

Old wine in new bottles: C-reactive protein (CRP) is a promising tumor marker in thymic epithelial tumors

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Tumor markers in the serum of cancer patients, regardless whether they are "molecular" (such as cell free tumor DNA and others) or biochemical, are an indispensable tool for the screening and monitoring of patients with malignant diseases. The fact that hardly any of the most broadly used tumor markers is specific for a given tumor entity does not diminish their great value for multiple purposes, which range from screening and diagnosis (e.g., germ cell tumors) to staging or prognostication.

The management of patients with thymic epithelial tumors (TET) (thymomas and thymic carcinomas) is highly challenging: these are rare tumors in a difficult anatomic region with a confusing variety of histological subtypes and an unpredictable and often protracted clinical course. Relapses as late as 20 years after primary surgery are on record (1), making long-term, or, in these mostly elderly patients, lifelong clinical follow-up mandatory. Expert knowledge about the biology of these tumors and the optimal follow-up modalities is usually limited even in large tertiary centers. Thus, the addition of tumor markers that aid in the monitoring of patients is highly desirable.

In their recent publication in *Oncotarget* (2), Janik et al. provide compelling evidence that C-reactive protein (CRP) might be a promising tumor marker in TET. While testing for CRP in patients with inflammatory or infectious disease is of course long established, its application in oncology, e.g., in the prognostication in pancreatic cancer patients (3), is only emerging. The authors found that increased preoperative CRP levels in patients with TET are associated with high tumor stage at diagnosis, an increased risk of relapse at 5 and 10 years

after surgery with a moderate drop after surgery and a significant elevation at relapse. The particular value of their finding lies in the fact that CRP was predominantly increased in high-risk patients with aggressive B3 thymomas and carcinomas. Follow-up of these patients is often difficult since postoperative changes (such as scars) can make the interpretation of CT scans or PET CTs problematic and may obscure residual tumors or early relapses. In thymomas, deterioration or de novo manifestation of paraneoplastic myasthenia gravis (MG), or increased levels of autoantibodies such as anti-titin, anti-ryanodine receptor, anti-IL12 or anti-IFN-alpha (4-7) is often a harbinger of relapse. Postoperative CRP monitoring is inexpensive, available worldwide, and may be able to aid in the detection of MG-negative thymomas and thymic carcinomas. Centers should be encouraged to include this item in their follow-up schedules to test its clinical usefulness.

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