Ca125 as a Marker for the Follow-up of Relapsing Polyserositis: A Case Report

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Introduction

Ca125 is a well-known marker of many malignant and non-malignant diseases the majority of which are characterized by serosal involvement [1]. Mesothelial secretion of Ca125 rather than direct production by the neoplastic or inflammatory cells seems to underlie this phenomenon [2]. Thus, Ca125 qualifies as a marker of serosal, either peritoneal or pleural, involvement. Not surprisingly, rising levels of Ca125 have been reported to characterize recurrent polyserositis in the context of familiar Mediterranean fever or systemic lupus erythematosus [3]. In these cases it was observed an increase in Ca125 concentration in patients with active disease, but Ca125 has not been used as marker of exacerbations.

We report a case of recurrent polyserositis in which exacerbations were heralded by increased Ca125 serum levels, making thus the periodical and on demand measurement of Ca125 a valuable means for a preclinical diagnosis of the recurrence.

Case Report

In November 2008 a 69 year old lady came to our attention for recurrent polyserositis. Her clinical history dated back to May 2008, when she was hospitalized elsewhere for fever, abdominal tension and dyspnea. Erythrocyte sedimentation rate was 23 mm/h, ferritin 341 mg/dl (normal values [n.v.]: 11-307 mg/dl), LDH 542 mg/dl (0-250 mg/dl), GGT 113 mg/dl (0-48 U/l), total bilirubin 2.3 mg/dl (n.v. 0.3-1 mg/dl), indirect bilirubin 1.8 mg/dl (0-0.4 mg/dl), Ca125 57 mg/dl/ml (n.v. 0-35 U/ml). Mucoproteins were 187 mg/24H (n.v. 0-6 mg/dl), D-dimer 2338 mg/ml (n.v.<259 mg/dl). The HbsAg and HbsAb, HBsAb and HBCAb (IgG) were positive, as were the HAVAb IgG. Anti-toxoplasmosis and anti-citomegalovirus IgG were 5.1 U/ml (n.v.<12 U/ml) and 246.7 U/ml (n.v.<14 U/ml), respectively, the Widal-Wright test was negative. Serologic tests for ANA, ANCA, rheumatoid factor and ENA screening were all negative. The lymphocyte phenotype showed CD4 1341 cells/mm 3 (n.v. 700-1100/mm3), CD4/CD8 3.2 (n.v.: 1-1.5). A CT scan showed pulmonary consolidation, pleural and pericardium effusion, ascitic fluid and a hepatic nodular lesion in the VII segment having a diameter of 17 mm. A tentative diagnosis of 3 hepatic malignancy and polyserositis was made and levovacin 300 mg, furosemide 30 mg and prednisone 3 mg prescribed with remission of symptoms.

In September 2008, after discontinuation of prednisone, she had ascites and Ca125 rose to 122 mg/dl. A MNR of the abdomen showed peritoneal and intralobular focal activity interface; intralobular accumulation of finely granular brown pigment in the cytoplasm of perivenous hepatocytes, groups of histiocytes containing ceroid pigment, outbreaks of hepatocyte degeneration with cytoplasmic ballooning. Immunohistochemistry showed positivity for HBsAg and negative for HBCAg Laboratory exams showed negative quantiferon and absence of antibodies against mitochondria.

In 2009, pleural and peritoneal effusions relapsed, with observed values of Ca125 of 961 U/ml. A genetic study did not disclose MEFV mutation consistent with familial Mediterranean fever. The diagnosis of recurrent polyserositis was eventually confirmed and treatment with methylprednisolone 30 mg started and, then, tapered gradually over 3 months.

Two months after steroid discontinuation, a new relapse occurred and responded well to a new course of steroids. Afterwards, the patients was carefully monitored for relapsing pleural peritoneal effusion by recording the weight, and a course of corticosteroid was administered at first signs of relapses, which usually were abdominal "fullness", dyspnea, edema and low grade fever. Later on, Ca125 was measured every three months, and prednisone was started when this marker at least doubled with regard to the last basal value, which occurred three times during one year, preventing thus the new onset of symptoms. This strategy has proved effective so far, although in the last couple of years the frequency of exacerbations has increased, with only about two weeks free of symptoms before a new treatment course is needed (Figure 1).

This case report confirms that Ca125 may be an indicator of the activity of serositis [4]. However, we add to the current knowledge by showing that exacerbations of recurrent polyserositis could be prevented and the related needs of steroids decreased by measuring Ca125 periodically and in the event of alarming symptoms such as feeling of rising abdominal tension and fatigue. The early intervention allowed to prevent or abort the exacerbation through a shorter course and lower cumulative dose of steroids. Furthermore, it prevented major symptoms such as abdominal pain, leg oedema and dyspnoea.

Interestingly, Ca125 increase also preceded the rise in inflammatory markers, as if activation of mesothelial cells were the first step of the exacerbation. Obviously, the timing of Ca125 monitoring was tailored to our patient and might not be the most appropriate for another patient.

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Thus, a careful scrutiny of clinical history is mandatory to correctly use this early diagnostic strategy.

This steroid sparing strategy is also important to prevent steroid related side effects. This is especially true in patients, such as ours, with very limited range of activity and ensuing greater risk of osteoporosis, sarcopenia and insulin resistance.

A note of caution in considering this case report is needed because we cannot exclude that Ca125 serum levels to some extent fluctuate. In this event, the risk exists that a spontaneous fluctuation and not an impending exacerbation accounts for increasing Ca125. Thus, a better knowledge of the dynamic of Ca125 would allow optimize the Ca125 based follow up strategy. Nevertheless, it is clear that in our patient monitoring Ca125 could improve the health status and reduce the use of steroids.

In conclusion, Ca125 might be an useful diagnostic tool to diagnose impending exacerbations of polyserositis at a preclinical stage and to guide the therapy accordingly. Experience is needed to translate a single, yet well documented, case into rules of general interest.

References


