CASE REPORT

Incorrect biochemistry complicates prostate cancer management

Iain McAuley, MD,[1] Gary Steinhoff, MD,[1] Michael McNeely, MD,[2] Paul Blood, MD[3]

[1]Department of Urology, Capital Health Region, Royal Jubilee Hospital, Victoria, BC, Canada
[2]MDS Lab Services, Capital Health Region, Royal Jubilee Hospital, Victoria, BC, Canada
[3]Department of Radiation Therapy, Capital Health Region, Royal Jubilee Hospital, Victoria, BC, Canada

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A man with a prostate specific antigen (PSA) of 6.1 ng/mL, a clinical stage T2b prostate nodule and biopsies that showed Gleason sum 6 adenocarcinoma of the prostate underwent a radical prostatectomy. The final pathology showed organ-confined disease. His postoperative PSA remained elevated at 4.0 ng/mL. The PSA was repeated several times and was in the same range. It was re-evaluated at another lab facility and was unmeasurable (<0.02 ng/mL). He has an antibody that cross-reacts with an assay reagent causing this false reading. The most likely antibody is one against mouse immunoglobulin G (IgG).

Key Words: prostate, PSA, heterophile, antibodies

Clinical summary

DC is a 54-year-old man with a PSA of 6.1. He has a past medical history of non-insulin dependent diabetes, high cholesterol, a deep venous thrombosis 10 years ago and a pelvic fracture in the late 1960's. The left lobe of the prostate was firm and biopsies showed Gleason 3+3 = 6 adenocarcinoma of the prostate in one of the three cores from the left side. After considering his options, he elected for a radical prostatectomy.

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Address correspondence to Dr. Iain McAuley, 200-1121 Yates Street, Victoria, BC V8V 3N1 Canada
Tel: (250) 388-7334 Fax: (250) 995-0767

In his pre-operative evaluation, he underwent screening for autologous blood donation. The HIV test for HIV p24 antigen was positive. He has no history of blood transfusion, intravenous drug use or high-risk sexual activity. A confirmatory Western Blot was indeterminate and the polymerase chain reaction test (PCR) was negative.

His peri-operative and post-operative course was uneventful and the pathology revealed negative lymph nodes, a Gleason 3+3 = 6 adenocarcinoma on the right with a volume of 5% of the prostate, and a Gleason 3+4 = 7 adenocarcinoma on the left with a volume of 20% of the prostate. All margins were negative. There was no perineural or lymphatic invasion.

Three months post operatively he was continent. His PSA was 4.0 ng/mL. This was immediately

repeated and was 3.9 ng/mL. A bone scan was negative. The decision was made that, based on the favorable pathology report, radiotherapy was not warranted and observation would be continued. At 6 months post-op his PSA was rechecked and was 2.3 ng/mL. After discussion with the laboratory pathologist, it was repeated at another facility and the value was <0.02 ng/mL. His PSA has remained unmeasurable at the second lab facility.

Discussion

This man had two immunoassay tests that gave false positive results. The screening HIV test (AxSYM HIV ½ gO, Abbott Laboratories, Abbott Park IL) is a test for serum antibodies that react with HIV antigens in the assay reagents. The test is highly specific but is known to cause false positive results with recent Epstein-Barr infections (heterophile antibodies). The initial PSA determination that produced the factitious results (AutoDefia, Wallac, Turko, Finland) is a two-site fluoroimmunoassay that employs a mouse monoclonal capture antibody and a mouse monoclonal signal antibody. The second determination that produced values less than 0.02 ng/mL (AxSYM, Abbott Laboratories, Abbott Park IL) employs a goat polyclonal capture antibody with a mouse monoclonal signal antibody. The patient's serum produced non-linear AutoDefia PSA results when diluted. Incubation with a mixture of animal antigens (HBT, Scantibodies Laboratory Inc., Santee CA) caused significant reduction of the AutoDefia result, demonstrating the presence of a heterophile antibody against animal immunoglobulin. The composition of the assay reagents suggests that the heterophile reacts with mouse IgG but not goat immunoglobulin. Thus, the results of any immunoassay using mouse immunoglobulin in this patient must be considered suspect to error.

Errors in two-site immunoassay tests can result from heterophile antibodies that bridge the capture and signal antibodies of the reagent mixture. These antibodies may result from keeping pets, ingesting animal antigens, vaccinations, infections or blood transfusions. However, in most instances the source is unknown.[1] Such interferences have caused patients to undergo chemotherapy and surgery for conditions they did not have based upon incorrect diagnoses that have resulted from circumstances similar to our patient.[2]

The absolute prevalence of this problem is not known but has been reported to occur in 0.03%-0.5% of patients depending upon the assay. Since all conventional PSA tests are two-site immunoassays, it must be concluded that this is a rare but potentially significant problem for all PSA tests.[3]

Conclusion

Clinical and biochemical data must always be taken together in the management of patients. If the PSA is out of keeping with the patient's clinical picture, consider contacting the pathologist responsible for the laboratory to arrange repeating the test with another assay that uses a different antibody composition and possibly carrying out additional tests to confirm the presence of heterophile antibodies. □

References

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