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A RARE CASE OF PYREXIA OF UNKNOWN ORIGIN

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ABSTRACT

We present a case of a young male with 3 weeks of fever, evaluated extensively and was found to have a right atrial mass which turned out to be a metastatic deposit from the liver. Intracardiac masses are a rare and unusual cause for Pyrexia of Unknown Origin. The differential diagnoses of intracardiac masses include vegetation, thrombus or tumours. Malignant cardiac tumors are more common than benign tumors. Secondary or metastatic heart tumors occur comparatively more frequently, with an at least 100 times higher incidence than primary tumors of the heart. We present this case in view of its rarity.

KEYWORDS: **Fever, pyrexia of unkown origin, hepatocellular carcinoma, metastasis, intra cardiac mass**

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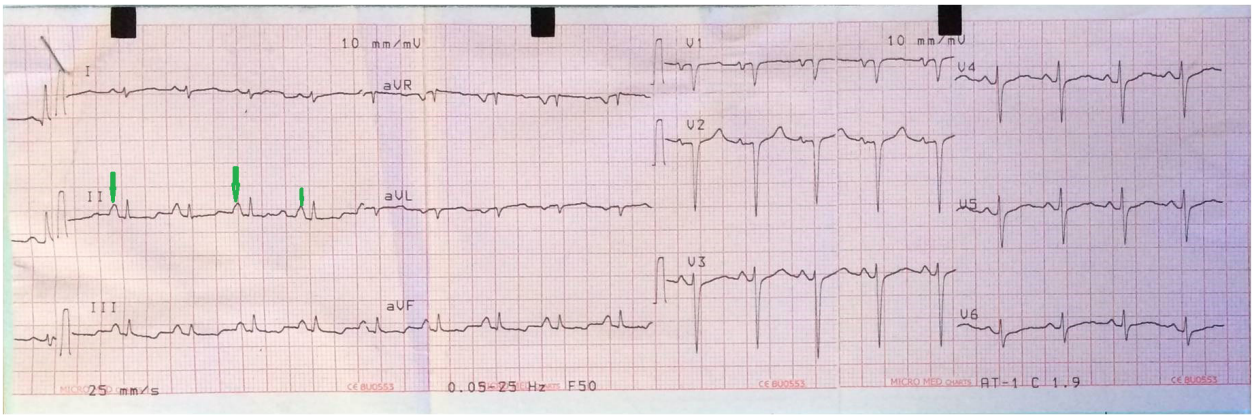
CASE DISCUSSION

Brief History

A young man aged 36 years came to the Medical OPD with complaints of fever for three weeks, low grade associated with chills, evening rise of temperature present. He also had dyspnoea Grade I – II for a few months. No history of chronic cough or loss of weight or appetite. No similar complaints in the past On examination he was afebrile, pulse 80 beats per minute, regular and of a normal volume. Blood pressure was 130/70 mm Hg in the right upper limb. His cardio-respiratory system examination was normal. On per abdomen examination, he had an enlarged liver, firm in consistency and with a smooth surface, without any bruit. He had been symptomatically treated earlier for the fever and was also diagnosed with enteric fever based on modestly raised widal titers. He was extensively re-evaluated at our institute. Laboratory investigations revealed elevated widal titers of 1:160 for both the O and H antigens, which had doubled from a week earlier. His blood counts revealed raised haemoglobin (17g/dl), total leucocyte count of 10700 cells/cubic mm of blood, differential count N - 78 L - 20 M - 1 E - 1, with mild thrombocytopenia (76000 cells/cubic mm of blood). His liver function tests revealed raised AST (103), ALT (53), Alkaline phosphatase 153, and GGT 156. His Prothrombin time, activated partial thromboplastin time and INR were elevated. He was also hepatitis B surface antigen positive. Other serological markers weren't done. He was also HIV 1&2 negative. Blood cultures were sterile

His ECG showed



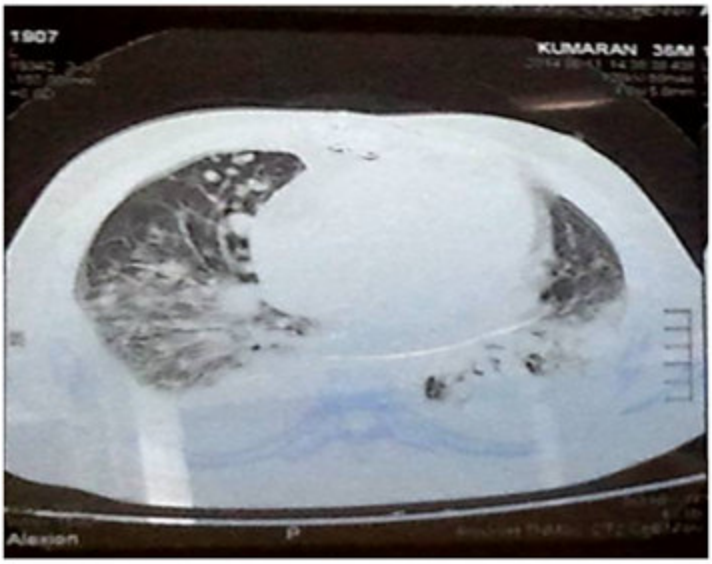
ECG

1. Sinus tachycardia
2. Right axis deviation
3. P pulmonale (green arrow)
4. S in Lead I
5. T inversion in Lead III
6. Poor R wave progression in chest leads.

Cardiologist's opinion was obtained. Echocardiography was done.

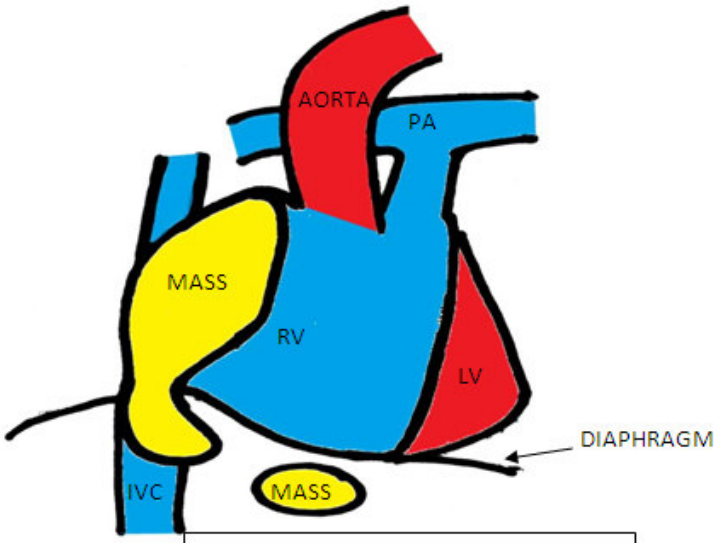
2D ECHO showed a large mass occupying 75 % of the right atrium extending up to the septal tricuspid leaflet (STL), (? RA myxoma or ? Large vegetation attached to STL). Meanwhile during his stay in the hospital his dyspnoea worsened to grade 4 with persistent tachycardia and appearance of central cyanosis. His arterial blood gas analysis showed persistent severe hypoxemia in spite of oxygen supplementation via face mask. He was shifted to the Medical ICU and was placed under 24 hour surveillance. Urgent Cardiothoracic surgeon's opinion was obtained who suggested surgery at the earliest following hemodynamic stabilisation

Plain Computer axial tomography of his chest



- B/L pleural effusion present.
- Multiple nodular lesions noted at the right ML medial and lateral segments, right LL anterior, posterior, medial and lateral basal segments, left side lingular, anterior, posterior basal and lateral basal segments.
- Impression : Bilateral pleural effusion. Metastatic nodules.

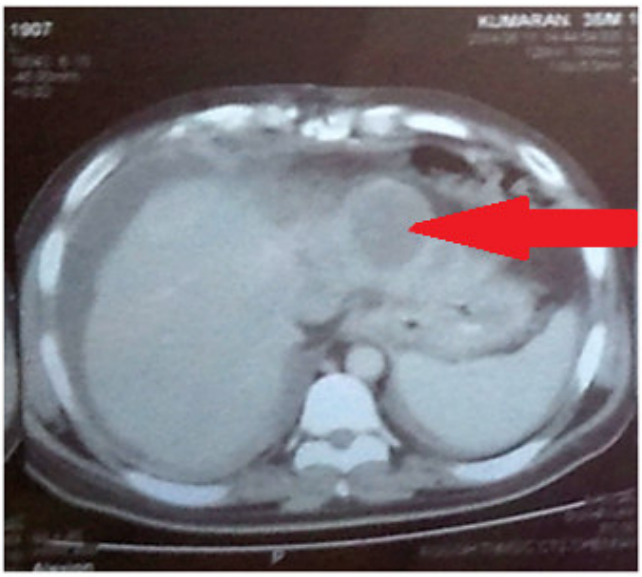
◈ He was posted for urgent right atrial mass excision. Intra Operative findings showed a huge friable mass in the right atrium extending into the IVC below the diaphragm of size: 10 x 8 cm plus a 5 x 5 cm hard mass felt through the diaphragm on the superior surface of liver. The mass was excised and was sent for histopathological examination.



INTRA OPERATIVE FINDINGS

He later became icteric and his total bilirubin rose to 14.3 mg /dl with elevated direct fraction (9.3) more than the indirect fraction (5.0).

Contrast enhanced computer axial tomography of abdomen

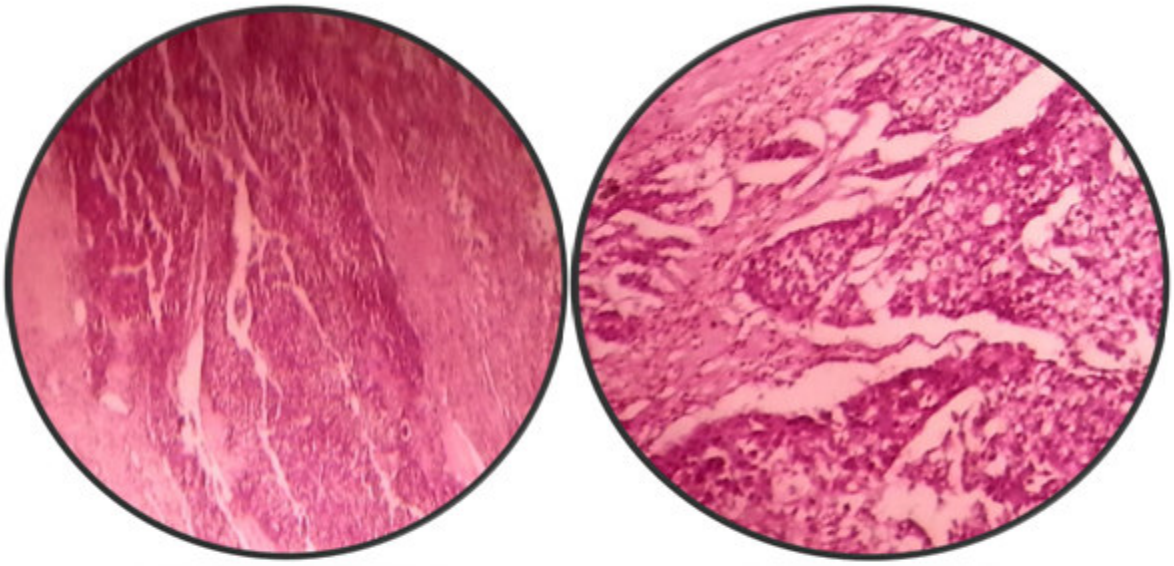


Liver - Nodular surface noted. Well defined peri portally extending hypodense lesion (red arrow) noted in the left lobe.

Histo-pathology

Macroscopically: Multiple greyish white and grey brown necrotic friable soft tissue fragments largest measuring 6 x 5.5 x 2 cm. Microscopically: Section shows sheets and nests of neoplastic cells showing vacuolated cytoplasm with vesicular nucleus admixed with cells with eosinophilic cytoplasm seen infiltrating into stroma showing congested vessels admixed with areas of necrosis and inflammatory exudate.

◈ ***Impression*** Metastatic clear cell carcinomatous deposits suggestive of hepatocellular carcinoma.



Low power field: Tumor cells infiltrating into the cardiac muscle

High power field: tumor cells with large nucleoli with clear cytoplasm

Liver biopsy was planned but was deferred in view of deranged coagulation parameters and hemodynamic instability. Since he had advanced hepatocellular carcinoma with multiple metastatic deposits he was only given palliative therapy for symptomatic relief.

DISCUSSION

PYREXIA OF UNKNOWN ORIGIN

Pyrexia of unknown origin (PUO) was defined in 1961[1,2] by Petersdorf and Beeson as the following

- a temperature greater than 38.3°C (101°F) on several occasions
- more than 3 weeks' duration of illness
- failure to reach a diagnosis despite 1 week of inpatient investigation.

A new definition which includes the outpatient setting (which reflects current medical practice) is broader, stipulating

- 3 outpatient visits or more than 3 days in the hospital without elucidation of a cause

or

- 1 week of "intelligent and invasive" ambulatory investigation

In an article from the *British Medical Journal*, Barbado et al[1] from La Paz University Hospital, Autonoma University, Madrid, Spain, they had compared the various etiologies and the methods of diagnosis in patients with PUO. They retrospectively compared 2 sets of patients who had presented with PUO during 1968-1981 and during 1982-1989 seen in the Department of Internal Medicine at La Paz University Hospital, Madrid, Spain. There was a statistically significant decrease in the percentage of infections and an increase in neoplasms and connective tissue disorders in the second series.In the first series of patients they found that the predominant etiology had been infections[1] and second were neoplasms (predominantly hodgkin's lymphoma). In the second series they found an increased prevalence of collagen vascular diseases and neoplasms compared to infections.

Intracardiac Masses

The differential diagnoses of intracardiac masses include vegetation, thrombus or tumours. Size, shape, location, mobility and attachment of the mass combined with the clinical findings help differentiate etiology.

Echocardiography became the gold standard test for the diagnosis of intracardiac masses and later on transesophageal echocardiography (TEE) further improved the accuracy. Magnetic Resonance Imaging (MRI) can identify the amount of fat with a high degree of specificity and can be used to diagnose cardiac lipomas. It is crucial to establish a correct diagnosis for proper management and therapy.

Cardiac tumors

Malignant cardiac tumors[3,4.5] are more common than benign tumors. Secondary or metastatic heart tumors occur comparatively more frequently, with an at least 100 times higher incidence than primary tumors of the heart.Intracavitary growth of secondary heart tumors, however, is unusual. Therefore, despite their frequency, metastatic heart tumors only rarely gain clinical attention. However, signs of cardiac involvement are often overlooked, since the symptoms of disseminated tumor disease prevail. Thus, like primary tumors of the heart, metastases may imitate valvular heart disease or cause cardiac failure, ventricular or supra-ventricular arrythmias, conduction defects, embolism, syncope quite often pericardial effusion. Today, two-dimensional echocardiography makes the detection of cardiac involvement in neoplastic diseases much easier. Metastases may reach the heart via the lymphatic or hematogenous route[3,4], or by direct or transvenous extension. Lymphatic spread tends to give rise to pericardial metastases, hematogenous spread preferentially gives rise to myocardial metastases. Only rarely are endocardial tumor deposits found. Owing to their topography and prevalence, carcinomas of lung and breast are the most common tumors originating cardiac metastases. Extracardiac tumors may also reach the atria and even the chambers of the heart by transvenous extension. Intraluminal growth of renal cell carcinoma (hypernephroma) through the vena renalis and vena cava inferior into the right atrium (in 1% of these tumors) has been reported . Furthermore, hepatocellular [3,4,5] carcinoma , leiomyoma of the uterus, nephroblastoma (Wilm's tumor) , pheochromocytoma and carcinoma of the adrenal cortex have been observed to extend through the inferior vena cava, and carcinoma of the lung and thyroid gland through the superior vena cava into the right atrium.

CONCLUSION

Pyrexia of unknown origin is a challenge for every physician and it is imperative not to be oblivious to the other less likely causes like neoplasms and they should not be missed when a definitive diagnosis cannot be made. Secondary heart tumors are common in patients with metastatic tumor disease, afflicting up to one-quarter of them. Clinically, secondary heart tumors usually remain silent.

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