CT of the abdomen and the pelvis, which demonstrated the absence of similar lesions in the intra-abdominal organs: liver, pancreas, spleen, kidneys, bladder, etc.

The result of fine-needle aspiration of the neck lump was relevant for the presence of fresh blood only, while the pathological report of the excisional biopsy of the same lesion concluded the diagnosis of ‘arteriovenous malformation’.

DIFFERENTIAL DIAGNOSIS

This was a typical case of BRBNS. Other similar cutaneous conditions with or without visceral involvement include: Klippel-Trenaunay-Weber syndrome, Peutz-Jeghers syndrome, Kaposi sarcoma, Maffucci syndrome, neurofibromatosis, diffuse neonatal haemangiomatosis and mucosal venous malformation. All these lesions have similar characteristic features.

TREATMENT

The patient was well supported by blood transfusion, iron therapy and a balanced diet.

OUTCOME AND FOLLOW-UP

The patient’s clinical course was eventless during the weeks following his current endoscopic evaluation. His blood indices

were significantly improved. We discussed possible future complications and long-term management planning for the gut and brain lesions with the patient, and a schedule for regular follow-up was fixed. As the patient is exposed to the risk of being infected with hepatitis B and C viruses, prophylaxis with hepatitis B vaccination had been arranged; however, hepatitis C vaccination is not currently available. As the cutaneous lesions, particularly those affecting his feet, are prone to bleeding from trauma, the patient was advised to be extra careful during daily activity.

DISCUSSION

It is worth mentioning that two famous people, Gascoyen in 1860 and William B. Bennett in 1958, were the first to describe BRBNS.^{9 10} According to the available literature, the estimated number of published cases until 2010 was around 200.¹¹ Although this disorder is still rare, that figure probably does not reflect the actual occurrence of such cases simply because many of them are neither recorded nor published, and other cases may remain undiagnosed or misdiagnosed particularly in the absence of a high index of clinical suspicion for diagnosis.

One of the major complications of this disorder is visceral involvement, especially that related to the gut. The lesions may occur anywhere in the gut but are most frequently found in the small intestine.^{2 12 13} In the present case, multiple gut lesions were encountered in the stomach, second part of the duodenum and colon. Comparable lesions in other organs and tissues such as liver, spleen, lung, CNS, kidneys, bladder, bones, joints, head and neck, etc, are well-recognised features of this disorder and have all been reported.⁴ Reports on head and neck lesions being

Figure 2 Purplish-blue sessile vascular lesions at the gastro-oesophageal junction, the gastric fundus and the second part of the duodenum.

Figure 3 Purplish-blue sessile vascular lesions at the sigmoid and the descending colon.

associated with gut lesions are very few. Starr *et al*¹⁴ reported a case of intestinal involvement with head and neck lesions. In the present case we recognised several extraintestinal lesions in the head and neck. Cutaneous lesions and iron deficiency anaemia are both considered the most important hallmarks of this disease, the latter is usually the outcome of bleeding from gut lesions.^{3 8 10 12 13} The anaemia in most instances tends to progress relatively slowly, resulting from minor, chronic occult blood loss. However, episodes of overt bleeding in the form of haematemesis or melaena, and bleeding per rectum can occur at any time and may be a serious complication of this disorder.^{4 13} In our case, the cutaneous manifestation and the signs of chronic iron deficiency anaemia (probably due to on-going occult blood loss) were obvious.

As almost all cases of BRBNS are listed as reporting cases, we lack any standardisation or guidance linked to the treatment of such a challenging disorder to date.

The modes of treatment are largely influenced by the site, severity of the lesion and doctor's perspective. Each mode has its specific indications, advantages, disadvantages and limitations. Cutaneous lesions, for example, may be solely removed for cosmetic reasons, while symptomatic intestinal and brain lesions may need an aggressive surgery. Endoscopic and pharmacological methods such as snaring, argon plasma, laser

photocoagulation, sirolimus (an antiangiogenic agent), steroid, interferon, octreotide, cyanoacrylate glue (a sclerotic agent), etc, are among the means of treatment of gut lesions for some patients.^{7 8 15–18} However, there is no evidence to support any supposed benefits of antiangiogenic or other pharmacological agents for this disorder.⁷

The initial step in our management strategy for treating the anaemia in this case was by offering supporting therapy; at the same time we also took into account the need for immediate endoscopic and/or surgical interference in the event of an episode of overt bleeding.

To achieve our final goal in the management of the gut lesions, a subsequent step will be surgical and/or endoscopic ablation of the lesions at an appropriate time to improve overall clinical outcome, as the presence of such lesions are potential sources of significant bleeding, which may threaten the patient's life.

The presence of the intracranial lesion in the case is another challenging issue that may need advanced neurosurgical intervention.

Learning points

- ▶ The evaluation of the gastrointestinal tract (GIT) for bleeding source(s) is mandatory in every case with unexplained iron deficiency anaemia and/or cutaneous lesions.
- ▶ Overt acute bleeding as well as chronic occult blood loss can both occur from gut vascular lesions in blue rubber bleb naevus syndrome (BRBNS).
- ▶ Surgical and endoscopic treatment of GIT lesions in BRBNS are sometimes challenging due to their vascular nature and tendency to recur.
- ▶ Always rule out the presence of intracranial lesions in patients with BRBNS especially when symptoms of central nervous system involvement are present.

Figure 4 Postcontrast MRI of the brain demonstrates the presence of an irregular intracranial vascular lesion at the left cerebellopontine angle with extension to the surrounding areas.

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