CASE REPORT

REVISED Case Report: Polyarteritis nodosa or complicated Henoch-Schonlein purpura (IgAV), a rare case [version 2; referees: 2 approved]

Previously titled: Case Report: Polyarteritis nodosa or complicated Henoch-Schonlein purpura, a rare case

Sajad Hasanzadeh[1], Seyedeh Maryam Alavi[1], Elahe Masnavi[2], Saeid Jokar[1], Maryam Rohani[2]

[1]Department of Internal Medicine, Yasouj University of Medical Sciences, Yasouj, Iran
[2]Department of Obstetrics and Gynecology, Yasouj University of Medical Sciences, Yasouj, Iran

v2 **First published:** 12 Jan 2018, **7**:49 (doi: 10.12688/f1000research.13295.1)
Latest published: 16 Apr 2018, **7**:49 (doi: 10.12688/f1000research.13295.2)

Abstract

Background: Polyarteritis nodosa (PAN) is a vasculitis that affects medium-sized arteries. PAN is a rare disease and requires a high clinical suspicion for diagnosis. PAN and HSP (newly named Immunoglobulin A-associated vasculitis) have narrowing differential diagnosis. Here, we reported a case of PAN.

Case presentation: Our patient was a 65-year-old woman that came to hospital due to abdominal pain and skin lesion on the right upper and right lower extremities. All rheumatologic tests were negative. A biopsy of the skin lesion was reported as mild hyperkeratosis, slight spongiosis with intact basal layer. The dermis showed moderate to severe perivascular PMN infiltration with vessel wall degeneration and extravasation of RBCs. A colonoscopy reported diffuse mucosal erythema and erosions were seen in the rectum until 6cm of anal verge. An electromyogram test and nerve conduction velocity study of the upper extremities reported bilateral mild carpal tunnel syndrome, and in the right lower extremities mononeuritis multiplex could not be ruled out. Abdominopelvic CT scan reported diffuse wall thickening of terminal ileum associated with mesenteric fat and narrow enhancement of inferior Mesenteric artery with patchy filling defect. After evaluation, the patient received corticosteroid pulses plus cyclophosphamide.

Conclusion: Diagnosis and treatment of PAN are important and PAN should be considered in a patient with skin lesions and neurological impairment.

Keywords

Polyarteritis nodosa, Henoch-Schonlein purpura (Immunoglobulin A-associated vasculitis), vasculitis

Open Peer Review

Referee Status: ✓ ✓

	Invited Referees 1	2
REVISED version 2 published 16 Apr 2018	✓ report	✓ report
version 1 published 12 Jan 2018	? report	? report

1 **Marco de Vincentiis**, Sapienza University of Rome, Italy

2 **Patricia Woo**, University College London, UK

Discuss this article

Comments (0)

Corresponding author: Maryam Rohani (m_rohani247@yahoo.com)

Author roles: Hasanzadeh S: Project Administration, Supervision; **Alavi SM**: Supervision; **Masnavi E**: Writing – Review & Editing; **Jokar S**: Data Curation, Validation, Writing – Review & Editing; **Rohani M**: Writing – Original Draft Preparation

Competing interests: No competing interests were disclosed.

How to cite this article: Hasanzadeh S, Alavi SM, Masnavi E *et al.* **Case Report: Polyarteritis nodosa or complicated Henoch-Schonlein purpura (IgAV), a rare case [version 2; referees: 2 approved]** *F1000Research* 2018, **7**:49 (doi: 10.12688/f1000research.13295.2)

Grant information: The author(s) declared that no grants were involved in supporting this work.

First published: 12 Jan 2018, **7**:49 (doi: 10.12688/f1000research.13295.1)

REVISED **Amendments from Version 1**

1. We added the exact course of the disease according to referees' comments

2. We added a new name for the Henoch-Schonlein purpura (IgAV)

3. We added other manifestations of the disease

4. We added new references based on referees' comments

See referee reports

Introduction

Polyarteritis nodosa (PAN) is a systemic vasculitis that mostly involves medium sized arteries, and sometimes involves small arteries[1]. The prevalence of PAN is estimated to be 2 to 33 million individuals[2,3]. The annual incidence in some areas of Europe estimate 4.4 to 9.7 per million population[4]. The diagnosis is most commonly made in middle-aged or older adults and increases with age, and its peak is in the sixth decade of life[2]. Polyarteritis nodosa can mimic the clinical manifestations of Henoch-Schonlein purpura (HSP) that is newly named Immunoglobulin A-associated vasculitis (IgAV). It is difficult to differentiate between PAN and HSP (IgAV), at an early stage. If PAN is not diagnosed and treated at an early stage, it has a high morbidity[5,6]. Considering that PAN is a rare disease and requires a high clinical suspicion for diagnosis, here, we report a case of PAN and the reasoning behind its diagnosis in our patient.

Case report

Patient information

The patient was a 65 year old woman from Yasouj (south of Iran) that came to our hospital due to abdominal pain and skin lesion on right upper and right lower extremities, which were was mostly on the distal of extremities, for since 2 weeks preadmission. Other complaints of the patient were diarrhea, vomiting, chills, fever, and anorexia. The patient did not complain of arthralgia. In the past medical history, the patient had Diabetes Mellitus, hypertension, and Bell's palsy one week pre-admission (treatment with 40mg prednisolone QD).

Clinical findings

On examination of the skin, the patient had palpable plaque in the erythematous and purpuric context with vesicular and bulla lesion on right upper and right lower extremities that mostly extended to the distal part (Figure 1). An abdominal examination revealed mild tenderness in the epigaster. The Right lower extremities were warm and end pulses were normal. In active and passive motion of the joints had not painful movements. Neurologic exam of the right lower extremity revealed decreased sense and motor function (muscle power 4/5).

Diagnostic assessment

Laboratory tests: HCV, HBV, HIV, ANA (antinuclear antibodies), cryoglobulin, anti-double-stranded DNA (dsDNA) antibodies, complement (C3 and C4), perinuclear antineutrophil cytoplasmic antibodies (P-ANCA and C-ANCA), all were normal. Urine analysis, Kidney performance (BUN and Creatinine) tests was normal, amylase and lipase levels were normal. ESR was 40mm/h (Normal under 20mm/h), occult blood one pluses positive, and hemoglobin was 11/9 g/L (Normal 13–16g/l).

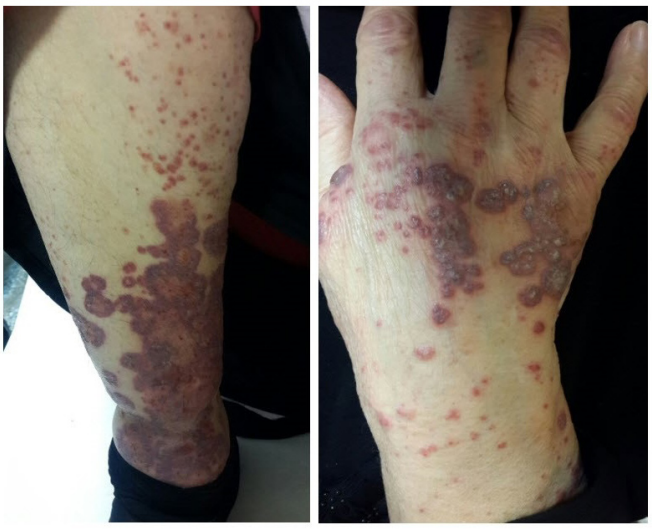

Figure 1. Palpable plaque in the erythematous and purpuric context.

Skin biopsy: Mild hyperkeratosis, slight spongiosis with intact basal layer. The dermis showed moderate to severe perivascular PMN infiltration with vessel wall degeneration and extravasation of RBCs. A diagnosis of a vasculitis leukocytoclastic variant (immunofluorescence is not available at our center).

Evaluation of patient anemia and GI tract were done via endoscopy and colonoscopy.

Endoscopy: Patchy erythematous lesions were observed.

Abdominopelvic CT scan (Figure 2): A 130mm of segment of terminal ileum had diffuse wall thickening (3–8mm) associated with mesenteric fat. Narrow enhancement of inferior mesenteric artery with patchy filling defect, poor enhancement of terminal branches. Therefore, suspicions were: 1)vasculitis, 2)mesenteric ischemia.

Colonoscopy: Diffuse mucosal erythema and erosions were seen in the rectum until 6cm of anal verge. Hemorrhoid without active bleeding in anus, few erythema and ophtus ulcer in cecum. Terminal ileum was not intubated. A diagnosis of a rectal erosion maybe due to vasculitis.

Electromyogram test and nerve conduction velocity: Upper extremities reported bilateral mild carpal tunnel syndrome, and in right lower extremities mononeuritis multiplex could not be ruled out.

Echocardiography: No evidence of any other disorder.

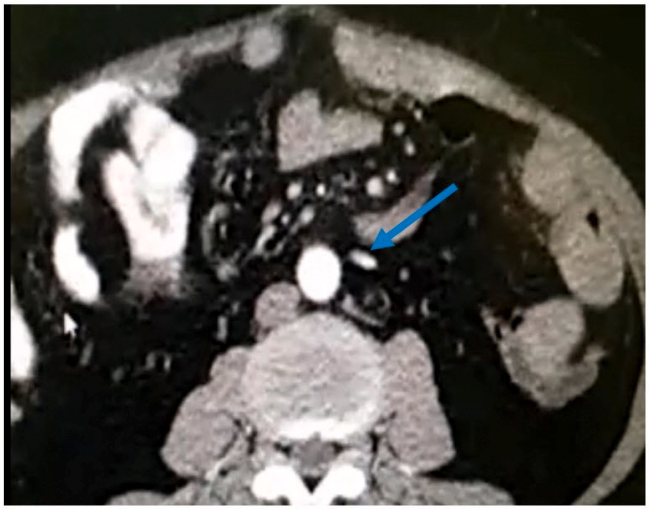

Figure 2. Abdominopelvic CT scan with IV contrast. Narrow enhancement of the inferior mesenteric artery can be observed (blue arrow).

Final diagnosis: Vasculitis PAN or complicated HSP (IgAV)

Therapeutic intervention

The patient received 1000 mg methylprednisolone IV pulse daily for 3 days, and 750mg cyclophosphamide IV pulse every two weeks for 3 weeks.

Follow-up and outcomes

After 24 hours of receiving corticosteroid pulses and cyclophosphamide, the symptoms of the patient subsided, with skin lesions going into remission. Currently, the patient is being treated with 50mg prednisolone daily, after 2 weeks, if there is no recurrence of patient symptoms we will taper off corticosteroids amount by 10%. We will reduce the dose of corticosteroids until we have control of patient symptoms, then we will make decisions depending on the patient's condition.

Discussion

Unlike other vasculitis's such as microscopic polyarthritis or Wegener's, PAN is not associated with ANCA[7]. The organs most often affected in PAN are the skin, renal and GI tract. Cardiac involvement can manifest itself with hypertension, or even ischemic heart disease[8]. In the skin, PAN may manifest by erythematous nodules, livedo reticularis, ulcer, bullous or vesicular eruption and purpura[7,9,10]. Gastrointestinal symptoms that may be seen include abdominal pain, nausea, vomiting, melena, bloody or non-bloody diarrhea, and life-threatening gastrointestinal bleeding[11]. One of the most common manifestations of patients with PAN is mononeuropathy multiplex that typically involves both motor and sensory deficits in up 70% of patients[7,12]. Some of the patients have sensorineural hearing loss[13] Most cases of PAN are idiopathic, although hepatitis B virus infection, hepatitis C virus infection, and hairy cell leukemia are important in the pathogenesis of some cases[3,4,14,15]. PAN can mimic the clinical manifestations of HSP (IgAV). It is difficult to differentiate between PAN and HSP (IgAV) at an early stage[5]. The biopsy pattern helps to differentiate between PAN and HSP (IgAV); in tissue studies of HSP (IgAV) leukocytoclastic vasculitis in postcapillary venules together with IgA deposition is observed[16]. As already mentioned, PAN is most commonly seen in middle-aged or older adults[3], while HSP (IgAV) is a childhood disease that occurs between the ages of 3 and 15 years[17]. Neurologic manifestation in HSP (IgAV) is rare. Single reports and case series document neurologic manifestations including headaches, intracerebral hemorrhage, focal neurologic deficits, ataxia, seizures, and central and peripheral neuropathy in children with HSP (IgAV)[18]. According to EULAR/PRINTO/PRES classification criteria, there was no renal failure, arthralgia and arthritis in this patient, but basis on other item, HSP (IgAV) could be diagnosis[19]. In the present case, using clinical manifestations and laboratory tests, we excluded another differential diagnosis apart from PAN. Considering that PAN and HSP (IgAV) have narrowing clinical manifestation, we differentiated between the two diseases by age and neuropathy. However, although the diagnosis of the present patient is PAN, for a better diagnosis, immunofluorescence of the biopsy was needed, which is not available in our center. Finally, diagnosis and treatment of PAN are important. PAN should be considered in a patient with skin lesions and neurological impairment.

Data availability

All data underlying the results are available as part of the article and no additional source data are required.

Consent

Written informed consent was obtained from the patient for the publication of the patient's clinical details and accompanying images.

Competing interests

No competing interests were disclosed.

Grant information

The author(s) declared that no grants were involved in supporting this work.

References

1. Sato O, Cohn DL: **Polyarteritis and microscopic polyangiitis.** In: *Rheumatology*, Klippel JH, Dieppe PA (Eds.), Mosby, St Louis; 2003.
Reference Source
2. Mahr A, Guillevin L, Poissonnet M, *et al.*: **Prevalences of polyarteritis nodosa, microscopic polyangiitis, Wegener's granulomatosis, and Churg-Strauss syndrome in a French urban multiethnic population in 2000: a capture-recapture estimate.** *Arthritis Rheum.* 2004; **51**(1): 92–9.
PubMed Abstract | Publisher Full Text
3. Ramos-Casals M, Muñoz S, Medina F, *et al.*: **Systemic autoimmune diseases in patients with hepatitis C virus infection: characterization of 1020 cases (The HISPAMEC Registry).** *J Rheumatol.* 2009; **36**(7): 1442–8.
PubMed Abstract | Publisher Full Text
4. Guillevin L, Mahr A, Callard P, *et al.*: **Hepatitis B virus-associated polyarteritis nodosa: clinical characteristics, outcome, and impact of treatment in 115 patients.** *Medicine (Baltimore).* 2005; **84**(5): 313–22.
PubMed Abstract | Publisher Full Text
5. Ozen S, Anton J, Arisoy N, *et al.*: **Juvenile polyarteritis: results of a multicenter survey of 110 children.** *J Pediatr.* 2004; **145**(4): 517–22.
PubMed Abstract | Publisher Full Text
6. Hočevar A, Rotar Z, Jurčić V, *et al.*: **IgA vasculitis in adults: the performance of the EULAR/PRINTO/PRES classification criteria in adults.** *Arthritis Res Ther.* 2016; **18**(1): 58.
PubMed Abstract | Publisher Full Text | Free Full Text
7. Kallenberg CG, Brouwer E, Weening JJ, *et al.*: **Anti-neutrophil cytoplasmic antibodies: current diagnostic and pathophysiological potential.** *Kidney Int.* 1994; **46**(1): 1–15.
PubMed Abstract | Publisher Full Text
8. Pagnoux C, Seror R, Henegar C, *et al.*: **Clinical features and outcomes in 348 patients with polyarteritis nodosa: a systematic retrospective study of patients diagnosed between 1963 and 2005 and entered into the French Vasculitis Study Group Database.** *Arthritis Rheum.* 2010; **62**(2): 616–26.
PubMed Abstract | Publisher Full Text
9. Gibson LE, Su WP: **Cutaneous vasculitis.** *Rheum Dis Clin North Am.* 1995; **21**(4): 1097–113.
PubMed Abstract
10. Karlsberg PL, Lee WM, Casey DL, *et al.*: **Cutaneous vasculitis and rheumatoid factor positivity as presenting signs of hepatitis C virus-induced mixed cryoglobulinemia.** *Arch Dermatol.* 1995; **131**(10): 1119–23.
PubMed Abstract | Publisher Full Text
11. Levine SM, Hellmann DB, Stone JH: **Gastrointestinal involvement in polyarteritis nodosa (1986–2000): presentation and outcomes in 24 patients.** *Am J Med.* 2002; **112**(5): 386–91.
PubMed Abstract | Publisher Full Text
12. Moore PM: **Neurological manifestation of vasculitis: update on immunopathogenic mechanisms and clinical features.** *Ann Neurol.* 1995; **37**(Suppl 1): S131–41.
PubMed Abstract | Publisher Full Text
13. De Virgilio A, Greco A, Magliulo G, *et al.*: **Polyarteritis nodosa: A contemporary overview.** *Autoimmun Rev.* 2016; **15**(6): 564–70.
PubMed Abstract | Publisher Full Text
14. Hasler P, Kistler H, Gerber H: **Vasculitides in hairy cell leukemia.** *Semin Arthritis Rheum.* 1995; **25**(2): 134–42.
PubMed Abstract | Publisher Full Text
15. Carpenter MT, West SG: **Polyarteritis nodosa in hairy cell leukemia: treatment with interferon-alpha.** *J Rheumatol.* 1994; **21**(6): 1150–2.
PubMed Abstract
16. Jennette JC, Falk RJ: **Small-vessel vasculitis.** *N Engl J Med.* 1997; **337**(21): 1512–23.
PubMed Abstract | Publisher Full Text
17. Gardner-Medwin JM, Dolezalova P, Cummins C, *et al.*: **Incidence of Henoch-Schönlein purpura, Kawasaki disease, and rare vasculitides in children of different ethnic origins.** *Lancet.* 2002; **360**(9341): 1197–202.
PubMed Abstract | Publisher Full Text
18. Nadrous HF, Yu AC, Specks U, *et al.*: **Pulmonary involvement in Henoch-Schönlein purpura.** *Mayo Clin Proc.* 2004; **79**(9): 1151–7.
PubMed Abstract | Publisher Full Text
19. Ozen S, Pistorio A, Iusan SM, *et al.*: **EULAR/PRINTO/PRES criteria for Henoch-Schönlein purpura, childhood polyarteritis nodosa, childhood Wegener granulomatosis and childhood Takayasu arteritis: Ankara 2008. Part II: Final classification criteria.** *Ann Rheum Dis.* 2010; **69**(5): 798–806.
PubMed Abstract | Publisher Full Text

Open Peer Review

Current Referee Status: ✔ ✔

Version 2

Referee Report 01 May 2018

doi:10.5256/f1000research.15802.r33221

✔ **Patricia Woo**
Division of Infection and Immunity, University College London, London, UK

The message is much clearer. Thank you. There are some typos, but I am happy to approve its indexing.

Competing Interests: No competing interests were disclosed.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Referee Report 17 April 2018

doi:10.5256/f1000research.15802.r33220

✔ **Marco de Vincentiis**
Department of Oral and Maxillofacial Sciences, Sapienza University of Rome, Rome, Italy

The authors addressed my comments and questions. The article can be indexed in the present form.

Competing Interests: No competing interests were disclosed.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Referee Report 13 March 2018

doi:10.5256/f1000research.14428.r31810

? **Patricia Woo**
Division of Infection and Immunity, University College London, London, UK

This is indeed a severe case of systemic vasculitis. The criteria used to classify the combined clinical and histological findings are not clearly referenced for discussion. The EULAR/PRINTO/PRES criteria

published in 2016 are more discriminatory with the addition of IgA immunofluorescence for IgA associated vasculitis (formerly known as HSP). Unfortunately the authors were not able to perform this test and the skin histology did not describe a necrotizing vasculitis. The authors are correct that mononeuritis multiplex would be a separator, but the evidence in this case is more circumstantial as reported. The time line of Bells palsy is suggestive. The nerve conduction report is equivocal. Renal dysfunction or joint involvement were not mentioned.

Both conditions can respond well to prednisolone alone, or in combination with cyclophosphamide depending on the severity.

Since the case report is to highlight the overlapping features of the vasculitides, I agree that the differentiating diagnostic features are important.

Is the background of the case's history and progression described in sufficient detail?
Partly

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?
Partly

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?
No

Is the case presented with sufficient detail to be useful for other practitioners?
Partly

Competing Interests: No competing interests were disclosed.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 16 Mar 2018

Saeid Jokar, yasouj university of medical sciences, Iran

Hi Patricia
I corrected the article in accordance with your comments.
Thank you for advising us on improving the content of the article.

Best Regards

Competing Interests: No competing interests were disclosed

Referee Report 25 January 2018

doi:10.5256/f1000research.14428.r29766

Marco de Vincentiis
Department of Oral and Maxillofacial Sciences, Sapienza University of Rome, Rome, Italy

The authors present a case of a 65 year old woman that was admitted to the authors' hospital due to abdominal pain and skin lesion on the right upper and right lower extremities, with negative rheumatologic tests. After careful diagnostic workout, the final diagnosis was vasculitis (Polyarteritis nodosa or complicated Henoch-Schonlein purpura). The paper is interesting, also due to the rarity of the disease. However, there are some points that need to be improved before final approval:

1. The authors report Bell's Palsy in patient's medical history; it would be interesting to know when this occurred. Since this was treated with corticosteroid therapy, it is important to know if it was present when the patient already had PAN lesions - and in this case if they also improved during therapy - or if it occurred prior to PAN-related lesions arose.

2. Timing details are missing: in the case presentation - follow up and outcomes - the authors report that the patient "is being treated with 50mg prednisolone daily and then we will taper this amount". It is important to define for how long the patient is being treated, how much time past from initial diagnosis and therapy, and how the authors intend to reduce treatment.

3. Sensorineural Hearing Loss is often reported in PAN and, in some cases, may occur as the presenting symptom. Hearing Loss is typically bilateral and symmetrical, with sudden or rapidly progressive onset. It would be interesting to know if hearing impairment was reported by the patient, or investigated.

4. In the discussion we recommend to further discuss the findings that led to PAN diagnosis in this case.

5. The paper has several English language typos and grammar mistakes that should be corrected by a native English speaker (i.e. "which were was mostly", etc).

References

1. De Virgilio A, Greco A, Magliulo G, Gallo A, Ruoppolo G, Conte M, Martellucci S, de Vincentiis M: Polyarteritis nodosa: A contemporary overview.*Autoimmun Rev*. 2016; **15** (6): 564-70 PubMed Abstract | Publisher Full Text

Is the background of the case's history and progression described in sufficient detail?
Partly

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?
Partly

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?
Partly

Is the case presented with sufficient detail to be useful for other practitioners?

Yes

Competing Interests: No competing interests were disclosed.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 29 Jan 2018

Saeid Jokar, yasouj university of medical sciences, Iran

Hi Marco,

Thank you for attention in review of our article. I will correct the article by your statements.

1. One week pre-admission the patient was under corticosteroid treatment because bell's palsy.

2. After 2 weeks, if the no recurrent of patient symptoms we will taper off corticosteroids amount 10 %. We will reduce the dose of corticosteroids until reaches to control of patient symptoms, then by the patient condition will decide about it.

3. Thank you - I add your statement to the manuscript

Other comments are considered.

Competing Interests: No competing interests were disclosed.