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RESEARCH ARTICLE

A CASE OF HEADACHE TURNING INTO MYELOPROLIFERATIVE NEOPLASM-A CASE REPORT

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Abstract

Headache is an important clinical symptom commonly encountered by practising physicians. Thorough history and physical examination is a must for arriving at differentials of headache. Headache is divided into- primary and secondary. Myeloproliferative neoplasm induced hyper viscosity and associated headache is an important though a rare entity in clinical medicine. This is the case report of a 60 yr. old female who presented with history of chronic headache which was induced by polycythemia vera, an important myeloproliferative neoplasm. Treatment of MPN associated headache is different from that of normal headache, as it involves treatment of underlying disorder. Main treatment modality involve phlebotomy, cytoreductive therapy-hydroxy urea, low dose aspirin, JAK -1/2 inhibitor-Ruxolitinib. Splenectomy is rarely indicated in present clinical scenario.

Introduction:-

Headache is a very common and debilitating neurological symptom that is encountered by all at least once during their lifetime. Headache can be attributed to many common and uncommon causes. Careful elicitation of history and proper clinical examination is very important in diagnosis and management of headache. Broadly it is divided as primary and secondary headaches.

Primary headache	Percentage	Secondary headache	Percentage
Tension type	69	Systemic infection	63
Migraine	16	Head injury	4
Idiopathic Stabbing	2	Vascular disorders	1
Exertional	1	SAH	1
Cluster	0.1	Brain tumor	0.1

Primary headaches result in affecting the quality of life of patient and are associated with disease itself while secondary is caused by exogenous disorder.

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Case Report
60 yr. old female presented with history of chronic headache of 1 yr. duration. Patient was evaluated elsewhere and had taken multiple medications for same but symptoms not subsided.

Headache was chronic in onset and gradually progressive usually lasted for about 6 to 8 hrs aggravated by exposure to sunlight and stress, relieved by intake of NSAIDS only to reoccur in the next few days. Pain occurred in about 2 – 3 episodes per week.No diurnal variation for headache. There were no associated symptoms or warning signs of headache like blurring of vision, neck pain, fever, vomiting, weakness, vertigo or tinnitus. Hence she was admitted in our institution for evaluation of headache.

Within few hours of admission, she developed deviation of angle of mouth and slurring of speech. No associated weakness of limbs. No sensory or cerebellar involvement or history suggestive of other cranial nerve involvement. Was observed in ward for next 24 hrs for progression of weakness. There was no further progression

O/E – Patient was conscious and cooperative
Vitals – stable. No pallor,icterus,cyanosis,clubbing,lymphadenopathy or edema
CNS- Higher mental function-normal

Cranial nerves- all normal except for involvement of 7^{th} nerve. Deviation of angle of mouth to right and loss of nasolabial fold on left. There was drooling of saliva through left side. Plantar –B/L mute

Motor system, Sensory system, cerebellar system, ANS and peripheral nerves – WNL

Per Abdomen- Splenomegaly 6cm below left coastal margin, rest normal

Examination of other systems-WNL

Considering the present status of patient, proceeded with the following investigations: -

Investigations

Hb-**18**	BU/Cr-29/0.9	URE-NAD
Tc-11000	Na/K-136/3.5	ECG- NAD
Dc-P60L38	TB-0.7	
Plt-5.5 lakh	Tp/Alb-6.7/3.5	
RBC Count-**6.8 million/microL**		
PCV-54%	OT/PT/ALP-24/28/200	
P smear- Normocytic normochromic RBC Count-Increased WBC- Normal Plt-Normal No abnormal cells.	CT Brain- Acute infarct in right corona radiata	

Considering the clinical history and lab values, polycythemia was attributed to headache and acute stroke. Next aim was to determine the etiology of polycythemia. Hence S. EPO level and JAK-2 mutation were sent.
S.EPO- 2 Mu/ML (4-26)
JAK-2 Mutation- POSITIVE

Dx- POLYCYTHEMIA VERA

Treatment
Five serial phlebotomies were performed.
Patient was started on low dose aspirin and hydroxy urea.
Patient symptomatically improved upon treatment and discharged with advice to review after 1week.
On review patient was symptom free with the following lab parameters.
Hb-15.9
PCV-45.6%

RBC-5.6 million/mcl
Tc-9000
Plt-4 lakh
Patient was counselled about need for prolonged treatment and frequent followups.Therapeutic phlebotomies were periodically repeated to maintain PCV level below 45%.

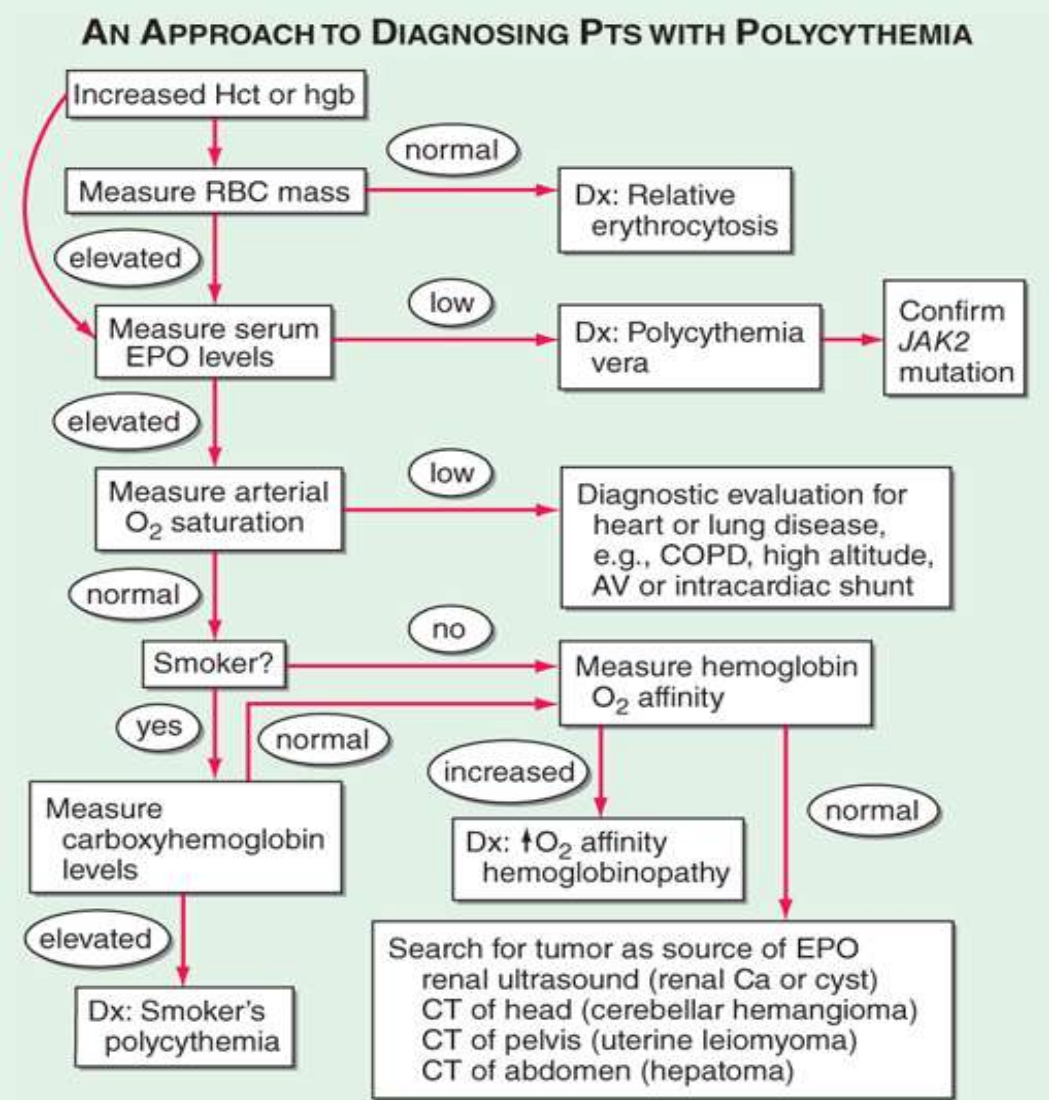
Discussion:-

Relatively few cranial cranial structures are pain producing which include scalp, meninges, Dural sinus, falx cerebri, proximal part of large pial arteries. Ventricular ependyma, choroid plexus, pial veins, and brain parenchyma are not pain producing. Important structures involved in primary headache are mainly the intracranial vessels, dura mater and peripheral terminals of trigeminal nerve. It became very important to identify certain warning signs that helps to differentiate serious from non-serious headache.

Red Flag Signs…
1.Sudden onset headache
2.First severe headache
3.Worst headache ever
4.Vomiting that precede headache
5.Subacute worsening over days or weeks
6.Pain induced by lifting, bending or cough
7.Pain that disturb sleep or present immediately upon awakening
8.Known systemic illness
9.Onset after 55yrs
10.Fever or unexplained clinical signs
11.Abnormal neurologic examination
12.Pain associated with local tenderness eg.in region of temporal artery

Apart from these, understanding specific disorders that present with headache is important for investigation of additional diagnostic approaches. Myeloproliferative neoplasms, including polycythemia vera and essential thrombocythemia are associated with thromboembolic events. Nearly 30 per cent of patients with MPN develop vasomotor symptoms that present with transient neurological features including headache or other visual symptoms. Polycythemia vera is essentially a stem cell disorder in which phenotypically normal red cells, granulocytes, and platelets accumulate in absence of recognizable physiologic stimulus. Isolated thrombocytosis, leucocytosis or splenomegaly may be initial manifestation of PV but most often the disorder is incidentally detected. Usually associated hyper viscosity symptoms like vertigo, tinnitus, headache, visual disturbance, transient ischemic attacks, systolic hypertension. Any vessel may be affected but usually cerebral, cardiac, and mesenteric vessels are commonly involved.Absorption and proteolysis of hmw vwD Factor may lead to acquired vwD and can sometimes present as bleeding.

Understanding approach to diagnosis of polycythemia is very important in ruling out secondary causes from polycythemia vera.



Conclusions:-

PV is generally an indolent disorder. Thrombosis due to erythrocytosis is early and important complication and treatment is aimed at preventing thrombosis. Target of treatment is to maintain Hb level <14 g/dl (PCV <45%) in men and <12g/dl (PCV <42%) in women. Serial phlebotomy helps to achieve iron deficient state and thus prevent further red cell mass expansion and once iron deficiency is achieved only 3 monthly phlebotomies is required. JAK1/2 inhibitor Ruxolitinib, PUVA therapy and hydroxyurea have become an important method of treatment in polycythemia vera. Acquired vwD is treated with EACA. Symptomatic splenomegaly can be treated with Ruxolitinib and PEG INFalpha. Hydroxyurea is preferred agent but this does not prevent either thrombosis or myelofibrosis in polycythemia. The drug itself is leukemogenic and should be used for short time as possible.No role for bone marrow transplantation is described in this disorder. Treatment of headache associated with MPN is essentially different from neurological headache. However, to date no studies have investigated whether aspirin or cytoreductive therapy have influences on number of headaches per month.

References:-

1. Headache Classification Committee of the International Headache Society (IHS) The international classification of headache disorders 3rd edition Cephalalgia. 2018;38:1–211.
2. Sohn JH, Choi YJ, Kim BK, Chung PW, Lee MJ, Chu MK, et al. Clinical Features of Probable Cluster Headache: A Prospective, Cross-Sectional Multicenter Study. Front Neurol. 2018 Oct;9:908.

3. Martins IP, Gouveia RG, Parreira E. Cluster headache without autonomic symptoms: why is it different? Headache. 2005 Mar;45((3)):190–5.
4. Drummond PD. Dissociation between pain and autonomic disturbances in cluster headache. Headache. 1990 Jul;30((8)):505–8.
5. Khalil M, Yoga B, Ahmed F. Cluster-like headache responsive to phlebotomy. BMJ Case Rep. 2014 Jun;2014(jun04 1):2014
6. Quintás-Cardama A, Kantarjian H, Cortes J, Verstovsek S. Janus kinase inhibitors for the treatment of myeloproliferative neoplasias and beyond. Nat Rev Drug Discov. 2011 Feb;10((2)):127–40.
7. Röder S, Steimle C, Meinhardt G, Pahl HL. STAT3 is constitutively active in some patients with Polycythemia rubra vera. Exp Hematol. 2001 Jun;29((6)):694–702.
8. Rittner HL, Machelska H, Stein C. Leukocytes in the regulation of pain and analgesia. J Leukoc Biol. 2005 Dec;78((6)):1215–22
9. Neeb L, Hellen P, Hoffmann J, Dirnagl U, Reuter U. Methylprednisolone blocks interleukin 1 beta induced calcitonin gene related peptide release in trigeminal ganglia cells. J Headache Pain. 2016;17((1)):19.
10. Ickenstein GW, Klotz JM, Langohr HD. [Headache caused by polycythemia vera. Classification of a headache under the heading of metabolic disturbances] Schmerz. 1999 Aug;13((4)):279–82.
11. Gaul C, Krummernerl P, Tamke B, Kornhuber M. Chronic daily headache in hereditary hemochromatosis treated by venesection. Headache. 2007 Jun;47((6)):926–8.
12. Stovner LJ, Hagen K, Waage A, Bjerve KS. Hereditary haemochromatosis in two cousins with cluster headache. Cephalalgia. 2002 May;22((4)):317–9
13. Mampreso E, Maggioni F, Viaro F, Disco C, Zanchin G. Efficacy of oxygen inhalation in sumatriptan refractory "high altitude" cluster headache attacks. J Headache Pain. 2009 Dec;10((6)):465–7.
14. Britze J, Arngrim N, Schytz HW, Ashina M. Hypoxic mechanisms in primary headaches. Cephalalgia. 2017 Apr;37((4)):372–84
15. Aamodt AH, Borch-Iohnsen B, Hagen K, Stovner LJ, Asberg A, Zwart JA. Headache prevalence related to haemoglobin and ferritin. The HUNT Study. Cephalalgia. 2004 Sep;24((9)):758–62.
16.Harrison principles of Internal Medicine 20th Edition page :84-89,733-735.
17.S.H. Swerdlow, E. Campo, N.L. Harris, E.S. Jaffe, S. Pileri, H. Stein, *et al*.WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues.4th ed., International Agency for Research on Cancer
18.J.L. Spivak.Polycythemia vera: myths, mechanisms, and management.Blood, 100 (2002), pp.
19.R. Rai, T. Pieters.An unusual psychiatric presentation of polycythaemia "Difficulties lie in our habits of thought rather than in the nature of things" Andre Tardieu.Case Rep., 2013 (2013),
20.A. Tefferi, T. Barbui.Polycythemia vera and essential thrombocythemia: 2019 update on diagnosis, risk-stratification and management.Am. J. Hematol., 94 (2018), pp. 133-143
21.M.F. McMullin, D. Bareford, P. Campbell, A.R. Green, C. Harrison, B. Hunt, *et al*.
Guidelines for the diagnosis, investigation and management of polycythaemia/erythrocytosis.
Br. J. Haematol., 130 (2005), pp. 174-195
22.J. Haber.Psychosis in polycythemia vera.J. Nervous Mental Dis., 115 (1952), pp. 537-540
23.M. Levin.Erythremia (polycythemia) with a psychosis.Am. J. Psychiatry, 87 (1930), pp. 407-410
24.S. Röder.STAT3 is constitutively active in some patients with Polycythemia rubra vera.
Exp. Hematol., 29 (2001), pp. 694-702.