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Case Report

Rare case of pernicious anaemia from a university hospital of Nepal: A case report

Suyesh Raj Shrestha, Pramit Ram Shrestha *, Abhyuday Kumar Yadav, Sneha Shrestha, Ashish Shrestha, Pawan Katwal

Kathmandu University School of Medical Sciences, Dhulikhel, 45210, Nepal

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ABSTRACT

Introduction: Pernicious Anaemia is a rare autoimmune disorder prevalent among 0.1% of the general population and is characterised by decreased cobalamin absorption. This condition is overlooked because of its rarity, insidious onset of non-specific symptoms and clinically asymptomatic state. Elevated serum intrinsic factor antibody level along with reduced Vitamin B12 level confirms the diagnosis.

Case presentation: Pallor and abdominal tenderness was present. Haematological investigations showed elevated platelet count, elevated Mean Cell Volume reduced haemoglobin level(11.4 g/dl), reduced Vitamin B12 and high serum intrinsic factor antibody level. Serum parietal cell antibody was positive. The patient responded well to parenteral Vitamin B12.

Discussion: In Pernicious anaemia, serum intrinsic factor antibody and parietal cell antibody are high which are responsible for reduced Vitamin B12 absorption. Studies have also shown positive correlation between H pylori and Pernicious Anaemia. Neurological symptoms are less common but may present as paraesthesia, changes in gait or spasticity due to peripheral neuropathy. It is also associated with autoimmune diseases. Untreated pernicious anaemia can lead to neurological and gastrointestinal complications.

Conclusion: Pernicious Anaemia is an overlooked condition because of its insidious onset of non-specific symptoms, clinically asymptomatic state, rarity and therefore timely diagnosis of Pernicious Anaemia still remains a challenge.

1. Introduction

Pernicious Anaemia is a complex disorder with haematological, gastric, immunological and neurological alterations characterised by cobalamin deficiency [1,2]. The prevalence is 0.1% in the general population, manifests usually in people above 30 years and increases with age [1]. This progressive autoimmune disease is due to the auto antibodies that work against intrinsic factor secreted by stomach and gastric parietal cells resulting in deficient Vitamin B12 absorption [2]. Pernicious Anaemia requires lifelong treatment with intramuscular Vitamin B12 injection along with iron deficiency monitoring [3]. Here we report a rare case of Pernicious Anaemia with *H. pylori* induced Peptic Ulcer Disease. The diagnosis of Pernicious Anaemia imposes great clinical burden on the hospital level. Economic burden of Pernicious Anaemia is high because of difficulty in diagnosis, greater lengths of stay and lifelong treatment [4]. This case report has been prepared in line with SCARE guidelines [5] (see Fig. 1)

2. Case report

A 40-year-old male presented to the outpatient department with a history of abdominal pain for 2 months. It was acute on onset, over the epigastric region, gradually progressive, diffuse, stabbing character and was associated with nausea and vomiting. There were 2–3 episodes of vomiting for the prior 7 days. The vomitus contained food particles and was not bile stained or bloodstained. History of the occasional black tarry stool was present suggestive of malena. He also has a history of numbness and tingling sensation of the hand and feet for one month. Water Brash and loss of appetite was present. There is no significant past medical and surgical history. He was diagnosed with Peptic Ulcer Disease. One week prior to the presentation, the patient visited a nearby hospital where he was diagnosed with Peptic Ulcer Disease and his stool

* Corresponding author.
E-mail addresses: suyesh311@gmail.com (S.R. Shrestha), pramit.shrestha.prs@gmail.com (P.R. Shrestha), abhyudayjnk1999@gmail.com (A.K. Yadav), snehashrestha091@gmail.com (S. Shrestha), drashishshresthakums@gmail.com (A. Shrestha), drpawankatwal91@gmail.com (P. Katwal).

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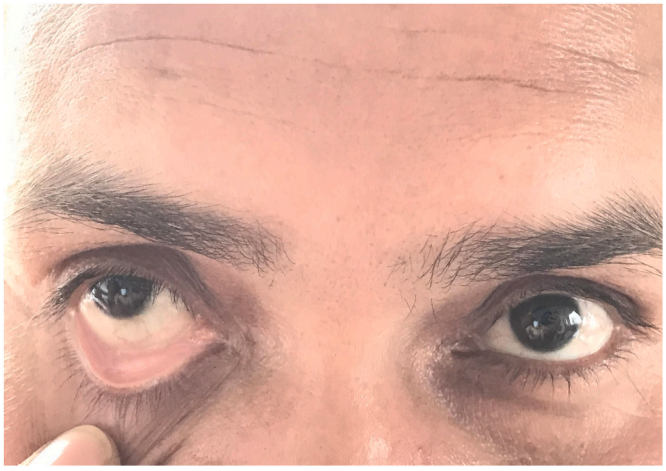

Fig. 1. Figure showing pallor in the palpebral conjunctiva of right eye diagnostic of anaemia.

antigen came positive for *Helicobacter pylori,* for which a triple regimen had been started.

Pallor was present on the general examination. Abdominal tenderness was present on abdominal examination. On haematological investigations, haemoglobin level was reduced with value 11.4 g/dl. Platelet count was elevated with value 598,000 per microliter blood. Vitamin B12 level was 83 ng/l diagnostic of Vitamin B12 deficiency. Folic acid level was 14.4. Mean Cell Volume was 114 fl which was higher than the normal level (80–100 fl) showing macrocytic anaemia. Serum intrinsic factor antibody level was 121 units, also much higher than the normal level(<20) and serum parietal cell antibody came positive which confirmed the diagnosis of PA.

Test	Result	Units	Reference Range	Remarks
Haemoglobin level	11.4	g/dl	13–17	Low
Platelets Count	598	× 10^3/ µL	150–450	High
Mean Cell Volume	114	fl	80–100	High
Vitamin B12	83	pg/ml	190–950	Low
Serum intrinsic factor antibody level	121	units	<20	High
Serum parietal cell antibody	Positive	_	_	

The patient was admitted in the hospital and intramuscular cyanocobalamin was given daily for one week. Then, he was discharged and he took intramuscular cyanocobalamin once a week for a month. Haematological investigations were repeated one month later when he came for follow up which showed normal Hb level(13g/dl) and normal Vitamin B12 level.

3. Discussion

Pernicious Anaemia is a progressive autoimmune disease characterised by atrophy of the body and fundus of stomach, reducing the number of parietal cells that produce intrinsic factors responsible for cobalamin absorption [2]. The absorption of cobalamin also requires haptocorrin present in saliva and transcobalamin present in serum [1]. Two types of autoantibodies, Intrinsic factor antibodies and parietal cell antibodies, target the binding site of cobalamin as well as interfere with binding of IF to the epithelium of ileal mucosa decreasing the absorption of cobalamin [1].

Pernicious Anaemia usually predisposes in patients over 30 yrs with no gender predisposition; the prevalence however increases with age from 2.5 to 12% [2]. Our patient is a 40 year old male without any genetic predisposition.

There are some studies that say that *H. pylori* lipopolysaccharides and gastric mucosa share protein structures resulting in mimicry between *H. pylori* antigens and H + /K + ATPase of parietal cells which in turn stimulate parietal cell antibody production while some suggest genetic predisposition for the association [6]. According to different studies, the prevalence of *H. pylori* was 11%, 21% and 40% [7]. Also, the prevalence of *H. pylori* antibody was 83% in a study of 30 patients of Pernicious Anaemia showing past exposure to *H. pylori* infection [7]. Our patient came positive for *H. pylori* antigen on conducting a stool antigen test showing active bacterial infection. So, *H. pylori* can be a risk factor for Pernicious Anaemia.

Pernicious Anaemia presents with nonspecific symptoms which are often insidious in onset. These may include lethargy, headaches, inability to concentrate, cardiac symptoms like chest pain and palpitations [1,8]. Gastrointestinal symptoms like anorexia, weight loss, diarrhoea, epigastric discomfort, abdominal pain can also occur in this case rarely [8]. Neurological symptoms are less common but may present as paraesthesia, changes in gait or spasticity [1,8]. The lack of cobalamin may attribute to changes in nerve fibres ranging from demyelination to axonal degeneration to even nerve death that may not be reversible even with Vitamin B12 replacement therapy [8]. Our patient had a history of abdominal pain, nausea, vomiting, anorexia, black tarry stool and paraesthesia probably due to peripheral neuropathy.

Association of Pernicious Anaemia with other autoimmune diseases like autoimmune hemolytic anaemia(AIHA) due to production of RBC antibodies, Hashimoto's thyroiditis, type 1 diabetes mellitus, Addison's disease, primary hypoparathyroidism, vitiligo, primary biliary cirrhosis, autoimmune hepatitis are commonly noted [8,9]. Autoimmune atrophic gastritis is caused by this autoimmune reaction by parietal cell antibodies. Moreover, Pernicious Anaemia may be associated with the production of red blood cell (RBC) antibodies leading to AIHA [10].

The diagnosis for Pernicious Anaemia can be made by measuring serum vit B12 level(less than 200ng/l), haemoglobin level, complete blood count, examination of peripheral blood smear(hypersegmented neutrophils), blood iron and folate level, autoantibodies to gastric parietal cells and intrinsic factor, bone marrow examination, levels of methylmalonic acid and homocysteine level [2]. Negative result of intrinsic factor antibody doesn't exclude the diagnosis of Pernicious Anaemia as only 40–60% of patients with Pernicious Anaemia have this antibody [8]. Measurement of parietal cell antibodies in conjunction with intrinsic factor antibodies aid in evaluation of patients with Pernicious Anaemia Yielding 73% sensitivity and nearly 100% specificity for Pernicious Anaemia [8]. In our case, haemoglobin level was reduced, platelet count was elevated, folic acid level was normal and Vitamin B12 level was 83 ng/l diagnostic of Vitamin B12 deficiency. Serum intrinsic factor antibody level was much higher than the normal level and serum parietal cell antibody came positive confirming Pernicious Anaemia.

Pernicious Anaemia is treated by prescribing Vitamin B12 in the form of intramuscular cyanocobalamin, hydroxocobalamin, or methylcobalamin, monitoring Vitamin B12, iron deficiency and looking for complications [11]. Hydroxocobalamin is a natural form of Vitamin B12 and is said to have better tissue uptake and storage than the other forms [11]. To prevent early relapse, a dose of 1000 µg daily for 1 week, followed by 1000 µg per week for 1 month, then a monthly dose of 1000 µg for life is given [11]. The treatment modality set for our patient is the same as above.

Untreated Pernicious Anaemia can lead to neurological complications like paraesthesia, ataxia, amnesia, combined sclerosis of spinal cord, cerebellar syndrome and parkinsonism but may have delayed clinical presentation as Vit B12 can be stored in the body and can last up to 10 years in certain individuals [11]. Iron deficiency anaemia may be seen in patients with Pernicious Anaemia secondary to their state of hypochloridia causing a defect in iron absorption [1]. Gastrointestinal complications are also present in long standing Pernicious Anaemia.

Pernicious Anaemia is considered to be a precursor to neoplastic lesions [6]. Individuals with Pernicious Anaemia have 2.84 fold higher

risk of developing gastric carcinoma(namely intestinal type of adenocarcinoma) compared to individuals without Pernicious Anaemia [11,12]. The higher risk is attributed to increase in gastric mucosa secondary to hypochloridia in Pernicious Anaemia and increase in abundance of nitroso amine producing microflora that may act as a carcinogen [6,8]. Carcinoid tumours are the most common neoplasms associated with Pernicious Anaemia with incidence varying between 4 and 7% depending upon the researcher [8,11].

4. Conclusion

Pernicious Anaemia is an overlooked condition because of its insidious onset of non-specific symptoms, clinically asymptomatic state, rarity and therefore timely diagnosis of Pernicious Anaemia still remains a challenge. Early diagnosis and treatment decreases the risk of disabling neurological and gastrointestinal complications in the future. Treatment of Pernicious Anaemia is simple and patients under treatment show remarkable improvement.

Ethical approval

As the case report contains information of retrospective period, we had obtained exempt for ethical approval from Institutional ethical committee.

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None.

Authors' contribution

Dr. Ashish Shrestha and Dr. Pawan Katwal contributed to clinical management and patient care.

Suyesh Raj Shrestha, Pramit Ram Shrestha, Abhyuday Yadav and Sneha Shrestha wrote, reviewed and edited the article.

Consent

Informed written consent was taken from the case in this case report. We also ensured, none of the identifying characteristics are included in the case report.

Declaration of patient consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Provenance and peer review

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Registration of research studies

1. Name of the registry:
2. Unique identifying number or registration ID:
3. Hyperlink to your specific registration (must be publicly accessible and will be checked):

Guarantor

The Guarantor is the one or more people who accept full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish.

Declaration of competing interest

There are no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.104151.

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