Polycythemia in hepatits C seropositive end stage renal disease patients: Role of insulin like growth factor 1

Sir,

We present two end stage kidney disease patients who were initially erythrocyte sensitizing agent (ESA) dependent, but subsequently developed polycythemia in spite of stopping the ESA.

A 39-year-old gentleman with chronic glomerulonephritis was on maintenance haemodialysis since 2007. Serology for hepatitis C virus (HCV), hepatitis B virus (HBV) and human immunodeficiency virus (HIV) were negative. He was initially on weekly 4,000 units of erythropoietin alpha S/C. Since there was disproportionate rise in his hemoglobin with this, we stopped his erythropoietin in December 2011. But his hemoglobin continued to be in normal to high normal range (13.5-15.5 g%). Biochemical investigations are noted in Table 1. Secondary causes of polycythemia were ruled out. The yearly viral marker screening done in March 2012 showed positivity for HCV.

The second case, a 43-year-old man was on maintenance haemodialysis since March 2010. He was negative for HCV, HBV and HIV. He was on darbepoetin 40 µg on alternate weeks with which he maintained a haemoglobin between 10 g/dL and 11 g/dL. Since December 2011, a steady rise in haemoglobin was noticed which reached 15.5 g/dL. We stopped ESA in February 2012. Blood investigations noted in Table 1. Here again, secondary causes of polycythemia were ruled out. This patient was again detected to be positive for HCV in March 2012 during the yearly screening.

In short, we have two patients with end-stage renal disease (ESRD) having erythrocytosis in spite of stopping ESA. There were no obvious causes for secondary polycythaemia. They were subsequently detected to have HCV hepatitis on yearly screening. First patient is having features of iron overload and the second patient that of chronic inflammation, both of which can be explained by the presence of chronic hepatitis C infection.

Anaemia is invariabe in patients with chronic kidney disease except for some patients with cystic kidney disease.[1] Erythrocytosis has been observed in ESRD patients with hepatitis C.[2] HCV positivity, as in our subjects, was associated with absence of anaemia in a cohert of ESRD patients.[3] Another observation study has shown a decrease in erythropoietin requirement in ESRD patients who are HCV positive.[4] Liver can produce erythropoietin as is well known in *in utero* state. However, contradictory findings have been shown in different studies regarding association of elevated erythropoietin levels associated with erythrocytosis in ESRD.[2] Both our patients had low normal levels of serum erythropoietin levels. Insulin like growth

Table 1: Investigations in June 2012

Parameters	Case 1	Case 2
Hb (g/dl)	13	14.5
TLC (cumm)	8900	9400
PLC (lakhs/cmm)	1.9	2.2
pO_2 (mmHg)	98	96
pCO_2 (mmHg)	43	38
HCO_3 (meq/L)	22.7	23
S. *bilirubin* (mg/dl)	0.9 (15.39 µmol/L)	0.8 (13.68 µmol/L)
AST (IU/L)	47	33
ALT (IU/L)	33	35
ALP (IU/L)	313	282
Protein (mg/dl)	7.8	7.5
S. *albumin* (mg/dl)	3.9	3.6
S. *ferritin* (ng/dL)	>1650	1123
TIBC (250-450 µg/dL)	192	187
TSAT (mg/dl)	84.4	26.2
S. *iron* (µg/dL)	162	49
S. *epo* level (µ/mL)	8.13	4.04
S. IGF-1 level (ng/mL)	399 (109-284)	150 (109-284)

TLC: Total leucocyte count, DC: Differential count, N: Neutrophils
L: Lymphocytes, E: Eosnophils, PLC: Platelet count, TIBC: Total iron binding capacity, TSAT: Transferrin saturation, epo: Erythropoietin
IGF-1: Insulin-like growth factor 1, AST: Aspartate aminotransferase
ALT: Alanine aminotransferase

factor 1 (IGF-1) plays an important role in post-transplant erythrocytosis.[5] Serum IGF-1 levels are significantly elevated in ESRD patients and erythrocytosis compared to normal subjects and ESRD patients with anaemia.[1] It has been demonstrated that IGF-1 enhanced human erythropoetic progenitor cell growth *in vitro*.[6] Another study has shown increased sensitivity of haemopoetic cells to IGF-1 in ESRD patients without anaemia.[7] Thus HCV positivity has shown to be associated with erythrocytosis in ESRD. We postulate that in ESRD patients with HCV infection, IGF-1 (which is produced by liver)/IGF-1 related pathway may be responsible for erythrocytosis. Our first patient had elevated serum IGF-1 and the second had normal IGF-1. In the latter patient, increased sensitivity to IGF-1 may be mediating erythrocytosis. This requires further studies.

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