A case report of combined vascular malformations with progressively growing lymphatic malformation: a potentially alarming feature of Gorham–Stout syndrome

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ABSTRACT:

YEESIBSEAN N*, WANANUKUL S, PONGPRUTTHIPAN M*, BOONTAVEEYUWAT E*. A CASE REPORT OF COMBINED VASCULAR MALFORMATIONS WITH PROGRESSIVELY GROWING LYMPHATIC MALFORMATION: A POTENTIALLY ALARMING FEATURE OF GORHAM–STOUT SYNDROME. THAI J DERMATOL 2020; 36: 46-53.**

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Congenital vascular malformations are rare and potentially causing life-threatening consequences. Diagnostic as well as therapeutic approach can be very challenging, interdisciplinary team work is then required. We report a case of a young man with combined capillary-lymphatic-venous malformation (CLVM) on the right lumbar area. He presented with progressively growing, bluish compressible tissue lumps, overlaid with red plaque and small clear vesicles at the right side of lumbar area. Radiographic skeletal survey showed lumbar spine's scoliosis. No osteolytic lesions were found. Contrast MRI revealed slow flow serpentine infiltrative vascular malformation. Combined CLVM without other anomalies was diagnosed. However, Gorham–Stout syndrome (GSD) with delayed osteolysis bone development, could be the case for our patient as progressive combined lymphatic malformation could be considered as a clinical crucial clue in clinically suspecting and diagnosing GSD later on. A long term close monitoring particularly bone pain and potentially high risk of fracture was mandatory. Minimal invasive procedure, percutaneous sclerotherapy, was arranged due to unresectable condition.

Key words: Capillary- lymphatic- venous malformation, Vascular malformations, Gorham-Stout syndrome, sclerotherapy

Case presentation

A 23-year-old Thai man presented at our dermatology clinic with growing deep red plaque at the right side of the front lumbar area since birth (Fig. 1), which initially presented as a flat red patch. He was not aware of the progression of the patch, nor lump development underneath until the last two years. His right flank grew disproportionately larger as well as the patch became raised and irregular. He also occasionally had deep pain inside the affected area. He was otherwise well with unremarkable antenatal record and normal child development. His family members have physically normal.

Physical examination revealed ill-defined, bluish, soft, compressible, dermal to subcutaneous masses at the right side of lumbar of 10x13cm; the front hypochondriac areas, of 10x 16cm., overlaid with (i) deep red papules and plaques and (ii) multiple small clear vesicles (Figure 1 A-D); 4x 5 cm solitary light brown patch at the left buttock (Fig. 2). There was no vascular pulsatile; bruits over the masses; physical bone nor limb overgrowth.

Radiographic skeletal survey showed lumbar spine's scoliosis convex to the left centred at the L2-3 with curves of 15° by Cobb angle measurement. No osteolytic lesions were found (Fig. 3).

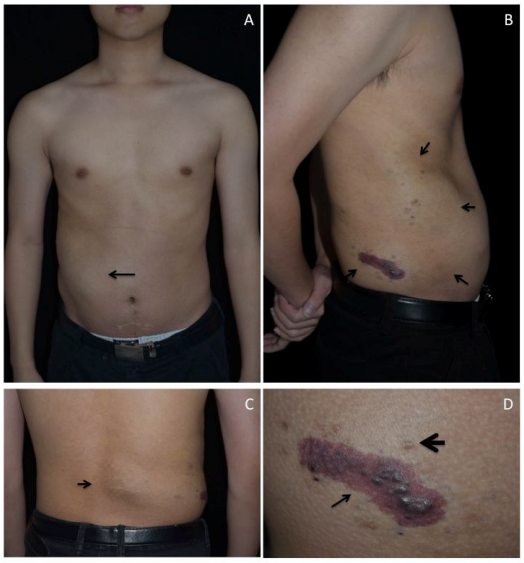

Figure 1 A-C, Ill-defined, bluish, compressible, soft, tissue mass at the right side of lumbar area of 10 x 13 cm., as well as, the front hypochondriac areas, of 10 x 16 cm. overlaid with **D,** (i; thin arrow) well-defined deep erythematous papules and plaques of 2 x 4 cm (ii; thick arrow) multiple discrete small clear vesicles scattered on their surface.

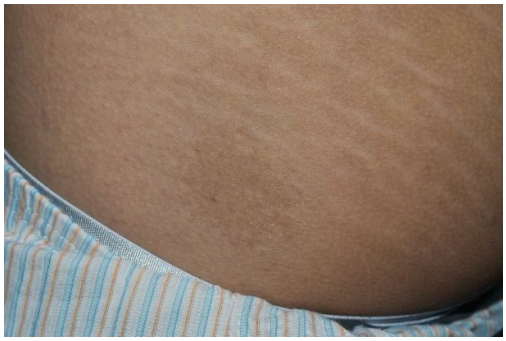

Figure 2 A 4 x 5 cm solitary light brown patch at the left buttock, compatible with cafe´-au-lait macule.

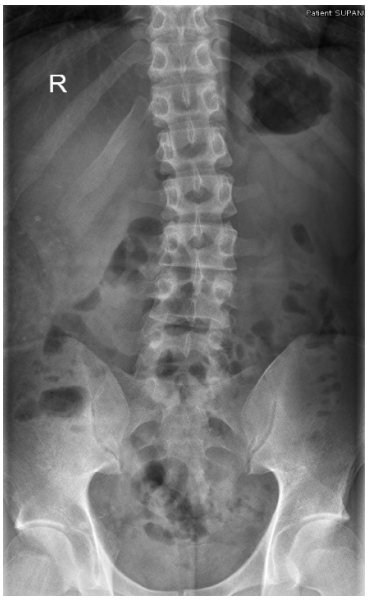

Figure 3 LS spine AP radiograph disclosed lumbar spine scoliosis with 15° apex at L 2-3 level.

In the view of suspected vascular malformation, ultrasonography (USG) and contrast-enhanced magnetic resonance imaging (MRI) were also undertaken. USG demonstrated increase of muscle and subcutaneous tissue thickness at the entire palpable region of the right flank both front and the back with ill-defined inhomogenously hyperechoic pattern and suspected slow flow vascular malformation. Contrast MRI revealed abnormal serpentine infiltrative vascular lesions from the right lumbar, hypochondriac areas, subcutaneous fat, and muscle extending to the right lateral peritoneal cavity and spleen. 3-minute, 5-minute and 10-minute delayed vascular like lesional

enhancement MRI reflected slow-flow patterned venous lesions. Multiple calcified spots in the abnormal veins as well as in the vascular lesions at the right abdominal wall and intraperitoneal region; enlarged spleen embedded with multiple delayed enhanced nodules were also found (Fig. 4).

The differential diagnosis included combined slow-flow vascular malformations with other anomalies including Gorham Strout Syndrome (GSD); or slow-flow vascular malformations without anomalies.

Percutaneous sclerotherapy for venous malformations (VMs) and laser therapy for superficial capillary part combined was initially arrange for him**.**

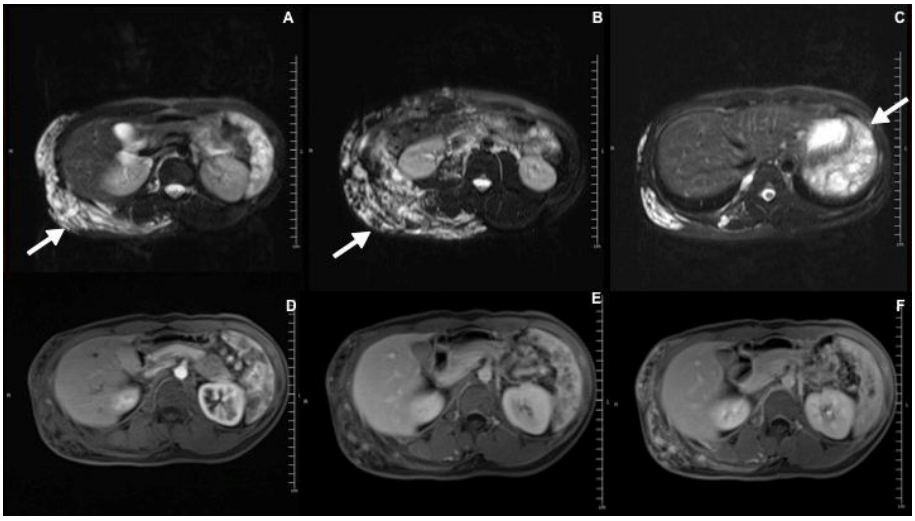

Figure 4 Upper abdominal contrast MRI

A-C; Axial T2 FS demonstrated bright fluid of serpentine infiltrative vascular lesions from the right lumbar extending to the right lateral peritoneal cavity and multiple delayed enhanced nodules in enlarged spleen.

D-F; Postcontrast fat-suppressed spoiled gradient-echo demonstrated 3-minute, 5-minute and 10-minute delayed vascular like lesional enhancement.

Discussion

Congenital vascular anomalies are one of the most complex diseases. Precisely defining a classified type following ISSA classification (2018); tumour vs malformation; simple vs combined component; with vs without other anomalies (Fig. 5)[1] is a crucial approach leading to treatment plan decision.

Diagnosis of vascular anomalies is based on clinical findings and imaging studies including USG

and contrast-enhanced MRI, USG is widely used[2] and should be performed in every patient to assess exact extension and dynamic vascularity. MRI is essentially providing vascular enhancement pattern, soft tissue involvement and other associated anomalies, is also needed particularly for pre-interventional assessment and follow-up after invasive therapy.

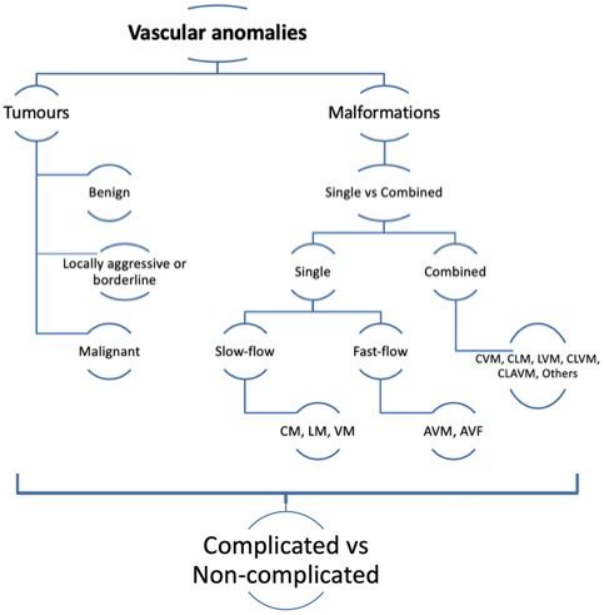

Figure 5 Approach diagram to vascular anomalies (adapted from ISSVA Classification for vascular anomalies. Approved at the 20th ISSVA workshop, Melbourne, April 2014, last revision May 2018); CM, Capillary malformation; LM, Lymphatic malformation; VM, Venous malformation; AVM, Arteriovenous malformation; AVF, Arteriovenous fistula; CVM, Capillary-venous malformation; CLM, Capillary-lymphatic malformation; CAVM, capillary-arteriovenous malformation; LVM, Lymphatic-venous malformation; CLVM, Capillary-lymphatic-venous malformation; CLAVM, Capillary-lymphatic-arteriovenous malformation.

Our patient presented with progressively enlarged deep red plaque as well as bluish, soft, compressible masses without a period of involution at his right flank. The masses had no sign of bruit, nor pulsation together with evidence of slow-flow complex venous channels indicate the most likely venous malformation. The two different coloured lesions, red plaques and clear vesicles, overlaid on the mass are in keeping with capillary and lymphatic malformation[1], respectively. He was therefore initially diagnosed as combined capillary- lymphatic- venous malformation (CLVM) with splenic involvement.

Table 1. Cutaneous manifestrations reported in GSD ; M, Male; F, Female; NA, No data available

Publication	Number of reported patient (s)	Sex	Age at diagnosis of GSD	Cutaneous manifestrations related GSD		
				Clinical presentations	Histology	Time duration between cutaneous vascular anomalies found and bone symptoms developed (years)
Fornasier VL. 1970	1	M	59	Small purple to red hemangiomas since birth	Hemangiomas	59
Aviv R.I, 2001	2	NA	NA	Lymphangiomatosis	Lymphangiomatosis	NA
Hsu TS, 2001	1	F	42	Hemangiomas	NA	NA
Stefanidou M, 2004	1	M	43	Angiomatous and dark-red to purple Kaposi-like plaques since birth	Vascular malformations	43
Takahashi A, 2005	1	F	2	Hemangiomatous change	Hemangiomas	NA
Bruch-Gerharz D, 2007	1	M	21	Skin-colored papules and vesicles	Lymphatic malformations	7
Johnstun J, 2010	1	F	37	Hemangiomas	Hemangiomas	NA
Venkatramani R, 2011	4	F	11	Lymphangiomatosis	NA	NA
		F	9			
		M	14			
		M	7			
Leite I,2013	1	F	7	Progressive purple–brown plaque on LS area since birth	Lymphatic malformations	7
Reipschläger M, 2018	1	M	12	Progressive dilated cutaneous venules	Lymphatic malformations	8.9
Wang Z, 2019	1	F	3	Firm, violaceous, and depressed plaque	NA	NA
Ozeki M, 2019	2	M	18	Lymphorrhea	NA	NA
		M	20			

Other potential anomalies were subsequently investigated in order to define CLVM is either isolated or syndromic. Mild scoliosis and an irregular border cafe´-au-lait macule (CALM) on the left buttock were revealed. No osteolytic bone lesions nor other system abnormalities were found. A few CALM can be considered a finding in normal population without clinical significance[3].

Gorham–Stout syndrome (GSD) characterized by progressive proliferation of endothelial-lined vessels in bone resulting in progressive osteolysis with devastating bone cortex destruction[4], can cause significant functional impairment to death. Most patients with GSD reported only presentation specifically resulted from particular parts of bone invasion including localized pain, weakness, breathing difficulty, neurological defects and paralysis[5]. There have been, however, 15 cases worldwide, reported concomitant various cutaneous vascular anomalies. Progressive combined lymphatic malformation could be considered as a clinical crucial clue in clinically suspecting and diagnosing GSD later on (Supplemental Table 1). The duration from the suggested clue to bone invasion development can range from 7 to 43 years. This could be the case for our patient regarding progressively growing lymphatic malformation. Therefore, long-term monitoring symptoms related to bone cortex destruction would provide early detection as well as prompt management to prevent possible serious consequences.

The treatment of peripheral vascular malformations needs a multidisciplinary team in order to determine an individualized treatment strategy. Aim of the treatments generally is to relieve devastating symptoms and prevent further potential consequences. Visceral organ involvement including gastrointestinal, genitourinary tracts can cause from minor to life threatening bleeding. However, splenic involvement is usually found in a form of splenic haemangiomas[6] of which bleeding or other forms of serious complications has rarely been reported. Monitoring its extension particularly to other hollow viscus organs would be the best way to ensure early therapeutic intervention if necessary. Treatment for slow-flow peripheral vascular malformation, include fitted compression garments, general pain-relieving agents and more invasive therapy such as sclerotherapy and surgery[7]. There has been also promising medical therapy including sirolimus[8], an mTOR inhibitor; sildenafil[9], reported having some benefits for vascular anomalies. However, long term efficacy and adverse events data are still limited. Percutaneous sclerotherapy for VMs was indicated for our patient who had symptomatic CLVM, bodily pain and disfigurement. Sirolimus which might also benefit our patient, would be considered as a next-line of treatment.

We are presenting a case of CLVM with progressively growing lymphatic malformation which is the most common feature found in potentially life-threatening GSD. Long-term monitoring is vital to early detect potential complication. Awareness of these rare conditions amongst dermatologists and general physicians, who usually are the frontline professional providers, would provide much benefit to affected individuals in term of early detection and treatment for possible life-threatening consequences.

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