Case Report

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Cystoid Macular Oedema Due to Cancer Associate Retinopathy: A Rare Presentation and Its Response to Intravitreal Bevacizumab Injection

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Abstract

We here present a cancer associated retinopathy with gradually progressive moderate diminution of vision in a patient of gall bladder carcinoma. There was bilaterally symmetrical cystoids macular oedema (CME) and was treated with intravitreal Bevacizumab injection with partial improvement in the vision and CME.

Keywords: Cancer Associated Retinopathy; Gall Bladder Carcinoma; Cystoids Macular Oedema; Intravitreal Injection; Bevacizumab; Anti-VEGF.

Introduction

Cancer associated retinopathy (CAR) is the most prevalent paraneoplastic retinopathy of the spectrum of diseases called autoimmune retinopathy. Still being a rare disease approximately only 100 cases of cancer-associated retinopathy have been reported in the literature [1].

The case reported here by us is a CAR patient with gall bladder carcinoma with local metastasis as the primary contributory disease. This association has not yet been reported in literature and another unusual presentation was of Cystoid Macular Oedema (CME) as manifestation of CAR. we present here the Optical Coherence Tomography (OCT) findings of the case and response to treatment by intravitreal Bevacizumab injection.

Key Messages

Cancer associated retinopathy (CAR) can present as gradually progressive bilateral moderate diminution of vision with cystoids macular oedema and gall bladder carcinoma can be one of the causes of CAR.

Case History

A 62 year old female patient presented in September 2014 with painless progressive diminution of vision in both eyes for last 4 months. At the time of presentation the patient did not have any systemic illness.

On ocular examination the patient vision had visual acuity of 6/24 (Log MAR 0.6) in both the eyes with no improvement with refractive correction. Early bilateral immature senile cataracts were present but did corroborate the significant vision loss. On fundus evaluation bilateral cystoids macular oedema (CME)was seen with no other associate findings. The OCT showed bilateral CME with central macular thickness of 503 micron and 514 micron in right eye and left eye respectively. (Figure 1. Figure 2. OCT macula Right eye and Left eye respectively showing increased macular thickness with typical cystoids spaces). There was no known systemic disease at the time of presentation.

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Patient's blood investigations including blood sugar, hemogram, and kidney function tests were normal. However, the Liver function tests revealed marginally raised serum glutamic oxaloacetic transaminase (SGOT) (58.0 IU/Lt) and Alkaline Phosphatase enzymes (163.6 IU/Lt).

Patient was administered intravitreal Bevacizumab for cystoid macular oedema in both the eyes and was kept on follow up. Repeat OCT during follow up after 6 weeks of the intervention,showed reduction in CME (Figure 3. Figure 4. OCT macula of right and left eyes respectively after 6 weeks of intravitreal Bevacizumab injections) and the visual acuity improved to 6/18 in both the eyes.

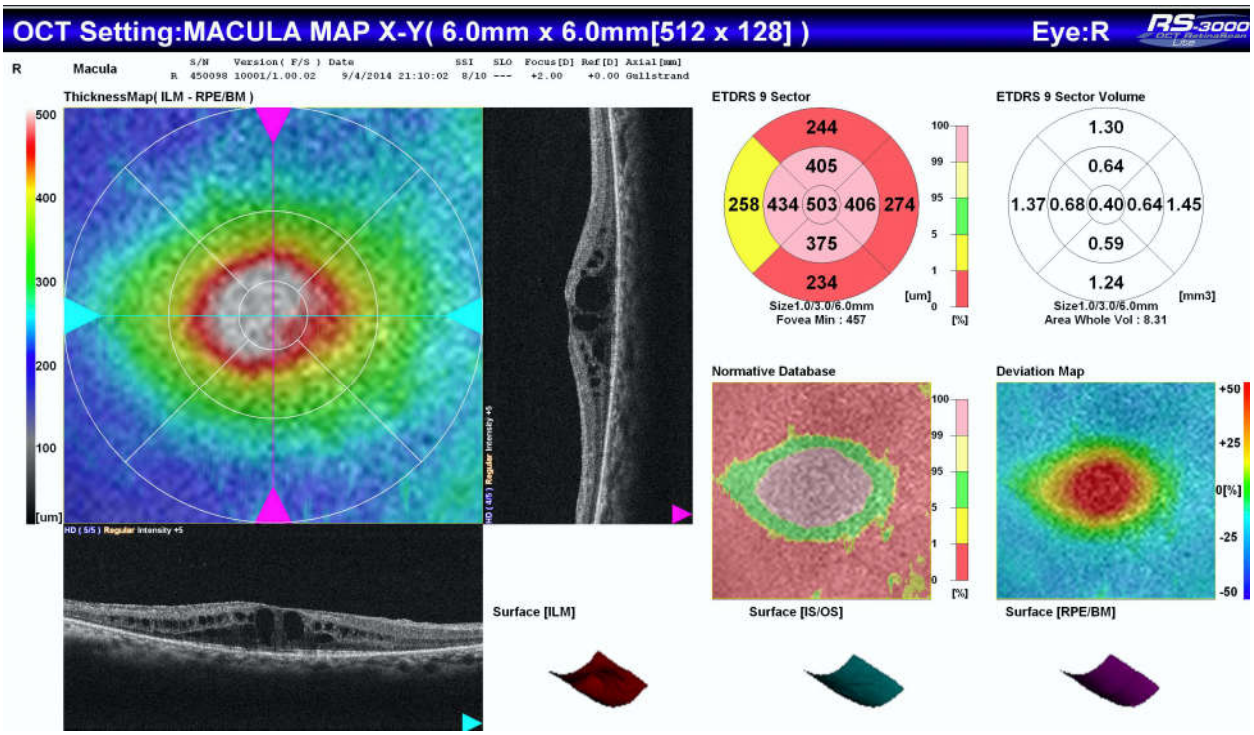

Fig. 1:

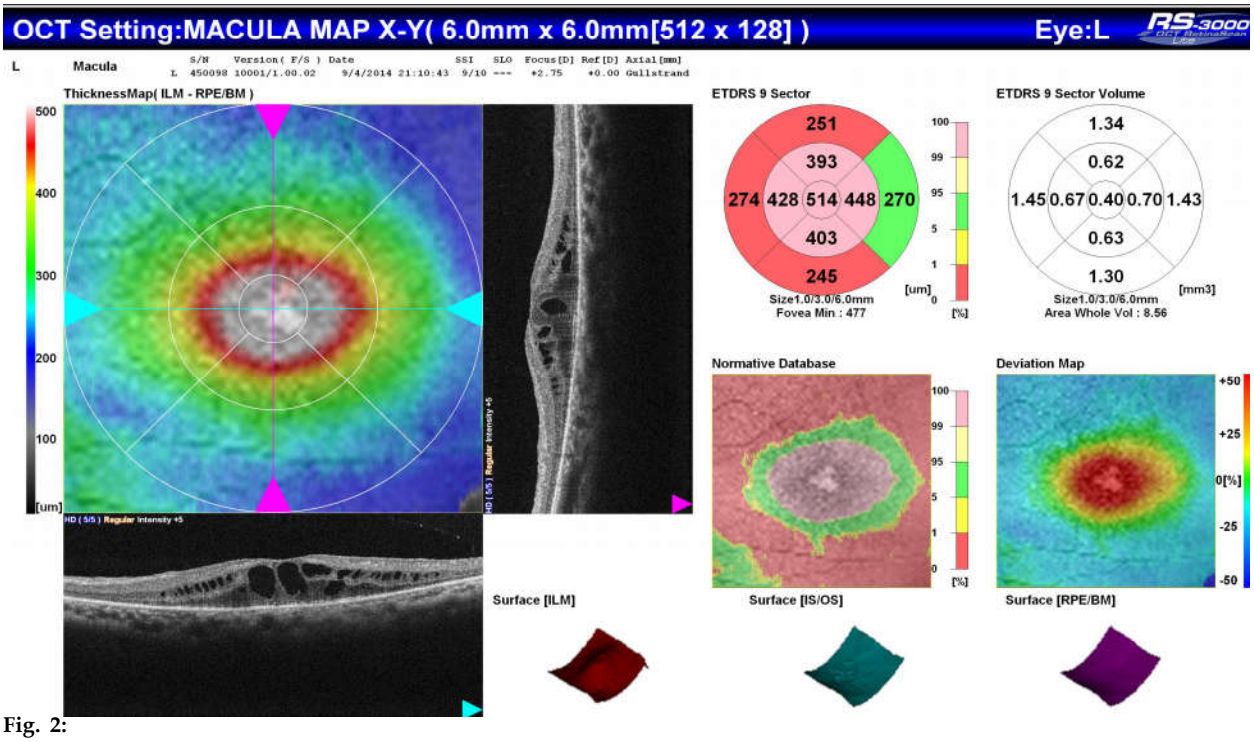

Fig. 2:

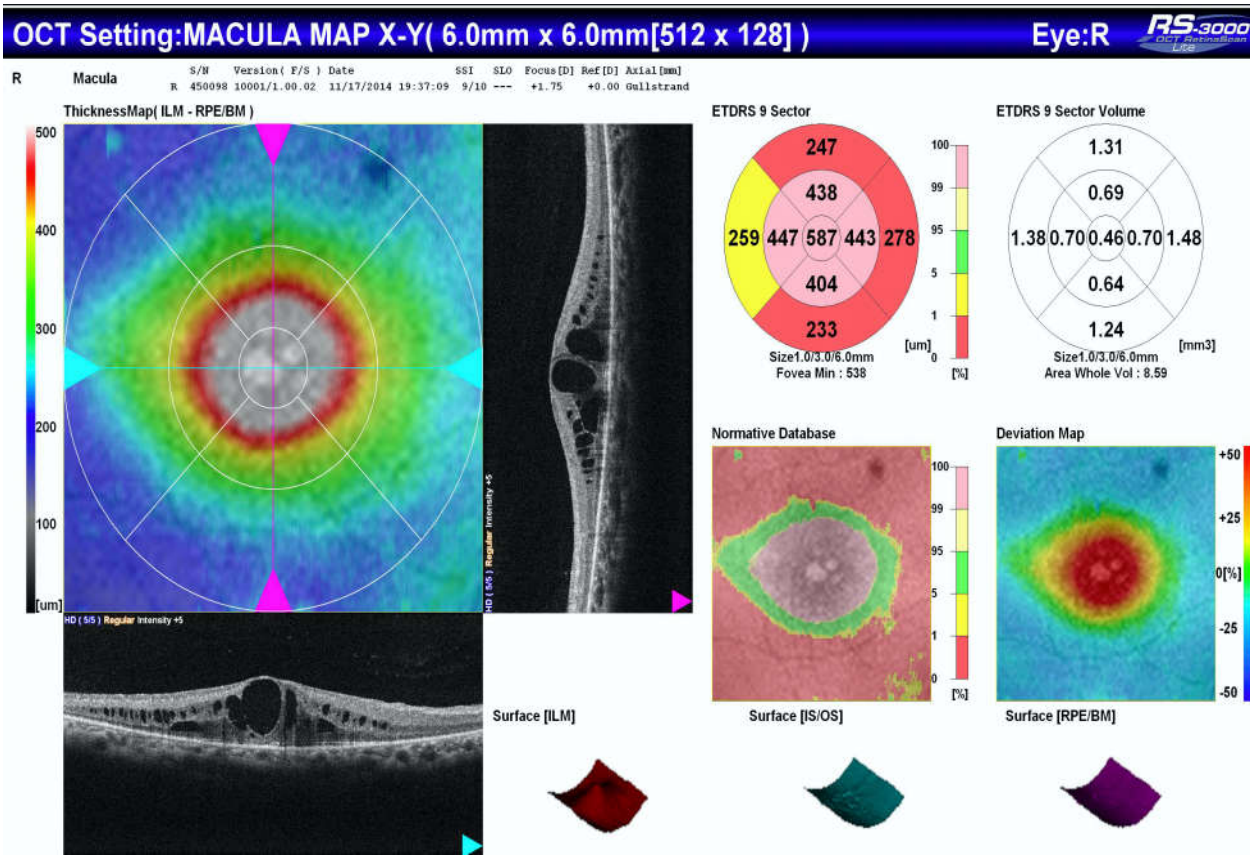
OCT Setting:MACULA MAP X-Y(6.0mm x 6.0mm[512 x 128])
Eye:R
R Macula
ThicknessMap(ILM - RPE/BM)
ETDRS 9 Sector
247
438
259 447 587 443 278
404
233
Size1.0/3.0/6.0mm
Fovea Min : 538
ETDRS 9 Sector Volume
1.31
0.69
1.38 0.70 0.46 0.70 1.48
0.64
1.24
Size1.0/3.0/6.0mm
Area Whole Vol : 8.59
Normative Database
Deviation Map
Surface [ILM]
Surface [IS/OS]
Surface [RPE/BM]

Fig. 3:

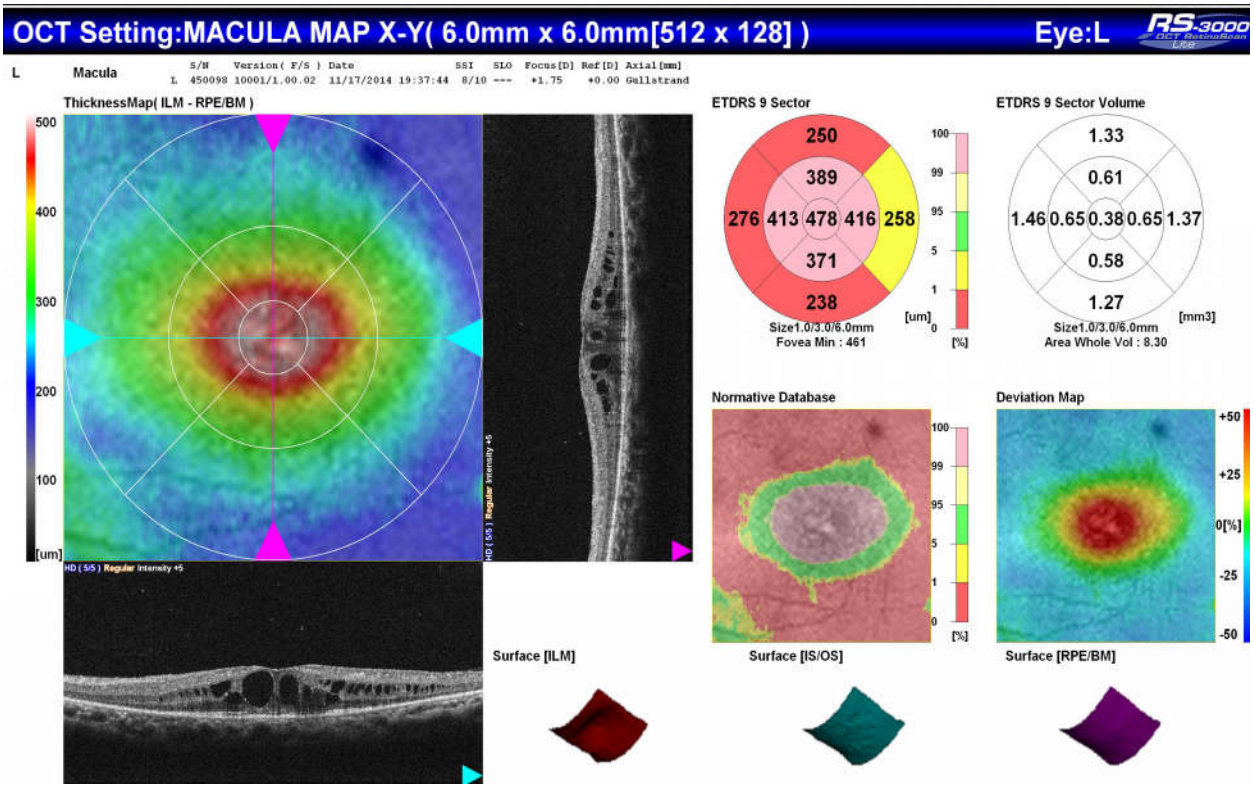
OCT Setting:MACULA MAP X-Y(6.0mm x 6.0mm[512 x 128])
Eye:L
L Macula
ThicknessMap(ILM - RPE/BM)
ETDRS 9 Sector
250
389
276 413 478 416 258
371
238
Size1.0/3.0/6.0mm
Fovea Min : 461
ETDRS 9 Sector Volume
1.33
0.61
1.46 0.65 0.38 0.65 1.37
0.58
1.27
Size1.0/3.0/6.0mm
Area Whole Vol : 8.30
Normative Database
Deviation Map
Surface [ILM]
Surface [IS/OS]
Surface [RPE/BM]

Fig. 4:

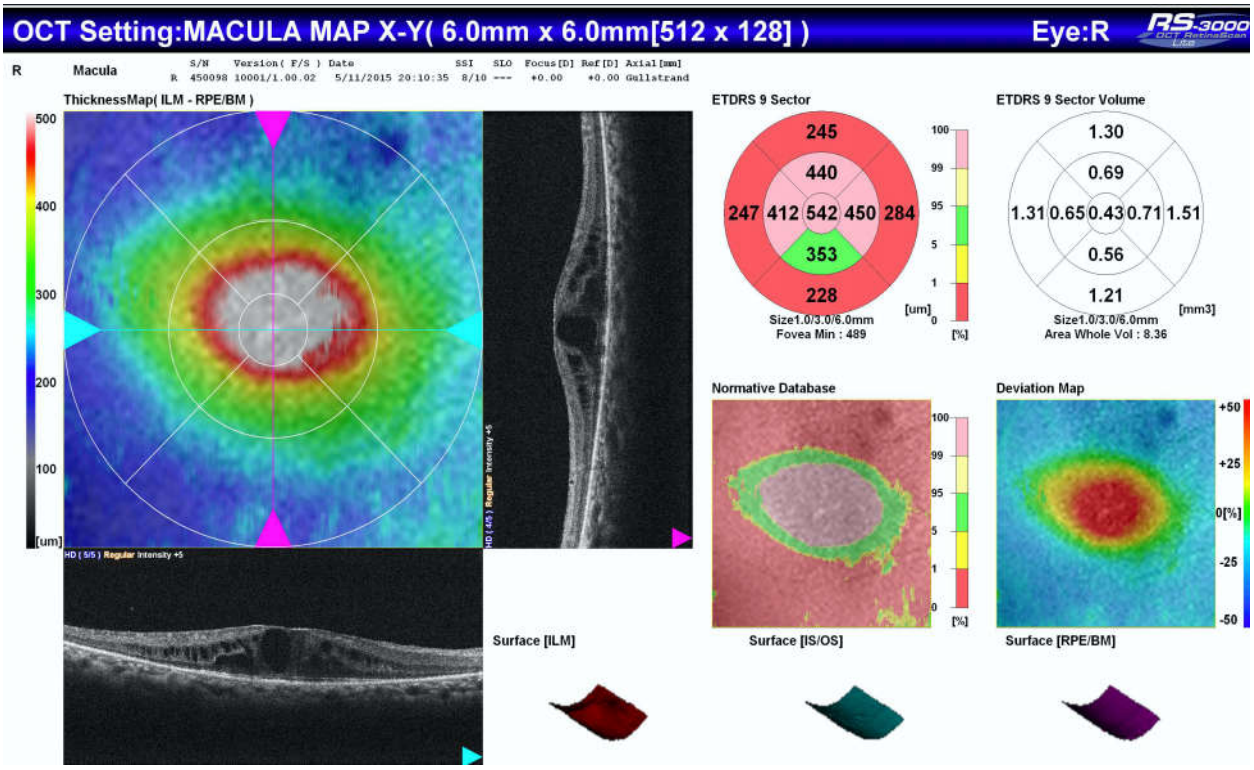
OCT Setting:MACULA MAP X-Y(6.0mm x 6.0mm[512 x 128])
Eye:R
R Macula
ThicknessMap(ILM - RPE/BM)
ETDRS 9 Sector
245
440
247 412 542 450 284
353
228
Size1.0/3.0/6.0mm
Fovea Min : 489
ETDRS 9 Sector Volume
1.30
0.69
1.31 0.65 0.43 0.71 1.51
0.56
1.21
[mm3]
Size1.0/3.0/6.0mm
Area Whole Vol : 8.36
Normative Database
Deviation Map
Surface [ILM]
Surface [IS/OS]
Surface [RPE/BM]

Fig. 5:

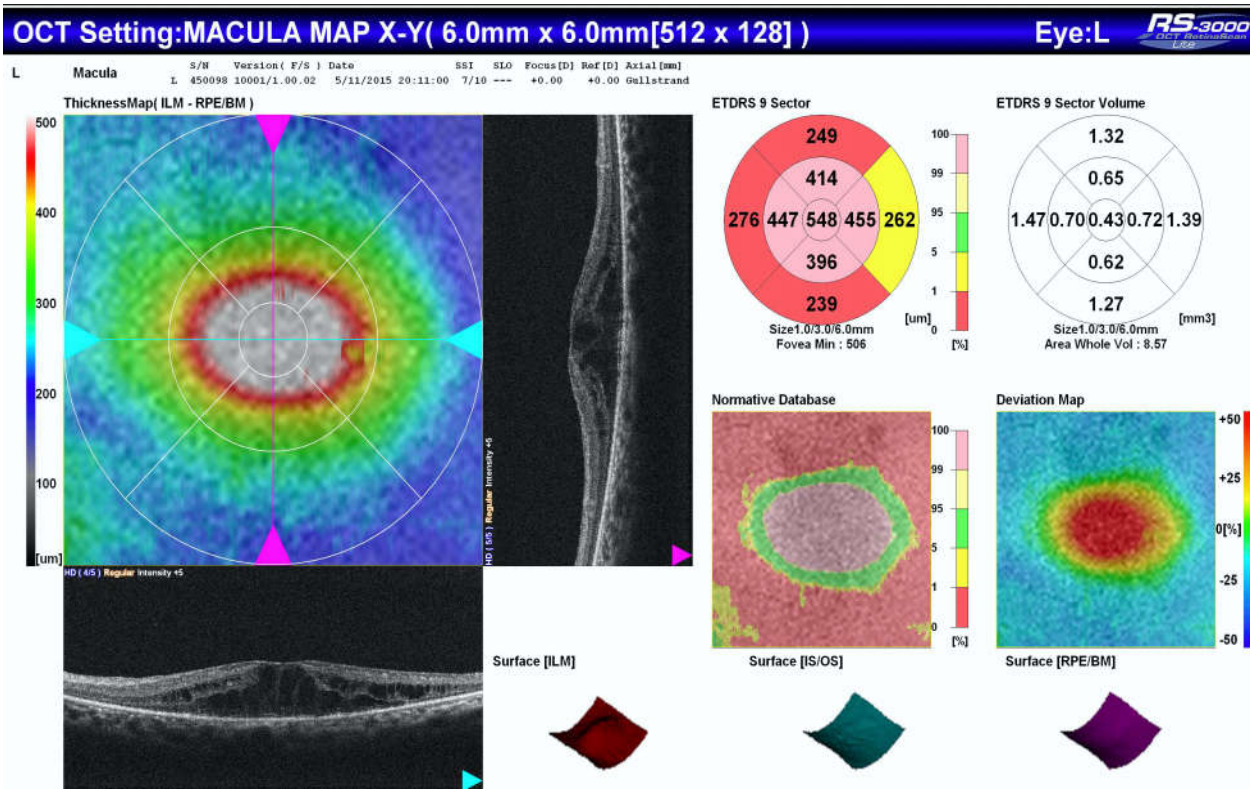
OCT Setting:MACULA MAP X-Y(6.0mm x 6.0mm[512 x 128])
Eye:L
L Macula
ThicknessMap(ILM - RPE/BM)
ETDRS 9 Sector
249
414
276 447 548 455 262
396
239
Size1.0/3.0/6.0mm
Fovea Min : 506
ETDRS 9 Sector Volume
1.32
0.65
1.47 0.70 0.43 0.72 1.39
0.62
1.27
[mm3]
Size1.0/3.0/6.0mm
Area Whole Vol : 8.57
Normative Database
Deviation Map
Surface [ILM]
Surface [IS/OS]
Surface [RPE/BM]

Fig. 6:

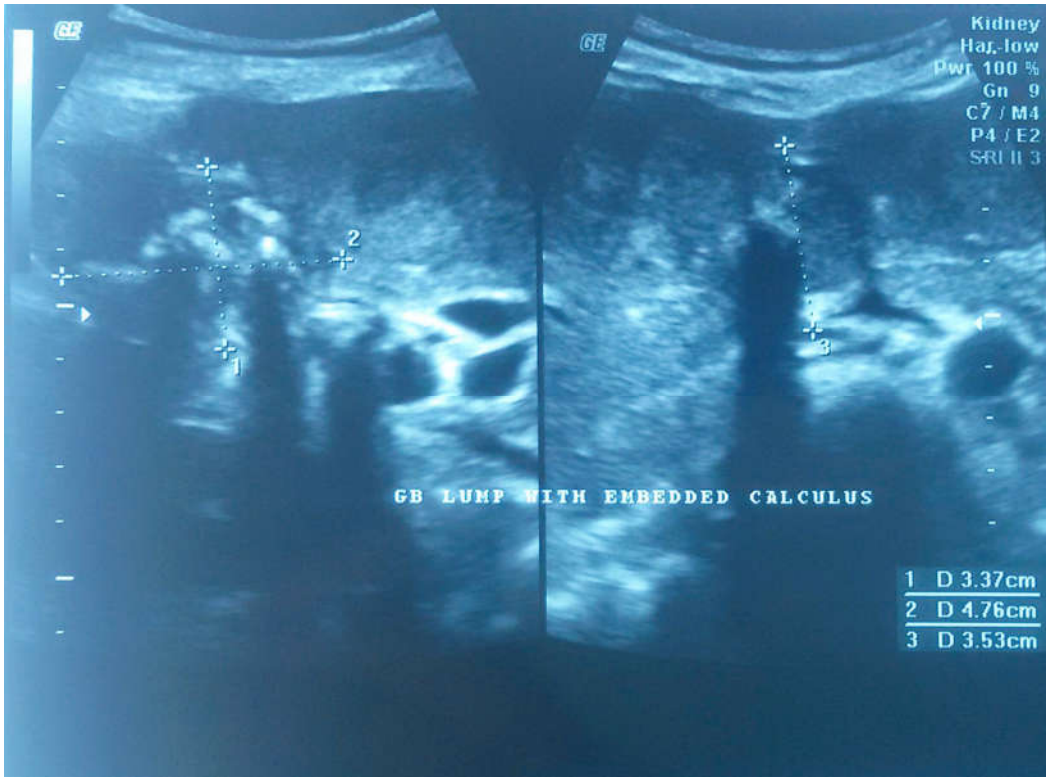

Fig. 7:

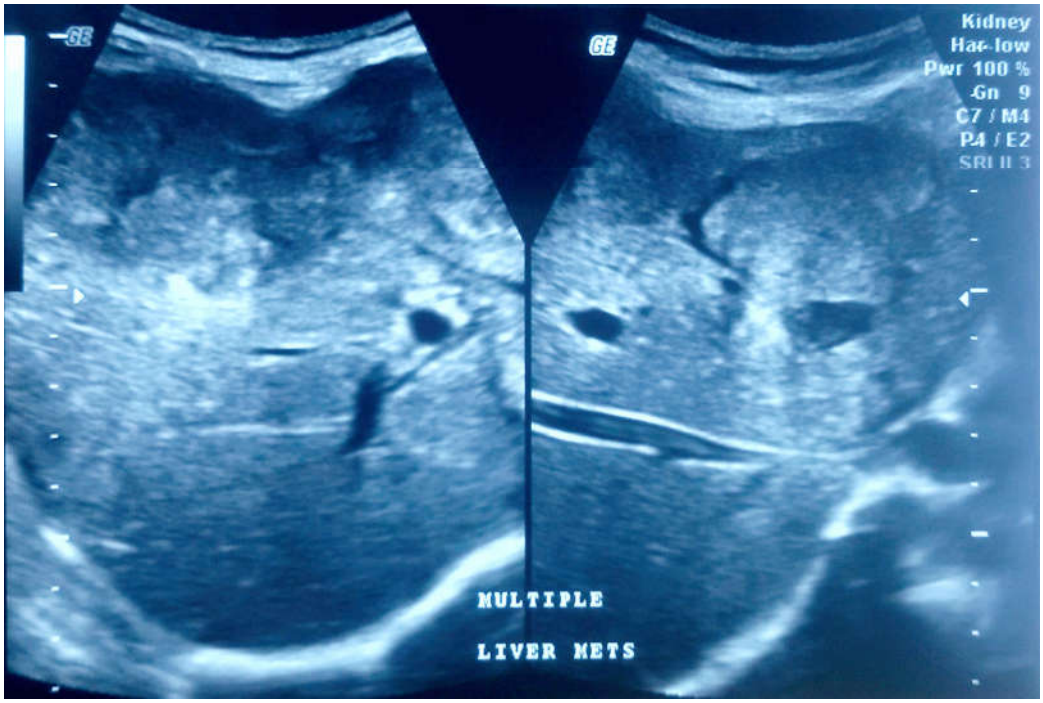

Fig. 8:

In May 2015 patient again presented with similar symptoms of painless progressive diminution of vision with Best Corrected Visual Acuity of 6/24 and recurrence of CME in both the eyes (Figure 5. Figure 6. OCT macula of right and left eyes respectively showing increased macular thickness and cystoids changes indicating recurrence of CME). Patient was planned for intravitreal steroids for recurrent CME as there had been only partial response to earlier intravitreal injections of Bevacizumab.

Before this therapy could be administered, patient started having symptoms of abdominal pain and loss

of appetite with weight loss. Patient was seen by the family physician and was diagnosed to have lump in abdomen in relation to liver. Ultrasonography of abdomen was done on in June 2015 which revealed a complex mass of mixed ecogenecity with embedded calculi (mass measured 3.4 x 4.8 x 3.5 cm). The liver was normal in size but showed multiple hypo echoic masses of variable sizes in both the lobes (Figure 7). Ultrasound abdomen showing gall bladder lump with calculi, Figure 8. Ultrasound abdomen showing Multiple liver metastasis). A provisional diagnosis of gall bladder carcinoma was made and the patient was referred to an oncologist.

The disease was too advanced at the time of presentation for any curative treatment and hence patient was put on palliative treatment consisting of Opioid analgesics and other supportive treatment to aid nutrition. The patient succumbed to the disease in august 2015.

Discussion

Cancer Associated Retinopathy (CAR) was first described by Sawyer et al. in 1976 with three cancer patients with blindness caused by diffuse retinal degeneration. In CAR, retinal degeneration occurs in the presence of auto-antibodies that cross react with tumour-tissue and retinal-tissue antigens which are recognized as foreign. In many instances, visual loss from CAR precedes the diagnosis of cancer [2].

CAR is Commonly associated with small-cell lung cancer, followed by gynaecologic and breast cancers, non–small-cell lung cancer, Hodgkin lymphoma, and pancreatic, prostate, bladder, laryngeal, and colon cancers [3]. Association of CAR with gall bladder carcinoma has not been reported as per the literature search at the time of reporting.

The temporal association of CAR with reported malignancies is very variable (from years before the malignancy is detected to months after the diagnosis of malignancy) [4]. The gall bladder carcinoma is known to have median survival period of 3 months [5] and in most patients the disease is incurable at the time of presentation, and many patients can be offered only palliative treatment [6]. Similarly our case was also diagnosed late, when there was local spread of the tumour and only palliative treatment was possible.

CME due to CAR can be considered a very rare presentation of autoimmune retinopathy due to paraneoplastic syndromes because majority of patients of CAR have been reported to have normal fundus findings at presentation, rest had vascular attenuation, or RPE changes [10]. Thinning of the inner retinal layers has been demonstrated with optical coherence tomography (OCT) in CAR [7]. On literature search we could find only one single case report by Moyer K et al describing cystoid macular oedema as a manifestation of CAR in a case of small cell carcinoma of lungs in a male patient [8].

The visual loss was painless progressive and was moderate at the time of presentation in contrast to the progressive optic atrophy and rapid severe vision loss as reported in autoimmune cancer related retinopathies in other series [9].

There was partial response to the anti-VEGF therapy with moderate improvement in vision and reduction in the CME as seen on OCT done 6 weeks after the therapy. The role of intra-ocular anti-VEGF (Bevacizumab) has not been reported in these patients yet.

We could not test the patient for anti-retinal antibodies for various reasons but though the presence of antibodies to various antigens (recoverin, enolase, transducin, carbonic anhydrase, arrestin, retinal bipolar cells, and transducin) [10] have been identified but the value of these in establishing the diagnosis is still on [11, 12] and in majority of cases the diagnosis is based on clinical findings.

The Case Report of this Patient with CAR Highlights That

1. CME can be a presenting sign of CAR and the associated vision loss is moderate with gradual progression.
2. The gall bladder carcinoma can be a cause of CAR and CME may be the presenting condition.
3. The treatment of such cases of CME is partially responsive to intraocular anti-VEGF (Bevacizumab) therapy in form of improvement in vision and changes as seen on OCT.
4. A check up by a physician should be recommended in patients with CME, in the absence of any contributory / risk factor. We could have probably diagnosed the malignancy earlier significantly altering the eventual outcome had search for cause been undertaken at first presentation.

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