Case Report

Medium Vessel Vasculitis - Classic PAN (Case Report)

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ABSTRACT

Medium vessel vasculitis or Polyarteritis nodosa is a rare condition with incidence of 8 cases per million adult cases.[1] There is no specific data on incidence of PAN in India. It is characterised by necrotizing inflammation of medium sized or small arteries without glomerulonephritis or vasculitis in arterioles, capillaries or venules. Classic PAN is rare with Annual incidence of < 1 / million. HBV associated PAN incidence is reducing due to the impact of vaccination.

PAN can present with involvement of any organ in the body but commonly the muscles, joints, intestines, nerves and skin are affected.

We present a case with mesenteric involvement diagnosed on small bowel biopsy after patient underwent emergency laparotomy for suspected small bowel obstruction with or without gangrene.

Key words : Medium vessel vasculitis, polyarteritis nodosa, mesenteric involvement, HBV associated PAN, systemic vasculitis.

Introduction :

As per Chapel Hill Consensus conference (1994), Polyarteritis nodosa is defined as Necrotizing inflammation of medium sized or small arteries without glomerulonephritis or vasculitis in arterioles, capillaries or venules.

ACR 1990 classification criteria for PAN

As per these criteria, PAN is diagnosed if 3 or more criteria out of ten are present, with 82.2% sensitivity and 86.6%specificity.[2]

1) Weight loss : unintentional weight loss more than 4 Kg from the onset of illness.
2) Livedoreticularis : mottled reticular patterns over the skins of extremities or torso.
3) Testicular pain or tenderness : not due to infection, trauma or other causes
4) Myalgias, weakness, or leg tenderness: diffuse myalgias (excluding shoulder or hip girdle) or weakness of leg muscles.
5) Mono or polyneuropathy : development of mono, multiple mono or polyneuropathy.
6) Diastolic BP > 90 mmHg
7) Elevated urea or creatinine : BUN > 45 mg/dl or Creatinine > 1.5 mg/dl not due to dehydration or obstruction.
8) Hepatitis B virus: either HBsAg surface antigen or antibody in the serum.
9) Arteriographic abnormality : presence of aneurysms or occlusions of visceral arteries, not due to arteriosclerosis, fibromuscular dysplasia or other non-inflammatory causes.
10) Biopsy of small or medium vessel : Histological changes showing presence of medium sized artery containing PMN granulocytes or granulocytes and mononucleolar leucocytes in the artery wall.

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Case Report :

29 years old male, teacher by profession, non-smoker, with no significant past medical history presented to emergency department with history of abdominal pain mainly in the periumbilical area for 7 days, intermittent colicky type not radiating, dull to moderate severity. He was seen by ED doctor and found no sinister abdominal signs. His abdominal X-ray showed non-specific bowel shadowing and hence was discharged home.

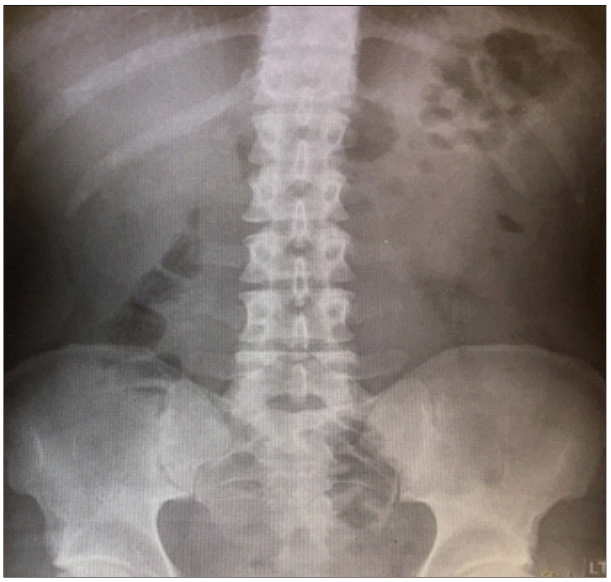

Figure 1 : **Plain Abdominal X-ray**

Patient went home and developed diarrhoea on the next day with some fresh bleeding P/R. There was no h/o constitutional symptoms or weight loss. Patient revisited Emergency Department. Patient was seen by medical team and was admitted to Acute Medical Unit. His vitals were normal and abdominal examination revealed mild tenderness over right iliac fossa, but no guarding or rigidity and bowel sounds were present in all 4 quadrants. His investigations showed Na-132 mmol/L, K-3.9 mmol/L, U-4.3 mmol/L, creatinine 67 micromoles/L, eGFR > 90 Ml/min/1.73 meter square, CRP-75 mg/L, Alb-34 gm/L,ALT-45 U/L, AlkPO 44-49 IU/L, Bil-11 mg/dL, GGT-45 U/L, WBC-17.7 x 109/L, N-15.4 x 109/L rest were normal. Patient was started on oral Cipro after review by Consultant Physician and requested Gastro review. Patient Improved over next 24 hours, bleeding P/R settled, started eating and drinking, Sent Home on next day.

After 2 days, his symptoms worsened. His abdominal cramps worsened, and diarrhoeal frequency also increased. He could not bear the pain and so returned to emergency department. Patient was seen by A & E Consultant who documented lower abdominal distension and a diagnosis of? IBD was kept and referred to Medical team.

His blood investigations showed raised WBC-18.5 x 109/L and was CRP - 168 mg/L, His liver function tests were ALT - 82 U/L, GGT - 81 U/L and Amylase was 48 U/L. His kidney function tests showed Na - 130 mmol/L, K - 4.5 mmol/L,U -3.9 mmol/L, eGFR > 90 ml/min / 1.73 meter square and Lactate-1.4 mmol/L. His Stool Culture which was sent during previous admission was negative for Salmonella, shigella, campylobacter and E. coli.

Patient was seen by Consultant Physician on Post take ward round. On examination his abdomen was soft, no guarding and rigidity, bowel sounds were present. The clinical impression was likely Inflammatory bowel disease and a plan to do have a Gastroenterology review and flexible sigmoidoscopy after diarrhoea settles.

Next day of admission patient's condition deteriorated a d his diarrhoea worsened, and bleeding P/R continued. Gastroenterology Consultant reviewed the patient and advised to treat like campylobacter / salmonella gastroenteritis. Patient's WBC count increased progressively from 23.6 x 109/L to 39.9 x 109/L and CRP from 86 mg/L to 189 mg/L.

Next 48 hours patient remained stable and his diarrhoea stopped, and patient managed to eat some food. However, on 4th day of his admission he developed severe abdominal pain and became unwell. His WBC increased to 40.3 x 109/L and CRP to 230 mg/L. Patient had bilious vomiting and he developed abdominal guarding and hence CT abdomen was requested, and a surgical opinion was sought.

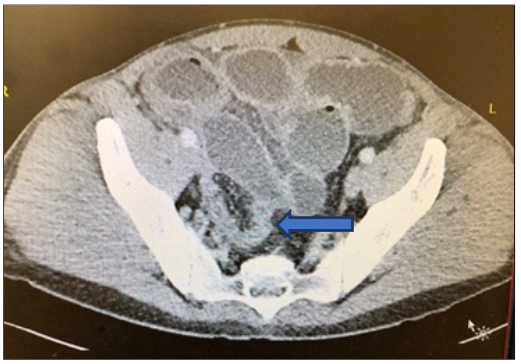

Figure 2 : **CT showing short collapsed terminal ileum as indicated by blue arrow**

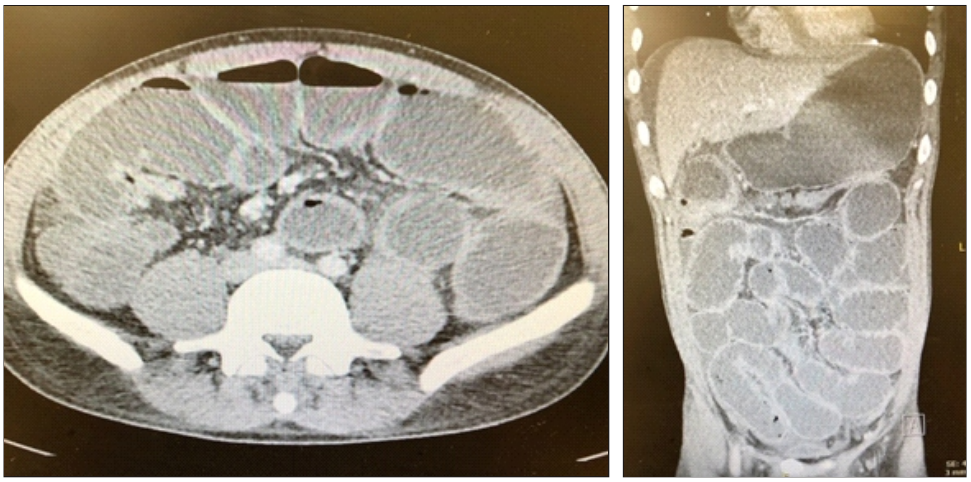

Figure 3 & 4 : **CT showing dilated small bowel loops with air fluid levels suggestive of small bowel obstruction in axial and coronal section**

His CT abdomen and pelvis showed distal small bowel obstruction. There was a short collapsed terminal ileum.

Patient was reviewed after CT Abdomen and pelvis by Surgeon and Gastroenterologist together and decided to proceed with Diagnostic Laparoscopy +/- Proceed if required.

Patient underwent Small bowel resection + anastomosis as 1- foot necrotic small bowel segment had to be removed. Patient had stable post-operative period and made rapid recovery. His CRP and WBC counts started improving and patient was mobilised on 2nd day & discharged on 7th Post-operative day.

His Histopathology report was sent to the surgeons and Gastroenterology Consultant 8 days post operatively. His report was as follows :

Macroscopicexamination : 40 cm length of bowel with 2 cm viable looking bowel at the joined stapled ends. No mass lesions seen.

Microscopicexamination : The resection margins show moderate ischaemic changes but are viable. There is a severe ischaemia throughout the length of the bowel with areas of complete full thickness bowel infarction.

There is a patchy active vasculitis within the medium sized blood arteries within the bowel wall. The inflammation is patchy even within the same vessels. No giant cells or granulomas seen. Some small thrombi seen within the similar sized vessels. The large vessel in the high tie region doesn't show any thrombosis or vasculitis.

Impression : Severe small bowel ischaemia secondary to medium sized arterial vasculitis with severe ischaemia and infarction with viable margins.

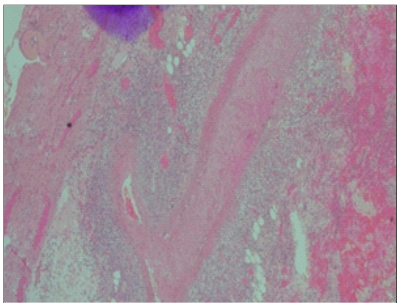

Figure 1 : **Histological features of medium size arterial vasculitis**

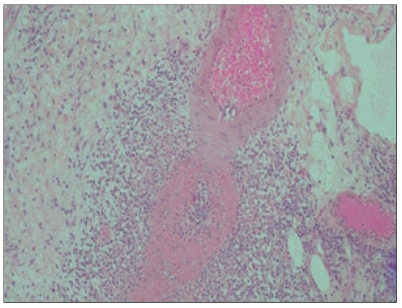

Figure 2 : **Histological features of medium size arterial vasculitis like infiltration of inflammatory cells in the vessel wall with occlusion of lumen**

After the histopathological report was available, patient was given 30 mg prednisolone daily till his Urgent Rheumatological appointment was through.

Patient was reviewed in Rheumatology clinic in 3 days. A detailed Rheumatological assessment was done. Patient was found to have nail fold infarcts in left thumb, right great toe and left 4th toe. In view of the recent history and histopathology report, a diagnosis of Systemic vasculitis? polyarteritis nodosa was kept and patient was given Intravenous Methyl prednisolone 500 mg daily for 3 days was given followed by Prednisolone 40 mg daily whilst waiting for induction of remission therapy in the form of cyclophosphamide to be arranged. All the investigations for vasculitis screening were sent.

Table 1 **: showing summary of the antibody tests done**

Sr No.	Name of the test	Result
1	ANA	Negative
2	ENA ab screening test (Ro,Ls,Sm,RNP,Scl-70,Jo)	Negative
3	dS-DNA	Negative
4	ANCA	Negative
5	Cryoglobulin	Negative
6	C3, C4	Normal
7	Serum electrophoresis	No paraproteins detected

Patient was referred to specialist centre for Vasculitis at St. Guys and Thomas Hospital, London under Proff. David Cruz, as per patients request for second opinion.

Patient was assessed at Vasculitis specialist centre and was advised CYCLOPS regimen as follows[3] as induction of remission.

TPMT (thiopurine methyl transferase) was checked on commencement of cyclophosphamide to ensure results were available prior to introduction of azathioprine maintenance therapy.

The first 3 pulses were given at intervals of 2 weeks, intravenously and then orally 3 pulses were given over 3 days with dose no more than 5mg/kg.

Patient went into remission after 6 pulses and hence conversion to azathioprine and Prednisolone was done after remission achieved. (Initially 2 mg/kg).

Maintenance of remission regime was started as follows :

Azathioprine was started 2 weeks after last cyclophosphamide dose after checking TPMT level along with prednisolone.

Prednisolone was started 1mg/kg and then reduced to 0.75 mg/kg on next week. Further dose was reduced to 0.50 mg/kg for 2 weeks and then reduced to 0.25 mg/kg till 3 months and then slowly tapered over next 15-18 months.

At the time of writing this case report patient is having a stable course and is on Prednisolone 5 mg and azathioprine 100 mg daily and his inflammatory markers are, ESR 4 and CRP <1.

Patient also has resumed his job as a teacher and is coming to us for Rheumatology follow up at 6 monthly follow up.

Table 2 : **showing cyclops regimen for induction of remission of systemic vasculitis**

Time in Weeks	Pulse number	Body mass in Kg	Route	Dosage
0	1		Intravenous	15mg/kg
2	2		intravenous	15mg/kg
4	3		intravenous	15mg/kg
7	4		Intravenous/oral	15mg/kg
10	5		Intravenous/oral	15mg/kg
13	6		Intravenous/oral	15mg/kg
16	7		Intravenous/oral	15mg/kg
19	8		Intravenous/oral	15mg/kg
22	9		Intravenous/oral	15mg/kg
25	10		Intravenous/oral	15mg/kg

Discussion :

This is a classic case of systemic vasculitis where the diagnosis is often missed due to some commoner clinical diagnosis. In this case patient was seen by 5 experienced clinicians and twice by the Gastroenterology consultant. His presentation was like any acute gastroenteritis and later of an inflammatory bowel disease patient. The minor clinical clues suggesting of vasculitis are often missed where common clinical impression. When this patient was seen in Rheumatology clinic, important clinical signs of nailbed infarcts were obvious, and their relevance could have been correlated.

As polyarteritis nodosa and other systemic vasculitis syndromes not common one should always suspect these group of disorders where one of the following are present

- Systemic symptoms are disproportionate to clinical signs
- Very high ESR and CRP not matching with the presentation
- History of night sweats
- High platelet count
- Family history of autoimmune conditions or joint symptoms
- Skin rash

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