Cutaneous polyarteritis nodosa: Varied presentations in 4 cases and review of literature.

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ABSTRACT

Polyarteritis nodosa is uncommon vasculitis with poor prognosis involving medium sized arteries. Cutaneous polyarteritis nodosa (CPAN) is a rare vasculitis with involvement of blood vessels of the skin, musculoskeletal, and nervous system. It is limited form of polyarteritis nodosa and characterized by benign nature but associated with frequent relapses. Main involvement is skin as the name suggests but it can presents as myalgia and neuropathy as well and hence it is necessary to differentiate CPAN from PAN. Before making diagnosis of CPAN other conditions which has similar presentation should be excluded.

INTRODUCTION

In 1866, Kussmaul and Maier described polyarteritis nodosa (PAN) in a 27-year-old patient whose condition was characterized by fever, cough, proteinuria, abdominal pain, mononeuritis multiplex, muscular weakness, and subcutaneous nodules.[1] Thereafter, PAN was always described as a vasculitis with systemic involvement until Lindberg 's description in 1931 of two patients with skin lesions and necrotizing arteritis without end organ disease which later labelled as cutaneous polyarteritis nodosa (CPAN).[2] PAN is a systemic collagen disease with poor prognosis that shows necrotizing vasculitis of small and medium-sized arteries of multiple organs like kidney, liver, heart, and skin and Cutaneous symptoms are observed in 25–60% of PAN patients[3], whereas CPAN is a limited form of PAN with involvement restricted to skin, musculoskeletal, and nervous system[4]. The cutaneous form of PAN is distinct from the systemic form due to its chronic but recurrent course, lack of internal organ vasculitis.[5] Studies have shown that some cases of CPAN can progress to PAN hence periodic follow up is needed.[6,7]

Chen and Daoud *et al*. classified cutaneous PAN into three groups[6,8] (i) a mild cutaneous form consisting of nodular lesions and reticular livedo; (ii) a severe cutaneous form consisting of livedo, ulceration, and pain; and (iii) necrotizing livedo and gangrene.

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Epidemiology

CPAN affects both the adults and children. The age of reported patients with CPAN has ranged from 5-68 years.[9] CPAN equally affects males and females as against PAN which is more common in males. Systemic polyarteritis nodosa is a rare vasculitis and CPAN is even more rarely seen. Hence, the true incidence of CPAN is unknown.[10]

Clinical features

Cutaneous PAN is characterised by tender subcutaneous nodules, usually measuring 4 - 5 mm in diameter, along with infarcts presenting as purple or black patches and livedo reticularis that may ulcerate.8. The legs are affected 97% of the time, followed by the arms in 33%, and the trunk in 8%.[8] Additional involvement of the head and neck has been noted in nine of 23 patients (39%) with CPAN.[11] Patients may have systemic symptoms like malaise, fever and arthralgia. Mononeuritis can present as decreased reflexes and paresthesias. Myalgias occur with physical activity in 100% of those affected. Other symptoms may be associated with cutaneous PAN, including constitutional symptoms, musculoskeletal and neurological symptoms, limited to the affected areas.[6,12]

Laboratory abnormalities

Laboratory abnormalities that are frequently

encountered include mild anemia, moderate leukocytosis, and an elevated ESR.[11] Serologic testing for syphilis, ANA, rheumatoid factor, and ANCA are most of the time negative. However, perinuclear-ANCA positivity has been found in cases of minocycline induced CPAN.[13;14]

Skin biopsy is mainstay in diagnosis of CPAN. Four stages of histologic findings in CPAN have been described: degenerative, acute inflammatory, granulation tissue, and healed endstages.[15] In a study direct immunofluorescence performed on nine CPAN skin biopsy specimens showed C3 deposits were seen in 7 cases, IgM deposits in three cases, and the absence of deposits at the dermoepidermal junction in all the samples.[16]

Diagnosis

Tomoyuki Nakamura et al. has suggested diagnostic criteria for CPAN based on clinical presentation and histopathology with exclusion of diffenrential diagnosis.[17] CPAN is a nodular arteritis with neutrophilic infiltrate in the medium-sized vessels in the deep reticular dermis. Fibrinoid necrosis and leukocytoclastic vasculitis can also present.[18]

Treatment

Treatment for CPAN is primarily with systemic corticosteroids. Patients should be monitored continuously for the development of systemic symptoms of PAN. The data of a study showed persistent only cutaneous lesions until 18 and 19 years of follow up.[19] Remission can range from months to almost 4 years. CPAN has been treated successfully with low-dose methotrexate and it has demonstrated that CPAN lesions began to regress within 2 weeks of this therapy.[20] Colchicine and pentoxifyllin can be used in combination with steroids in cases with incomplete response.[12] IV immunoglobulin can be administered in resistant cases.[22]

Cases

Case 1:

A 38 year old lady was having lump in left breast associated with pain since 1 month. Then she started pain in both lower legs with swelling since 15 days associated with red painful rash. Mild fever and tiredness was associated with it. She never had similar episodes previously. She was not a hypertensive or diabetic. Examination revealed grade III synovitis of ankle with pedal edema and erythematous tender nodules 3-4 in number, about 1×2 cm in size in both lower legs. There was single ulcer of size 2×2 cm in left breast whose base had healthy granulation tissue. Margins were regular and erythematous. She was provisionally diagnosed as reactive arthritis versus sarcoidosis or Cutaneous polyarteritis nodosa. Her routine blood tests revealed elevated ESR (64 mm at the end of one hr) and positive CRP (26.0 IU/dl). Otherwise Hemogram was normal. Kidney function, liver function, hepatitis viral serology, Serum calcium ANA, ANCA all were negative. Biopsy from ulcer showed leaukocytoclastic vasculitis. She was diagnosed as Cutaneous PAN. She was treated initially with NSAIDs and steroid. But she had partial response hence methotrexate was added with which she responded and is in remission since 6 months.

Case 2:

A 35 year lady was presented with recurrent skin ulcers since 2 years over both the lower legs which used to get healed leaving deep scars. She visited for recent onset joint pain in small joints of hands and knee joints. Her routine laboratory work up was normal as in first case along with immunological tests. Biopsy from one of the active lesion showed leaukocytoclastic vasculitis. She was managed with combination of analgesics, steroids and azathioprine.

Case 3:

19 year girl was suffering from small red nodules over both the legs since 3-4 months. She also started burning paresthesia in both legs eventually. Clinical examination revealed normal vital parameters including normal blood pressure. Neurological examination revealed no focal neurodeficit. Laboratory work up was normal except elevated acute phase reactants. Skin biopsy revealed leukocytoclastic vasculitis. She was managed with combination of moderate dose steroid and NSAIDs. She achieved remission in about 6 months but the recurrences of symptoms were seen frequently. She lost to follow up in a year.

Case 4:

32 year old normotensive lady was presented with pain and swelling of both ankle and knee joints since 1

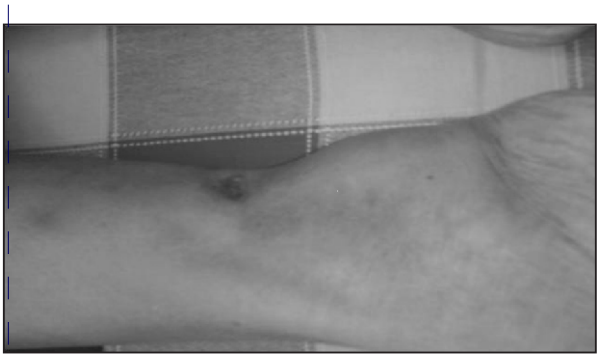
month. She was suspected of having early inflammatory arthritis and managed accordingly with steroid and NSAIDs. Within a week she developed red nodules over both legs multiple and painful. Her ESR was raised otherwise other laboratory reports including serology was negative. Biopsy from the nodule revealed leaukocytoclastic vasculitis. She was managed with steroid and colchicine. She is in remission since 3 years.

Table 1: clinical and laboratory characteristics of our cases

Case	Myalgia Neuropathy Other areas	Arthritis / Arthralgia	Livedo reticulares	Ulceration	Nodules	Fever	Organ Involve-ment	Leukocytosis	Anemia	Proteinuria, Leukocyturia, Hematuria, Elevated creatinine	Elevated ESR	HTN	HBV HCV	ANA RF Complement ANCAs
1	N	Y	N	Y	Y	Y	N	N	N	N	Y	N	N	N
2	Y	Y	N	Y	Y	Y	N	N	N	N	Y	N	N	N
3	Y	Y	N	N	Y	N	N	N	N	N	Y	N	N	N
4	Y	Y	N	N	Y	Y	N	Y	N	N	Y	N	N	N

Y=YES; N=NO/NEGATIVE

Figure 1: ulcerated nodule in case 2 which healed with scar formation.



Discussion

Since its first description in 1931 by Lindberg K [2], CPAN has been underreported as only case reports and few case studies. A reason for underdiangnosing CPAN may be the lack of any specific criteria for diagnosis and its benign, but relapsing and long-term course.[22] Diagnosis, treatment and follow up of CPAN is necessary as some studies have shown that it can progress to systemic PAN. A study of 20 CPAN patients undergoing long-term treatment and follow-up showed that two out of the 20 patients eventually progressed to PAN 18-19 years after their initial diagnosis of CPAN.[6] Another study showed a much higher incidence of seven out of nine CPAN patients eventually showing signs of systemic involvement over a period of 4 months to 14 years after the initial diagnosis of CPAN.[7] Other characteristics of our 4 patients was similar as other studies of CPAN. [6,8] Case 1 has ulcerative nodule in breast which is a very rare site of involvement of any vasculitis.

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