COMy

The 6th World Congress on

CONTROVERSIES IN MULTIPLE MYELOMA (COMy)

SEROLOGIC TESTING FOR SARS-CoV-2 IN MULTIPLE MYELOMA

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Introduction

During the novel coronavirus (SARS-CoV-2) outbreak several laboratories developed serologic tests with the aim of widespread screening of both ill and healthy populations. PCR screening at this magnitude is not only unfeasible from a laboratory capacity standpoint, it also provides no data about the population level immunity. Serology was proposed as a screening method for larger populations, but it is yet to be validated: its sensitivity and specificity depends greatly on the screened population, and in some patient groups this could present a potential problem. Low immunoglobulin levels are typical in multiple myeloma, which could interfere with the usability of serologic tests. Our aim was to determine the clinical usefulness of serologic testing in multiple myeloma.

Methods

Our day clinic cares for a multitude of multiple myeloma patients as well as provides treatment to general oncology and other hematology patients. We introduced routine serologic testing for SARS-CoV-2 from the beginning of April, following the screening longitudinally, with serology repeated each time blood samples were obtained (no more often than once weekly), looking out for newly attained IgM positivity and seroconversion. In the case of positive IgM results, we obtained detailed histories and PCR testing was carried out to rule out asymptomatic infection (patients with symptoms were tested with PCR automatically).

Results

During the month of April 2020, we have obtained SARS-CoV-2 serology from 238 patients, performing 351 tests evenly during the month as patients came for therapy appointments (Fig. 1). An overview of COVID testing results among our actively treated patients is presented by cohort in Table 1. In all three groups, the number of IgM positives was comparably low (Fig. 2.). The distribution of IgM positive results was even throughout the month (Fig. 3.) No one was PCR positive.

	oncology	other hematology	myeloma
N of patients	79	108	51
N of tests	132	139	84
IgM positivity (% of tests)	7 (5,0%)	3 (2.2%)	3 (3.6%)
IgG positivity (% of tests)	1 (0.7%)	4 (3.7%)	0 (0%)
PCR testing (% of patients)	5 (6.3%)	5 (4.6%)	1 (2.0%)

Table 1. Overview of SARS-CoV-2 testing by cohorts

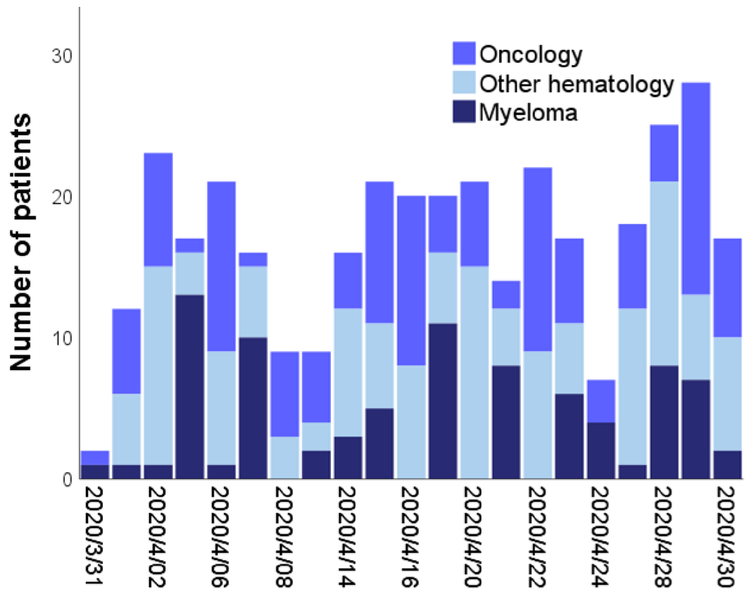

Figure 1. Number of patients by cohort throughout the month

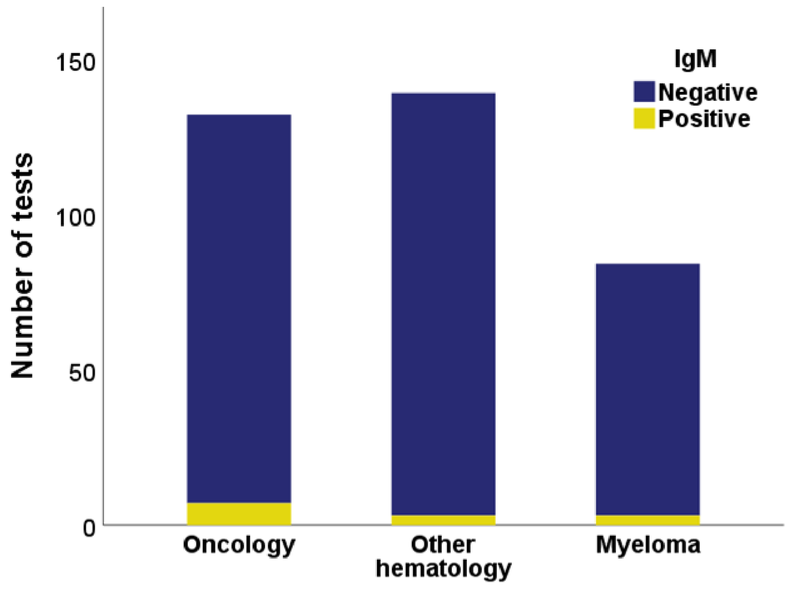

Figure 2. Number of IgM positive and negative tests by cohort

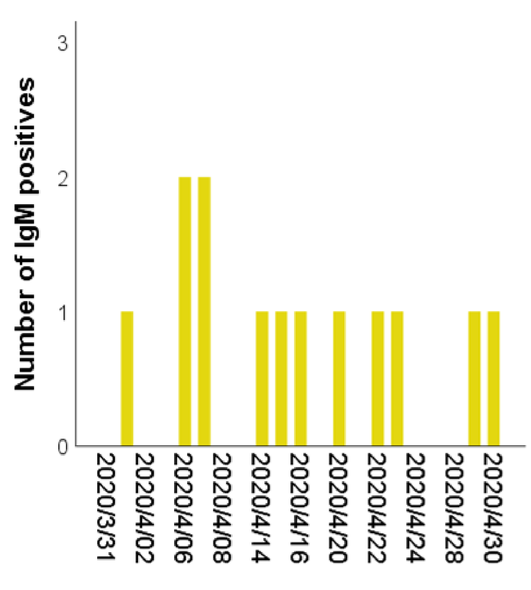

Figure 3. Number of IgM positive tests by date

Discussion

Following closely the news about the COVID pandemic and the rapidly changing circumstances in which we need to treat our patients, we have initiated testing at the beginning of April, expecting a surge of infections in the general population and among our patients. Thankfully however, the distancing measures introduced appear to have been successful in reducing the number of infected in Hungary, with PCR proven cases ranging steadily between 50 and 100 daily (roughly 0.5-1 infection/day/100 000 citizens). Even considering that the real number of infections must be higher than this, it is unsurprising that with infections quite scarce - among our highly isolated patients even more so - serology testing found few positives. Overall, only 3.7% of our tests were positive. Contrary to our previous expectations, the rate of positivity was comparable to the other two groups in patients with multiple myeloma. The rate of these positives among the cohorts and their relatively even distribution through time also support that they were false positives. If there was any clinical suspicion for a possible infection, PCR testing was carried out, all of them with negative result; other patients had been self-isolating for weeks beforehands and had no symptoms either at the time of the test or previously, making infection highly unlikely. None of these false positive patients developed IgG positivity later on.
Most interesting perhaps, is that known official specificity of this particular test is 85%[1]. Even assuming that all of our patients were indeed free of COVID-19, according to this data, at least 15% of them should have tested positive. Why then, are our data hinting at a much better specificity than previously published? On the one hand, it might be due to our relatively low number of patients. On the other hand, in a mixed group of affected and unaffected people, specificity and sensitivity are always measured against a gold standard, in this instant, PCR testing. This, however, may erroneously mark a number of affected or previously affected people negative, if PCR was performed after virus shedding stopped or indeed, because of lower sensitivity. These people may have rightly tested serologically positive afterwards, but then categorized as “false positives”, leading to a much worse specificity. Consequently, if those positive results were valid, it could mean a more widespread rate of immunity among the general population than previously estimated.

Conclusions

In Hungary, nationwide as well as personal isolation strategies had proven unexpectedly successful and we had no proven and very few suspected COVID-19 infections among our patients. Serology testing under these circumstances allowed us to validate the specificity of this test in a hemato/oncological setting. The unexpectedly low number of positive results raise the possibility for much better specificity of the test than previously published.
Longitudinal follow-up can be used to determine sensitivity of the test as well as evaluate any differences between myeloma and other patients.

References

[1]Vásárhelyi B, Kristóf K, Ostorházi E, Szabó D, Prohászka Z, Merkely B. (2020) Some rapid tests detecting specific IgM and IgG antibodies are not suitable for screening SARS-CoV-2 viral infection Orv Hetil. 2020; 161(20): 807–812.

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