

Spurious Leukocytosis Secondary to High Cryoglobulin Concentration in a Patient with Hepatitis C

Meredith A. Reyes, M.D.; Andy N.D. Nguyen, M.D.

Department of Pathology and Laboratory Medicine, University of Texas-Houston Medical School

ABSTRACT

We report a case of spurious leukocytosis secondary to the presence of a very high concentration of cryoglobulin in a patient with hepatitis C infection. Automated blood analysis with Coulter models GenS and LH755 resulted in a white blood cell count ranging from 36-39K/mm³, while manual count revealed a value of 7K/mm³ with amorphous basophilic material representing precipitated cryoglobulin. After warming of the sample, or with the use of a saline replacement technique, automated counts normalized. A review of literature reveals few case reports of spurious leukocytosis secondary to cryoglobulinemia, and none related to hepatitis C infection. This case demonstrates the importance of laboratory protocols to ensure that spurious results such as these not be reported until reviewed by a technologist and/or pathologist. With the ever increasing incidence of chronic hepatitis C infection, this is a complication that must be considered and has significant prognostic implications.

CASE HISTORY/ PATHOLOGICAL FINDINGS

This patient was a 46 year-old female who was referred to the emergency room for work-up of leukocytosis with reported white blood cell counts ranging from 40K-80K/mm³. Past medical history was significant for liver cirrhosis secondary to hepatitis C and hypertension. Multiple cultures of her ascitic fluid and abdominal and pelvic CT scans were negative. On pathologist review of the peripheral smear numerous clumps of amorphous, pink-purple material were appreciated in the background of the slide (Fig. 1), and a manual white blood cell count was 7.2K/mm³. These clumps represent a significant amount of precipitated cryoglobulin. After warming of the sample, or with the use of a saline replacement technique, automated counts normalized with marked decrease in cryoglobulin on peripheral blood review (Fig. 2). The WBC histogram showed artifacts introduced by cryoglobulin clumps which were counted as numerous large WBCs (Fig. 3).

MICROSCOPIC FINDINGS

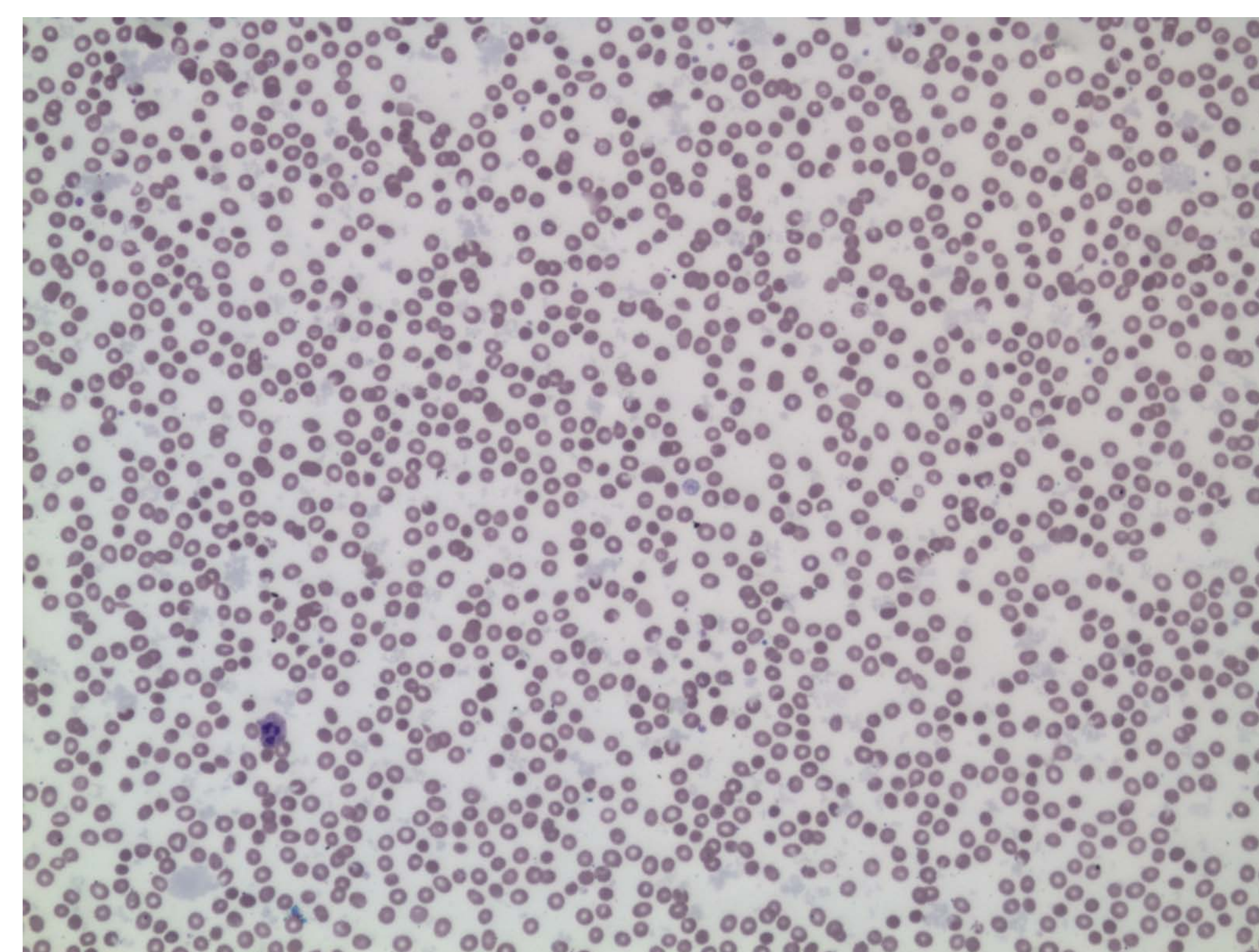


Fig. 1. The patient's peripheral blood smear with clumps of precipitated cryoglobulin (H&E 20X).

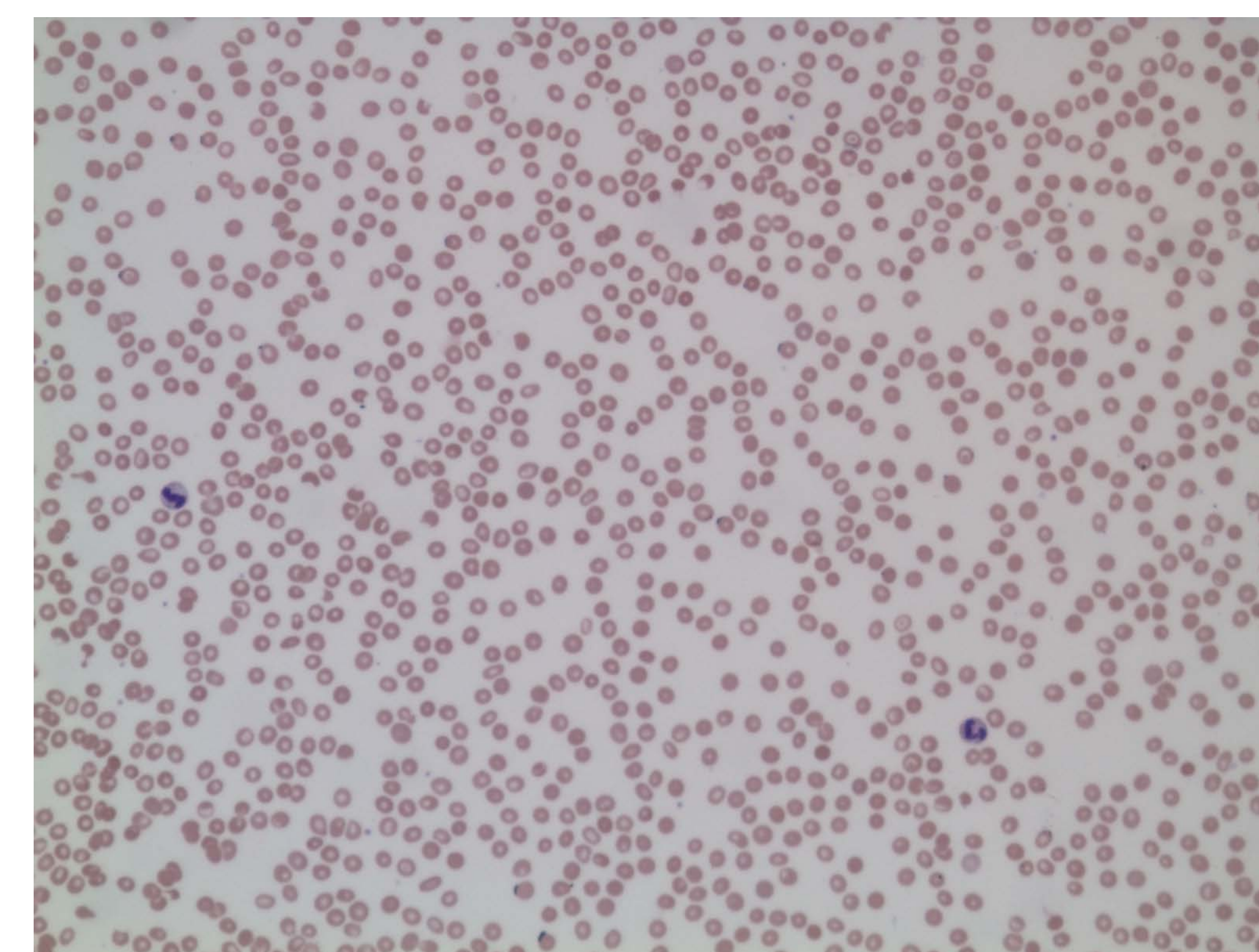


Fig. 2. The patient's peripheral blood smear after warming, with marked decrease in precipitated cryoglobulin (H&E 20X).

HISTOGRAM

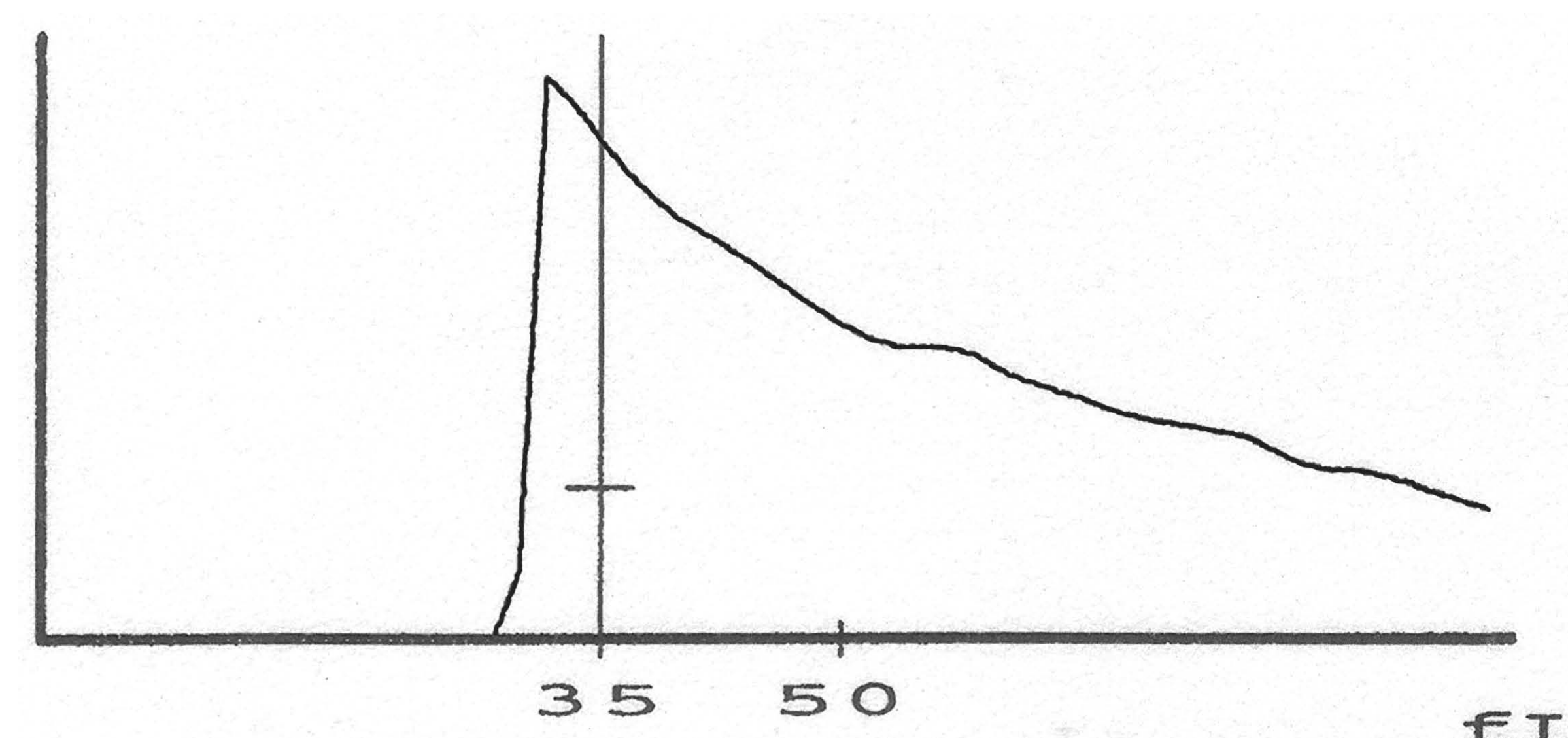


Fig. 3. WBC Histogram

A cryocrit was measured with a resultant value of 25%. Immunofixation of cryoglobulin aliquot showed a monoclonal protein of the IgM kappa isotype with polyclonal IgG (Fig.4). The patient also had decreased level of C4, normal level of C3, and a rheumatoid factor of 398 IU/ml. This is consistent with a type II cryoglobulinemia. Of note, this patient had complaints of generalized abdominal pain and arthralgias, and slightly elevated BUN and creatinine levels, all common complications of a high cryoglobulin level.

CRYOGLOBULIN IMMUNOFIXATION

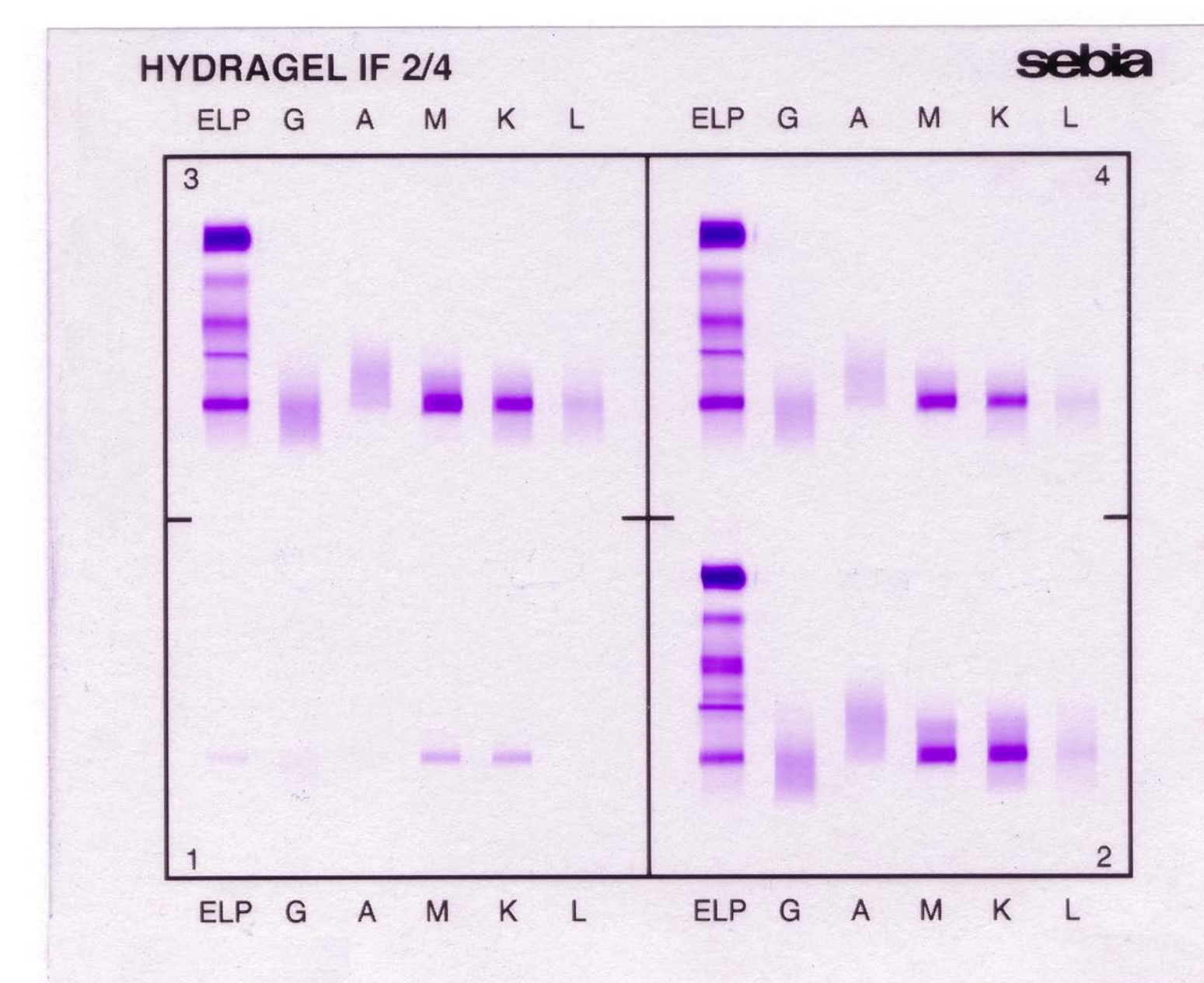


Fig. 4. Immunofixation of cryoglobulin shows a monoclonal IgM kappa with polyclonal IgG

DISCUSSION

The association of cryoglobulinemia and hepatitis C virus infection is well-known. Most of these patients have a type II cryoglobulinemia. The development of a cryoglobulin seems to show no relation to the genotype of hepatitis C infection. These patients have an increased rheumatoid factor level and decreased early complement components. With a cryocrit of greater than 2%, the patient is at a greater risk for severe, early fibrosis of the liver and a higher risk of transplant failure. In addition, we found that the presence of a large amount of cryoglobulin can severely affect the accuracy of automated blood counts. In this case, this patient was referred to the hospital for work-up of possible malignancy or severe infection due to reported white blood cell counts of 40K-80K/mm³. However, these results were found to be automated counting errors secondary to cryoglobulinemia. This case demonstrates the need for stringent laboratory protocols regarding technologist and/or pathologist review of flagged results. Proper identification of cryoglobulins can eliminate unnecessary diagnostic procedures, and has great impact on the prognosis and treatment plan for the patient. With the ever increasing prevalence of hepatitis C and chronic active hepatitis, this is a complication that must be considered.

REFERENCES

1. Banfi G, Grazioli V, Dolci A, Murone M, Bonini PA: Detection of a case of pseudoleukocytosis due to cryoglobulins: J Clin Lab Anal. 1990;4(5):319-23
2. Banfi G, Bonini PA: Detection of cryoglobulins by Coulter Counter model S-Plus IV/D: Clin Lab Haematol. 1988;10(4):453-9
3. Peng SL, Schur PH: Overview of cryoglobulins and cryoglobulinemia: Up to Date, 2006