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POLYMYALGIA RHEUMATICA(PMR) ASSOCIATED WITH INFLAMMATORY FOCAL COLITIS: A DIAGNOSTIC CHALLENGE

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Abstract : Polymyalgia rheumatica is a rare disorder with no known cause. It usually poses a diagnostic challenge but should be considered in a patient with fatigue and chronic pains and non-specific elevated C-reactive protein and erythrocyte sedimentation rate (ESR) inflammatory tests. We present a 44-year-old man who came with fever, fatigue, early morning pains at the shoulder and neck, weight loss and anemia. Laboratory tests indicated an inflammatory process and a histologic diagnosis of inflammatory focal colitis. He was managed with prednisone with marked improvement. This case shows that a diagnosis of inflammatory focal colitis associated with polymyalgia rheumatica poses a diagnostic challenge and can easily be missed.

Key words- **Polymyalgia rheumatica, inflammatory, inflammatory bowel disease, focal active colitis**

INTRODUCTION

This patient had anemia, thrombocytosis, and fever of unknown origin. This may be a sign of inflammatory, neoplastic, rheumatologic, hematological, or collagen vascular disease. Polymyalgia rheumatica (PMR) is rare and involves the release of inflammatory cytokines that affect the joints and blood vessels, and treatment involves the use of glucocorticoids for at least two years (Lundberg et al., 2022). Polymyalgia rheumatica is known to commonly occur in adults aged greater than 50 years (Schmidt & Warrington, 2011) but our case report is in a male less than 50 years.

CASE REPORT: We admitted a 44-year-old male with fever, weakness, weight loss, left shoulder pain and passage of melena stools. He complained of feeling stiff for up to an hour most mornings. When asked about his past medical history, it was discovered that he had carried out a colonoscopy 4 months prior to presentation. The result was normal, and it was done as a work-up for passage of melena stool which occurred after taking NSAIDs.

Physical examination showed an adult who was weak with no signs of thyroid, liver, rheumatic, or vasculitic disease. Thorough laboratory investigations were done and shown in the table below are the reports.

Table 1: Full blood count results

	I	II	III	IV	V	VI
DATE	16/9/2023	21/9/2023	3/10/2023	6/10/2023	12/10/2023	26/10/2023
HEMOGLOBIN (g/dl)	10.8	10.6	8.5	9.2	8.9	9.4
PCV (%)	37.5	32	26	30	31.3	31
WBC(TOTAL) (mm3)	8200	3500	9000	12,000	9700	7.73
NEUTROPHILS (%)	76.7	37	75	68	68.8	55.7
LYMPHOCYTES (%)	14.4	55	22	21	15.5	25
MONOCYTES (%)	1	5	1	6	1	1.16
EOSINOPHILS (%)	1	3	1	5	3	3.9
BASOPHILS (%)	1	1	1	1	1	0.4
PLATELETS (ul)	361,000	400,000	596,000	264,000	440,000	512,000
RBC (mil/cm^3)	4.59	3.34	2.71	3.00	2.92	3.87
MCV (fL)	81.7	81.0	80	80.2	81.5	80.1
MCH (pg)	23.5	24.8	31	26.0	23.2	24.3
MCHC (g/dL)	28.8	31.0	39	32.0	31.3	30.3

At presentation initial hemoglobin (Hb) concentration was 10.8 g/dl and PCV was 37.5%. Normocytic normochromic red blood cells were seen with a red blood cell count of 4.59 millions/cmm and a platelet count of 361 thousands/cmm. (Table 1 column I).
A few days to weeks later, hemoglobin (Hb) concentration reduced to 10.6 g/dl, and then to 8.5g/dl. Packed cell volume of 32%, reduced to 26%, while red blood cell count of 3.79 millions/cmm reduced to 2.71 millions/cmm. Platelet count of 400 thousands/cmm increased to 596,000 thousands/cmm giving a microcytic, hypochromic picture with thrombocytosis.
Peripheral blood smear results showed anisopoikilocytosis with anisochromia and thrombocytosis with platelet clumping.
Impression: i. Background dimorphic anaemia to rule out iron deficiency
ii. Thrombocytosis ? reactive to rule out chronic blood loss.

With the drop of the PCV from 32% to 26% (Table 1. Column II & III) with signs of decompensation, he was given two pints of blood. Post transfusion PCV done was 30%. (Table 1, Column IV). Reticulocyte count prior to transfusion was 0.5% (0.5-2.2%).
Helicobacter Pylori test was negative.
Stool occult blood test done one month prior to admission was positive and a repeat while on admission was also positive. A bleeding peptic ulcer disease was considered as a possible cause of chronic blood loss and an upper GI endoscopy was done which showed:
Oesophagus: The lower third is hyperaemic with few erosions. No evidence of recent bleed. Nil ulcers, varices or masses. Oesophago-gastric junction is irregular.
Stomach: The corpus and antrum are inflamed with few erosions, nil ulcers or masses. The mucosa of the cardia and fundus are not inflamed. Pylorus not deformed.
Duodenum: Bulb and second part: mucosa is normal, no deformities, no ulcers or masses seen.
Conclusion: Gastro-esophageal reflux disease LA Grade A.
He was started on triple regimen (Omeprazole, clarithromycin and metronidazole).
Pyrexia continued unabated and malignancy was considered. To rule out a colorectal cancer, the nonspecific tests (carcinoembryonic antigen (CEA) and Ca 19-9) were requested. The reports of these tests were essentially normal.

CEA: 0.58ng/ml (Normal 0-5.0 ng/ml)
Smokers <5
Non smokers <3
CA 19-9:1.2 U/ml (Normal 0-35 U/ml)
Iron serum level was markedly reduced at 2.3umol/l (Normal range: 12-30 umol/l) and the ferritin concentration was also markedly elevated (742.48 ng/mL Normal range: 10-150 ng/mL). Elevated serum iron and ferritin levels are usually a sign of hyperthyroidism, liver disease, iron storage disorder, such as hemochromatosis, rheumatoid arthritis, chronic disease process and other inflammatory conditions.
Liver function tests were normal. (Table II). Renal function tests were normal also. The non-specific inflammatory tests, C-reactive protein and ESR were requested. The C-reactive protein report showed a very high value of >200mg/l which is above the upper limit of the reference range for normal values (normal: 0-10mg/l). The erythrocyte sedimentation rate was also markedly elevated, >120 mm/h (normal: 0-24mm/h).
The human immunodeficiency virus 1/2, and the hepatitis A, B, C viruses were negative, Covid 19 RT-PCR test was negative.

Table 2. Liver function test results

TEST	VALUE
Albumin Serum Normal: (18-36 g/l)	31
Alkaline Phosphatase (ALP)	56
ALT(SGPT) Normal:(4 to 36 u/l)	47
AST(SGOT) Normal: (10-42u/l)	15
Bilirubin conjugated Normal:(2-20umol/l)	3.2
Total Bilirubin Normal (2-20umol/L)	6.1
Bilirubin Unconjugated Normal:(2-14 umol/L)	2.9
Total Protein Normal: (64-83g/l)	69
Gamma GT(GGT) Normal: (7-64 u/l)	47
Globulin Serum: Normal: (20-35 mg/l)	34
Albumin/Globulin Ratio Normal: (0.9-2.7mg/L)	1

Rheumatoid factor was negative. The urine microscopy, culture and sensitivity test done yielded no growth after 48 hours of incubation. A chest computed tomography scan was essentially normal while an abdominal computed tomography scan showed moderate hepatomegaly with a liver span of 17.9cm but no hepatic masses or hepato-biliary obstruction. There were two cortical cysts in the left kidney measuring 3.2cm × 2.4cm and 1.6cm × 1.3cm respectively. A cortical cyst was also noted in the right kidney measuring 2.0cm × 1.7cm. Conclusion: Multiple renal cortical cysts with moderate hepatomegaly (? Cause).

Inflammatory bowel disease (IBD) was considered, and colonoscopy was done and a biopsy taken and sent for histology showed: colonic mucosa with foci of crypt destruction by neutrophilic infiltrates. There is patchy lymphocytic infiltration in the lamina propria with mild basal lymphocytosis. Conclusion: Colonic tissue biopsy: Focal active colitis. No evidence of malignancy.

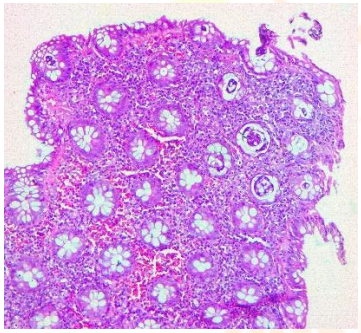

Figure 1. Colonoscopic biopsy showing colonic mucosa with cryptitis and formation of crypt abscesses. Haematoxylin amd eosin. x100 magnification.

The left shoulder pain was sharp, intermittent with no radiation, transiently relieved with pain killers and continued unabated despite adequate analgesics.
Magnetic Resonance Imaging of the cervical spine showed straightening of the cervical spine. The vertebrae are normal in height and marrow signal. No focal vertebral mass lesion.
There was mild left paracentral protrusion of C3/4 and C4/5 discs causing narrowing of the lateral recesses with exiting nerve root impingement. There was severe reduction in dorsal kyphosis and lumbar lordosis.
The thoracic and lumbar vertebral bodies with intervertebral discs were within normal limits. The posterior elements and facet joints were normal.

The spinal cord showed normal contour and signal intensity with the conus medullaris at L1 vertebral level. There was no evidence of cord compression or mass lesion.
The paravertebral soft tissue was unremarkable. Conclusion: Mild C3/4 and C4/5 left paracentral disc protrusions with lateral recess narrowing and exiting nerve roots compression. Cervical and thoracolumbar muscles spasm were noted.
This clinical scenario of fatigue with intermittent pain affecting the left shoulder and neck posed a diagnostic challenge and prompted the consideration of polymyalgia rheumatica (Lundberg et al., 2022). There was no history of vision difficulties, scalp tenderness and jaw pain. Biopsy of the temporal artery is not a routine recommendation and was not done for this patient.
Polymyalgia rheumatica is usually associated with giant cell arteritis but less often with inflammatory bowel disease. (Schmidt & Warrington, 2011). Prednisone was considered but the result of the lower GI endoscopy was waited. As soon as the result showed focal active colitis, prednisone was started. His relief was almost immediate, and the fever subsided by the next day. Over the course of the month after discharge from hospital, his hemoglobin levels started rising steadily. Two months after discharge on a maintenance dose of prednisone 5mg daily, the patient felt well.

DISCUSSION

Polymyalgia rheumatica is an inflammatory condition characterized by pain around the neck, shoulder, and hip with a high C reactive protein and ESR result (Florescu et al., 2023; Acharya & Musa, 2023). The cause is unknown but there are infectious, autoimmune, and chronic bowel inflammatory processes postulated to be associated with its pathogenesis (Scrivo et al.,2018; Mackie,2013; Guggino et al.,2018; Floris et al., 2018). Systemic symptoms such as fever, malaise, weight loss may also be seen in patients (Matteson & Dejaco, 2017). Normocytic anemia and thrombocytosis may be seen. Our case had normocytic anaemia at first then later microcytic anaemia with thrombocytosis.

Polymyalgia rheumatica is usually associated with giant cell arteritis (Ahmed, 2013; Nesher & Breuer, 2016) but less often with inflammatory bowel disease though studies have shown an association (Halling et al., 2017). Our case had no symptoms of giant cell arteritis, but the presence of gastrointestinal symptoms led to a provisional diagnosis of inflammatory bowel disease.
Histology of the colonic biopsy showed focal active colitis which meant there were no signs of chronic inflammation but a predominance of neutrophilic damage of focal crypts. Literature however has shown that a diagnosis of focal active colitis can herald a diagnosis of inflammatory bowel disease (Sinagra et al.,2017; Shetty et al.,2011) while others show no such correlation (Greenson et al.,1997; Volk et al., 1998). Sinagra et al, (2023) agree that larger prospective studies to explore the relationship between focal active colitis and inflammatory bowel disease need to be carried out as more recent literature seems to show it is a notable predictor.

Involvement of the gut and joints at the same time by disease processes have been described in literature. The pathogenesis though not fully understood has been thought to be through infectious, hypersensitivity and immune complex deposition mechanisms (Ashrafi et al., 2021). Genes associated with both inflammatory bowel disease and other immune mediated diseases (such as polymyalgia rheumatica) have been identified (Lees et al.,2011).

Polymyalgia rheumatica is Th1 mediated. Th17 cells in ulcerative colitis can induce a Th1 response which might explain the association. A study by Ma et al. (2023) found that the pathogenesis of polymyalgia rheumatica involved JAK signaling and as such alternatives to glucocorticoids use such as tofacitinib which is a Janus tyrosine kinase (JAK) inhibitor is welcome. Polymyalgia rheumatica can be associated with subclinical giant cell arteritis and a biopsy of the temporal artery is the gold standard for diagnosis (Mertens et al., 1995). However, a positron emission tomography– computed tomography which is non- invasive can be done where there is reluctance to do a biopsy as was the case in this patient and it would show inflammatory arteritis (Salvarani et al., 2012).

The association between polymyalgia rheumatica and giant cell arteritis has been widely documented in literature but the association with inflammatory focal colitis is rarer. This article adds to the body of evidence that such associations exist and should be investigated.

CONCLUSION

In conclusion, we admitted a 44-year-old male with fever, weakness, weight loss, left shoulder pain, passage of melena stools, anaemia, and thrombocytosis. An inflammatory state (inflammatory focal colitis) may be associated with polymyalgia rheumatica which is a rare diagnosis but should be considered in a similar setting as described in our case report. The challenge with this disorder is that response is dramatic but long-term use of steroids is fraught with complications.

RECOMMENDATION

Large population-based studies should be done to determine the association between immune mediated diseases such as polymyalgia rheumatica and inflammatory focal colitis with a view to understanding its pathophysiologic aetiology.

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CONFLICTS OF INTEREST

None of the authors have any conflicts of interest.

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