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Splinter hemorrhage as a telltale of active extra-cranial giant cell arteritis

A case report and review of the literature

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Abstract

Rheumatologists and general practitioners as a rule do not examine the nails when giant cell arteritis (GCA) is suspected, and may thus miss a simple yet valuable clinical sign. Splinter hemorrhage (SH) is a non-specific but significant clinical finding that can be seen in a wide range of conditions and by different medical specialists, among others: rheumatologists, infectious diseases specialists, dermatologists, nephrologists and endocrinologists. Rheumatologists usually look at the nail beds in search of SH when there is a suspicion of vasculitis, mostly anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis although SH has been described in other vasculitides as well. SH in GCA has rarely been described. Here are two cases with SH appearing during active disease in patients with extra-cranial GCA, illustrating the value of nail bed assessment and how it may provide important clues.

Keywords: Large vessel vasculitis, Extra-cranial giant cell arteritis, Giant cell arteritis, Splinter hemorrhage, Renal artery, Nails, Conjunctivitis.

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Introduction

SH is a non-specific indicator of vascular damage and presents a non-specific yet significant clinical finding that can be seen in many conditions. Within the rheumatological field SH is seen, inter alia, when vasculitis is involved. The present cases were found in a cohort of prospectively followed giant cell arteritis (GCA) patients reported elsewhere [1].

Case Reports

Case 1

Medical history and clinical presentation

A 65.5-year-old male had disease onset in the beginning of September 2013 with pains in both shoulders, later spreading to the neck accompanied with stiffness and still later jaw claudication, visual symptoms as flashes in both eyes and finally pain in the middle of the forehead. He had a medical history of long-lasting multiple sclerosis and a former hypertension. He was initially admitted to a general internal medicine unit and one day later diagnosed with GCA and started on prednisolone 60 mg/d.

Clinical findings at the first visit to the rheumatology clinic, with 5 weeks ongoing prednisolone, at visit 30 mg/d

The physical examination (including auscultation of the heart, peripheral vessels and cranial arteries; palpation of the peripheral vessels and temporal arteries (TA); joint examination; bilateral brachial and ankle pressure measurements) was unremarkable except for an ankle pressure difference of 20 mmHg. Laboratory analysis (before prednisolone) erythrocyte sedimentation rate (ESR) 81 mm/h, C-reactive protein (CRP) 74 mg/L, thrombocytes (Trc) 456 × 10^9/L; at visit ESR 18, CRP 1.2, Trc 255.

Investigations, treatment and disease course

Temporal artery biopsy (TAB) was positive. He exhibited frequent flares on high doses of steroids (laboratory ones when prednisolone < 20 mg/d and clinical ones when ≤ 15 mg/d). During prednisolone tapering from the middle of February 2014, incremental escalation of the systemic blood pressure and discreetly rising serum creatinine, ESR and CRP, could be observed. In the beginning of June a brachial pressure difference but no change in baseline ankle pressure difference was recorded, prednisolone 10 mg/d; ESR 13, CRP 2.0, Trc 312. The brachial pressure difference had disappeared and the ankle pressure difference was unchanged in the end of August, prednisolone 5 mg/d; ESR 27, CRP 6.9, Trc 307. A review of available computed tomography of the thorax and abdomen with contrast enhancement from October 2013 was done in the middle of December revealing moderate vessel wall thickening of the left common carotid, vessel wall thickening with contrast enhancement but no caliber shifts of the innominate artery and both subclavian arteries, dilatation of the coeliac trunk and a vessel wall thickening with significant luminal stenosis of both renal arteries from the ostium to the bifurcations.

In the end of January 2015 a vessel bruit in the left axilla, an increased blood pressure of 171/99 mmHg, some improvement of baseline ankle pressure difference and no brachial pressure asymmetry were noted. The patient had on his own discontinued prednisolone intake in the beginning of January; ESR 45, CRP 63, Trc 350. Prednisolone was reinstituted 60 mg/d. A recurrence of brachial pressure difference, a complete resolution of baseline ankle pressure difference and splinter hemorrhages in left fingernail dig III and right fingernails dig II+III were noted in the end of June; ESR 27, CRP 2.0, Trc 366. A computed tomography angiography (CTA) the same month showed total regress of the vasculitic changes in the innominate artery but

unaltered vasculitis in the left axillary/brachial artery. The resolution of vasculitis in the innominate artery caused the now lower blood pressure in the left arm.

Steroid sparing agent was discussed several times but the patient kept postponing the decision. Methotrexate was started orally in escalating doses to 30 mg/w, in the beginning of August. The brachial pressure difference improved but ankle pressure difference reappeared at visit end of October. During this visit the Methotrexate dose was reduced to 20 mg/w due to side effects. At last follow-up in the end of March 2016, both pressure differences remained unchanged with ongoing treatment Methotrexate 20 mg/w orally and prednisolone 12.5 mg/d. Methotrexate dose was further reduced to 15 mg/w since no improvement of the side effects had been achieved. The patient was approved for tocilizumab but declined.

Case 2

Medical history and clinical presentation

A 72-year-old male with an unremarkable medical history was referred to the cancer center unit November 2014 due to inflammation of unknown origin. He was diagnosed with polymyalgia rheumatica (PMR) and started on prednisolone 30 mg/d, then referred to the rheumatology clinic querying atypical PMR. Sometime June/July the patient had noted muscle weakness in the legs during gardening, muscle exhaustion of the upper arm muscles during physical activity and exercise pain from the back of the right thigh and calf that disappeared at rest. New was also whitening of the right big toe, coldness and sensory disturbance of the right foot, feeling of tightness of the chest and sweating the last 4-5 weeks prior to his visit to the rheumatology clinic. He denied any classical signs of GCA or of PMR. The patient had some memory difficulties (unclear how many years) but denied worsening during this period.

Clinical findings at the first visit to the rheumatology clinic, with 18 days ongoing prednisolone, at visit 30 mg/d

Normal cardiac and pulmonary auscultation but shortness of breath walking a short distance. Unequal brachial and ankle pressures of 10 mmHg and 45 mmHg respectively. Ankle-brachial index right 0.33, left 0.58. Vessel bruits bilateral axillary and the left common femoral artery. Prominent left TA without pulsation. Coldness of both feet and mild cyanosis of the right toe tips I+II+V. Laboratory analysis (before prednisolone) ESR 104 mm/h, CRP 64 mg/L, Trc 390 × 10^9/L; at visit ESR 44, CRP 1.2, Trc 346. The diagnosis of PMR was changed to claudication of the extremities.

Investigations, treatment and disease course

Since the patient described worsening of the symptoms the prednisolone dose was escalated to 80 mg/d. A CTA of the cervical and intracranial vessels was ordered to investigate a possible underlying vasculitis as cause to the memory difficulties and a CTA of the aorta to evaluate the extent of suspected large vessel vasculitis. The TAB was positive. The CTA-cervical and intracranial vessels showed vessel wall thickening of left subclavian, bilateral vertebral and internal carotid arteries, markedly thin and irregular right anterior cerebral artery and narrowed basilar artery. The CTA-aorta showed bilateral vasculitis of subclavian, brachial and superficial femoral arteries. One month later, prednisolone 70 mg/d, the shortness of breath, the leg claudication and the toe cyanosis had progressed why cyclophosphamide was added. At the second last pulse a mild conjunctivitis of the right eye and splinter hemorrhages in right fingernails dig III+IV could be noted; prednisolone 15 mg/d, ESR 14, CRP 3.2, Trc 298. A follow-up CTA showed progress of the vasculitic changes of the majority of the affected vessels. Two weeks after the last cyclophosphamide pulse leflunomide was initiated and because of the CTA results, tocilizumab was approved. A new CTA-aorta and CTA-intracranial vessels after six months of tocilizumab treatment, showed only some improvement in the arm arteries.

Discussion

Splinter hemorrhages have been described in connective tissue diseases such as systemic lupus erythematosous, anti-phospholipid syndrome, systemic sclerosis, primary Sjögren's syndrome and dermatomyositis/polymyositis [2-4]. SH are also seen in vasculitides, mostly ANCA-associated vasculitis i.e., granulomatosis with polyangiitis (GPA) [5], mikroskopisk polyangit (MPA) [6] and eosinophilic granulomatosis with polyangiitis (EGPA) but occurrence has also been described in other vasculitides like polyarteritis nodosa (PAN) [7,8], thromboangiitis obliterans [9] and Cogan's syndrome [10]. For GCA, a search of the English literature in Google, Embase and PubMed using the keywords "Horton's disease", "Temporal arteritis", "Giant cell arteritis", "Splinter hemorrhage", "Splinter haemorrhage", "Subungual hemorrhage" and "Subungueal hemorrhage" to the best of my ability, yielded no papers dedicated to this clinical finding.

In an unrelated search for floating thrombus in GCA, Singh et al. reported on a 77-year-old male with fatigue, proximal muscle stiffness, raised inflammatory markers and SH on examination. Investigation with transesophageal echocardiogram revealed extensive mural thrombus in the aortic arch and positron emission tomography-computed tomography (PET-CT) showed vasculitis of the aortic arch and its proximal branches consistent with GCA [11].

In another unrelated search regarding extra-cranial GCA and PET-CT in GCA, Tucker et al. reported on a 78-year-old female with anorexia, fatigue, night sweats, weight loss, breathlessness on exertion and swollen ankles who on examination had SH, systolic heart murmur, unequal brachial blood pressures and markedly raised ESR and CRP. A CT chest abdomen pelvis revealed small pericardial and pleural effusions and PET-CT demonstrated extensive aortitis consistent with GCA [12].

Lee and Marshall presented a case with a 68-year-old female with a 6 months history of fatigue, weight loss, dizzy spells and sudden coldness of the left hand and proximal myalgia of the shoulders the last four weeks. There were no classical signs of GCA. Physical examination revealed bilateral carotid bruits, absence of left radial pulse and SH in her left hand. ESR and CRP levels were raised. TAB showed GCA. Angiography showed stenosis of the left subclavian and vertebral artery and bilateral internal carotid arteries. Later PET-CT revealed active inflammation in all large vessels despite normal inflammatory markers on treatment with cyclophosphamide [13].

Lloyd et al. presented a 70-year-old female with three days

history of SH in all the fingers of the left hand and a three weeks history of left shoulder and thumb pain. There were no signs or symptoms of GCA or PMR and no constitutional symptoms. Examination revealed, besides SH, absence of left brachial, radial and ulnar pulses, equal brachial blood pressures and no vessel bruits. ESR and CRP levels were raised. TAB showed GCA. Ultrasound showed narrowing of both axillary arteries [14].

All the cases depict SH in the setting of active large vessel vasculitis (LVV), in some cases despite ongoing treatment and normal-low inflammatory markers and in others in untreated patients, making SH an independent clinical sign of LVV and a sign of disease activity in both grumbling and overt inflammatory states.

The existence of LVV in a large proportion of GCA patients is becoming more and more recognized. The approach to treatment is also changing towards differentiated therapy regimen for GCA patients with and without large vessel involvement, namely early/at baseline initiation of steroid-sparing drugs. The presence of SH should hence lead to a low threshold for imaging studies to assess the large vessels.

Conclusion

Besides anamneses, pressure measurements of the four extremities and analysis of the inflammatory markers, an assessment of the nails for splinter hemorrhages may provide additional sign of large vessel involvement. The presence of splinter hemorrhages may signal an active disease in GCA patients despite low-normal inflammatory markers.

References

1. Naderi N. giant cell arteritis-A report on systematic physical evaluation and large vessel involvement as a prognostic risk factor for complicated disease course, real life data. Arch Gen Intern Med. 2018;2:10-6.
2. Tunc SE, Ertam I, Pirildar T, et al. Nail changes in connective tissue diseases: do nail changes provide clues for the diagnosis? J Eur Acad Dermatol Venereol. 2007;21:497-503.
3. Garcia-Carrasco M, Galarza C, Gomez-Ponce M, et al. Antiphospholipid syndrome in Latin American patients: clinical and immunologic characteristics and comparison with European patients. LUPUS. 2007;16:366-73.
4. Elmansour I, Chiheb S, Benchikhi H. Nail changes in connective tissue diseases: A study of 39 cases. Pan Afr Med J. 2014;18:150.
5. Schattner A, Kozak N, Friedman J. Pulmonary nodules and splinter haemorrhages. Postgrad Med J. 2001;77:785-94.
6. Atzeni F, Carrabba M, Davin JC, et al. Skin manifestations in vasculitis and erythema nodosum. Clin Exp Rheumatol. 2006;24(1 suppl 40):S60-66.
7. Chasset F, Francès C. Cutaneous manifestations of medium- and large-vessel vasculitis. Clin Rev Allergy Immunol. 2017;53:452-68.
8. Young JB, Will EJ, Mulley GP. Splinter haemorrhages: Facts and fiction. J R Coll Physicians Lond. 1988;22:240-3.
9. Quenneville JG, Gossard D. Subungueal-splinter hemorrhage an early sign of thromboangiitis obliterans. Angiology. 1981;32:424-32.
10. Touloei K, Tongdee E, Smirnov B, et al. Cogan's Syndrome with Cutaneous Findings: A Case Report and Review of Dermatologic Manifestations. JAOCD. 2003;25-9.
11. Singh S, Michelena HI, Warrington KJ. The nails give it away. J Am Coll Cardiol. 2011;57:996.
12. Tucker LJ, Mankia KS, Magliano M. Extra-cranial giant cell arteritis: A diagnostic challenge. QJM Int J Med. 2015;108:823-5.
13. Lee JHM, Marshall T. 356. An atypical presentation of giant cell arteritis and the role of PET scanning. Rheumatology. 2006;45(suppl_1):i136-48).
14. Lloyd M, Brooks C, Leopold P. 357. The hands have it: giant cell arteritis presenting with unilateral finger splinter haemorrhages. Rheumatology. 2006;45(suppl_1):i136-48).

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