

High-Dose Hook Effect in a Grossly Elevated Tumour Marker: A Case Report of Delayed Diagnosis

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Abstract

The high-dose hook effect, in which a very high antigen concentration saturates both capture and detection antibodies in a two-site immunometric assay and produces a falsely low or even normal result, is a well-described but infrequently encountered analytical pitfall that can delay diagnosis when the falsely reassuring result does not match the clinical picture. We report a case in which a patient with advanced ovarian carcinoma had a CA-125 result within the reference range despite a clinical presentation strongly suggestive of advanced malignancy, delaying oncology referral by several weeks until an alert laboratory scientist, noting the mismatch, requested sample dilution, which revealed a true CA-125 concentration exceeding the assay's normal reportable range by more than one-hundred-fold. We describe the clinical and laboratory clues that should prompt consideration of a hook effect, and recommend conditions under which routine dilution should be considered for clinically discordant tumour marker results.

Keywords: Hook effect; Tumour marker; CA-125; Immunoassay interference; Delayed diagnosis

Background

The high-dose hook effect occurs in two-site immunometric assays when an antigen concentration far exceeding the assay's normal working range saturates both the capture and labelled detection antibodies independently, preventing the sandwich complex from forming correctly and producing a falsely low signal that the assay's calibration curve misreads as a low or even normal concentration rather than the very high true value actually present.^{[1][2]} The effect is well described for several tumour markers, including CA-125, and while modern assay designs and automated dilution protocols have reduced its incidence, it has not been eliminated and remains a recognised cause of a falsely reassuring tumour marker result.

The mechanism is specific to two-site immunometric ('sandwich') assay designs, where a capture antibody immobilised on a solid phase and a separate, labelled detection antibody are both required to bind the same antigen molecule simultaneously to generate a measurable signal; at antigen

concentrations far exceeding the assay's working range, excess antigen saturates the capture and detection antibodies independently before a sandwich complex can form between them, so that much of the antigen present goes undetected and the resulting signal corresponds to a concentration far below the antigen's true concentration in the sample.^{[1][2]}

This mechanism distinguishes the hook effect from most other recognised immunoassay interferences, such as heterophilic antibody interference, which typically produces a falsely elevated rather than falsely low result; the hook effect's tendency to produce a falsely low or normal result is precisely what makes it clinically dangerous, since a falsely elevated result would at least prompt further clinical and laboratory scrutiny, whereas a falsely normal or low result, as in this case, can be mistakenly reassuring.^[4]

Case Presentation

A 58-year-old woman presented with a six-week history of progressive abdominal distension, early satiety and unintentional weight loss. Abdominal examination and subsequent ultrasound raised strong suspicion of advanced ovarian malignancy with ascites. A CA-125 requested as part of the initial diagnostic workup returned within the reference range at 28 U/mL (reference <35), a result that did not match the strength of clinical suspicion.

The discordant result initially led to some diagnostic uncertainty and a delay of several weeks in oncology referral while alternative explanations for the presentation were considered. A laboratory scientist reviewing the result alongside the clinical details flagged the possibility of a hook effect given the marked mismatch between the clinical picture and the normal result, and requested manual dilution of the original sample.^[3]

Reviewing the case retrospectively, the degree of clinical-laboratory discordance was substantial: the ultrasound findings of extensive ascites and a complex pelvic mass, combined with the degree of weight loss and early satiety reported, were individually and collectively far more consistent with advanced malignancy than with a benign process that might plausibly explain a genuinely normal CA-125, underscoring in hindsight how strong the mismatch signal available to the clinical team already was before the laboratory scientist's dilution request ultimately resolved it.^[5]

Laboratory Investigation

The sample was manually diluted 1:100 and re-assayed, returning a corrected CA-125 concentration of approximately 4,200 U/mL -- more than one-hundred-fold above the original undiluted result and well into the range strongly associated with advanced ovarian malignancy.^[4] The patient was referred urgently to gynaecological oncology, and subsequent imaging and biopsy confirmed advanced high-grade serous ovarian carcinoma.

The magnitude of correction revealed by dilution in this case -- from 28 U/mL undiluted to approximately 4,200 U/mL at 1:100 dilution -- is substantially larger than the correction typically reported in published hook effect cases for CA-125, most of which describe an undiluted result in the hundreds or low thousands of U/mL being revealed as considerably higher on dilution, rather than an undiluted result within the normal reference range as occurred here, illustrating that this case sits toward the more extreme end of the hook effect severity spectrum described in the published literature.^[3]

Measurement	Undiluted Result	1:100 Dilution Result
CA-125 (U/mL)	28 (within reference)	~4,200 (markedly elevated)
Clinical impression	Discordant with imaging	Consistent with imaging

Table 1: Undiluted Versus Diluted CA-125 Result and Corresponding Clinical Impression.

Discussion

This case illustrates the specific diagnostic danger of the hook effect: unlike an assay failure that produces an obviously implausible or flagged result, a hook-effect-affected result can appear entirely unremarkable and fall comfortably within the reference range, giving no automatic signal to the requesting clinician or the reporting laboratory that anything is wrong with the result.^[5] The clue that prompted investigation here was not a laboratory-generated flag but the clinical team's persistence in reporting a mismatch between the result and the clinical picture, which depended on a laboratory scientist recognising the possibility of a hook effect specifically -- an outcome that relied on individual awareness rather than a systematic safeguard.

Some modern immunoassay platforms incorporate automated hook effect detection, comparing signal patterns at two different sample dilutions as part of routine processing, and laboratories using a platform without this feature should consider a standing policy of automatic dilution and re-assay whenever a tumour marker result is reported as notably discordant with the referring clinician's stated clinical suspicion, rather than relying on incidental recognition as occurred in this case.^{[6][7]} A structured comment on the report form inviting the requesting clinician to flag a strong clinical-result mismatch back to the laboratory would also support earlier recognition.^{[8][9][10]}

Clinical and Laboratory Clues That Should Prompt Hook Effect Consideration

Drawing on this case and the broader published literature, several clinical and laboratory clues should prompt consideration of a possible hook effect when a tumour marker result is received.

A clinical presentation strongly suggestive of advanced malignancy -- extensive imaging findings, marked constitutional symptoms such as significant unintentional weight loss, or a biopsy-confirmed diagnosis -- accompanied by a tumour marker result within or only mildly above the reference range is the single most important clue, as it was in this case, and should prompt the requesting clinician or the reporting laboratory to consider dilution testing rather than accepting the normal result as excluding or minimising disease burden.^{[5][6]}

A tumour marker result that falls unexpectedly, or shows a paradoxical decrease, between two time points in a patient with otherwise progressing disease on imaging or clinical assessment should also raise suspicion of hook effect, since advancing disease progressively increasing antigen burden can push a borderline-high result further into hook-effect-susceptible territory over time, converting a previously accurate elevated result into a falsely lowered one at a later time point.^[7]

Analytical Detection Methods for the Hook Effect

Beyond the manual dilution approach used to resolve this case, several analytical methods exist for detecting or mitigating hook effect risk, varying in how readily they can be implemented on a given assay platform.

Automated two-dilution signal comparison, available on some modern immunoassay platforms, compares the signal obtained at two different sample dilutions and flags a result for further investigation when the signal pattern is inconsistent with a simple linear dilution relationship, a pattern characteristic of hook effect; this automated approach removes the dependence on individual staff recognition that determined the outcome in this case.^{[1][6]}

A standing laboratory policy of automatic dilution and re-assay for any tumour marker result flagged by the requesting clinician as clinically discordant, even without automated two-dilution detection capability on the assay platform itself, provides a lower-technology alternative achievable at any laboratory regardless of its specific analyser's built-in hook detection features, and is the specific recommendation this report makes for laboratories without access to automated detection.

Why Automated Hook Detection Is Not Universally Implemented

Given that automated two-dilution hook detection capability exists on some platforms, it is worth considering why this feature is not universally implemented across all immunoassay platforms and laboratories.

Automated two-dilution testing approximately doubles the reagent cost and analyser time required for every tumour marker result, an overhead that is difficult to justify for every result given that the hook effect, while clinically significant when it occurs, remains an infrequent event relative to the overall volume of tumour marker testing performed, leading many laboratories to reserve automated or manual dilution confirmation for results meeting specific triggering criteria rather than applying it universally.^{[2][9]}

Defining those triggering criteria well -- balancing the cost of universal dilution testing against the risk of missing a hook effect case like this one -- is itself a significant practical challenge, and this report's recommendation of a clinical-discordance-triggered dilution policy represents one reasonable approach to this balance, prioritising detection sensitivity for exactly the scenario, a strong clinical-result mismatch, that proved decisive in resolving this case.

Comparison with Previously Published Hook Effect Cases

This case is broadly consistent with the pattern described in previously published hook effect case reports across various tumour markers and other immunoassay analytes, while illustrating some features specific to the CA-125 and ovarian carcinoma context.

Published hook effect cases span a range of analytes beyond CA-125, including human chorionic gonadotropin in the context of gestational trophoblastic disease and prostate-specific antigen in advanced prostate cancer, generally sharing the common feature of a very high true antigen concentration arising from advanced or bulky disease, consistent with this case's presentation of advanced, high-grade serous ovarian carcinoma with extensive ascites.^{[3][10]}

What distinguishes this case within the published literature is the specific degree to which the undiluted result fell within, rather than only mildly below, the reference range, since many published cases describe a hook-effect-affected result that is still mildly to moderately elevated, drawing at least some clinical attention, whereas this case's undiluted result at 28 U/mL would have appeared entirely unremarkable to a clinician without the specific knowledge of the strongly discordant imaging findings.

Implications for Laboratory Report Design

This case's resolution depended on a laboratory scientist independently recognising the discordance between the clinical picture, available to them only because it had been specifically communicated on the request form, and the reported result, and this dependency has direct implications for how tumour marker request and report forms might be better designed.

A structured field on the tumour marker request form explicitly prompting the requesting clinician to note the strength of clinical suspicion for malignancy, rather than relying on free-text clinical details that may or may not be read carefully by laboratory staff processing a high-volume workload, would make the kind of discordance identified in this case more readily and consistently visible to laboratory staff at the point of initial result review.^[8]

Equally, a reciprocal prompt on the report form inviting the requesting clinician to contact the laboratory if a reported result does not match their clinical impression would provide a second, clinician-initiated pathway to the same recognition this case achieved through laboratory-initiated scrutiny, broadening the routes by which a hook-effect-affected result can be caught beyond dependence on either party acting alone.

Study Limitations

As a single case report, this report's findings and recommendations should be interpreted with the limitations inherent to this study design.

A single case cannot establish the population frequency of clinically significant hook effect among tumour marker results more broadly, nor can it establish the specific sensitivity and specificity of a clinical-discordance-triggered dilution policy for detecting hook effect cases in practice, though the broader published case literature cited throughout this report provides some further context on the recognised range of hook effect presentations beyond this single case.^{[5][7]}

Future Directions

A prospective study implementing a clinical-discordance-triggered dilution policy across a laboratory network and measuring the resulting rate of hook effect detection, alongside the additional reagent and staff time cost incurred, would provide stronger evidence for the practical value of this report's recommended approach than this single case report can offer on its own.

Further work characterising which specific tumour marker assays and analyser platforms remain most susceptible to hook effect despite modern assay design improvements would help laboratories prioritise where a dilution-triggering policy, whether automated or discordance-based, is most likely to be clinically valuable.

Why This Case Was Reported Despite the Hook Effect Being Well Described

The high-dose hook effect is a well-established phenomenon in the laboratory medicine literature, and the decision to report this particular case despite that existing recognition reflects the specific severity of the diagnostic delay and the magnitude of discordance involved, rather than any claim that the underlying mechanism itself is novel.

Many clinicians, particularly outside laboratory medicine and specialist oncology, have limited exposure to the hook effect as a specific, named phenomenon despite broad general awareness that laboratory results can occasionally be misleading, and this case's several-week referral delay illustrates concretely how costly that specific knowledge gap can be when it coincides with an unusually severe presentation of the phenomenon.^{[5][8]}

Case reports of this kind serve an ongoing educational function for the broader clinical and laboratory community precisely because awareness of infrequent but consequential phenomena such as the hook effect does not remain uniformly distributed across all clinicians and laboratory staff over time, particularly as staff turnover introduces individuals without direct prior exposure to a case of this kind.

Interdisciplinary Coordination Between Laboratory and Oncology Teams

This case's eventual resolution depended on coordination between the laboratory scientist who recognised the possible hook effect and the clinical team who had communicated the strength of their clinical suspicion, and this coordination dynamic deserves further comment.

Establishing a direct, named point of contact between the laboratory and oncology or gynaecology services for urgent tumour marker result queries, rather than routing such queries through a general laboratory enquiry line, would plausibly shorten the interval between a clinical team's recognition that a result seems discordant and the laboratory's initiation of dilution testing, compared with the several-week delay that occurred in this case before the mismatch was specifically flagged and acted

upon.^[6]

Regular case-based teaching sessions, using de-identified cases such as this one, jointly attended by laboratory and oncology staff, would help sustain awareness of the hook effect and similar interference phenomena across both groups, rather than awareness residing primarily with individual, experienced laboratory staff whose knowledge may not be systematically transferred to colleagues or to the clinical teams they support.

Patient Communication Considerations

The several-week delay in oncology referral in this case carries direct implications for how the diagnostic delay should be communicated to the patient once the hook effect was identified as its cause.

Explaining to the patient, once the true diagnosis and extent of disease were established, that an unusual laboratory measurement artefact rather than any failure to act on an available correct result had contributed to the delay in referral is important both for patient understanding and for appropriately characterising the nature of the delay, since the delay arose from a genuine and recognised analytical limitation rather than from an error in clinical judgement once accurate information was available.^[4]

Equally, acknowledging to the patient that this delay, however explicable, may have had some impact on the timing of treatment initiation is an important component of honest, transparent communication about a diagnostic delay, regardless of its underlying cause, consistent with general principles of open disclosure following a recognised diagnostic delay.

Economic Considerations

Implementing a clinical-discordance-triggered dilution policy, or automated two-dilution hook detection where available, carries a modest but real cost that should be weighed against the cost of a delayed diagnosis of the kind this case illustrates.

The several-week referral delay in this case plausibly contributed to some degree of disease progression before treatment began, with associated potential costs in both clinical outcome and the subsequent intensity and cost of treatment required, costs that are difficult to quantify precisely in a single case but that provide a strong qualitative rationale for the modest additional reagent and staff time cost of a more systematic dilution-testing approach of the kind recommended throughout this report.^[9]

Applicability to Other Immunometric Tumour Markers

Although this case specifically involves CA-125, the underlying hook effect mechanism and the recommendations made throughout this report apply equally to other tumour markers measured by two-site immunometric assay design.

CA 19-9, carcinoembryonic antigen, and alpha-fetoprotein, among other commonly used tumour markers, are typically

measured using similar two-site immunometric assay designs and share the same underlying susceptibility to hook effect at sufficiently high true antigen concentrations, meaning the clinical-discordance-triggered dilution policy recommended in this report is not specific to CA-125 and should reasonably be applied to any tumour marker result that appears discordant with a strong clinical suspicion of advanced malignancy.^{[2][10]}

Regulatory and Quality Management Context

Laboratory accreditation and quality management standards generally require documented procedures for identifying and managing known sources of analytical interference, and the hook effect, despite being well described in the literature, is not always explicitly addressed within individual laboratories' documented interference management procedures.

Explicitly documenting hook effect as a recognised interference for applicable tumour marker assays within a laboratory's quality management system, alongside the specific triggering criteria and dilution procedure to be followed when discordance is identified, would both support accreditation compliance and provide the institutional memory needed to sustain consistent practice despite staff turnover, directly addressing the awareness-dependency concern raised earlier in this report.^{[6][7]}

Differential Diagnosis Considered Before Hook Effect Was Identified

Before the hook effect was identified as the explanation for the discordant CA-125 result, several alternative explanations were reasonably considered by the clinical team managing this patient, and reviewing these alternatives illustrates why the diagnostic delay occurred despite reasonable clinical reasoning at each step.

A CA-125-negative ovarian malignancy, recognised to occur in a minority of ovarian cancers, particularly certain histological subtypes, was initially considered as a plausible explanation for the normal result, a reasonable alternative given that CA-125 elevation, while common in high-grade serous ovarian carcinoma specifically, is not universal across all ovarian malignancy subtypes.^[5]

An alternative, non-malignant cause for the ascites and pelvic mass, such as a benign ovarian cyst with secondary ascites or a non-gynaecological intra-abdominal process, was also considered during the period of diagnostic uncertainty, reflecting appropriately cautious clinical reasoning that did not assume malignancy was certain simply because imaging findings were suggestive of it, even though the imaging findings combined with the degree of weight loss ultimately proved highly specific for advanced malignancy in this case.

Age and Clinical Context Considerations

This patient's age of 58 years and the specific pattern of her presentation are consistent with the typical demographic and clinical pattern of high-grade serous ovarian carcinoma, and considering this context helps situate the hook effect finding within a broader clinical picture rather than as an isolated laboratory curiosity.

High-grade serous ovarian carcinoma, the histological subtype ultimately confirmed by biopsy in this case, is specifically associated with some of the highest reported CA-125 concentrations among ovarian cancer subtypes, which plausibly explains why this case's true antigen concentration was high enough to produce such a severe degree of hook effect, since a less aggressively CA-125-producing tumour type might not have reached a sufficiently extreme antigen concentration to produce hook effect at all.^{[3][10]}

Role of Imaging in Resolving the Diagnostic Uncertainty

Although this report focuses primarily on the laboratory dimension of this case, the role of imaging findings in ultimately supporting the decision to pursue dilution testing, and in confirming the diagnosis once the corrected CA-125 result was available, deserves explicit mention.

The ultrasound findings of extensive ascites and a complex pelvic mass provided the specific clinical detail that, when communicated to the laboratory alongside the request for CA-125 testing, enabled the laboratory scientist to recognise the discordance with the normal reported result; without this specific imaging information being communicated to the laboratory, the normal CA-125 result alone would have offered no basis for suspecting a hook effect.^[8]

This dependency reinforces the structured-request-form recommendation made earlier in this report: the imaging findings that proved decisive in this case were available to the clinical team from the outset but required deliberate communication to the laboratory to become clinically useful in resolving the result discordance, rather than being inherently visible to laboratory staff without that specific communication step.

Practical Checklist for Laboratories Encountering Discordant Tumour Marker Results

Drawing together the recommendations made throughout this report, we propose the following practical checklist for laboratories encountering a tumour marker result that appears discordant with the available clinical information.

Confirm whether the clinical information available to the laboratory supports a strong suspicion of advanced or bulky malignancy; if so, and the reported result is within or only mildly above the reference range, request manual dilution and re-assay before accepting the original result as final; document the discordance and the rationale for dilution testing within the patient's laboratory record; and communicate the corrected result

promptly to the requesting clinical team along with a clear explanation of the hook effect mechanism if dilution reveals a markedly different result.^{[6][9]}

Where automated two-dilution hook detection capability exists on the analyser platform in use, confirm that this feature is enabled and appropriately configured for all applicable tumour marker assays, rather than assuming a modern analyser platform necessarily has this protection active by default without specific confirmation.

Why This Case Report Emphasises Systems Solutions Over Individual Vigilance

Throughout this report, the recommendations made emphasise systematic, structural solutions -- automated detection, standing dilution policies, structured request form fields -- over simply recommending that laboratory staff and clinicians exercise greater individual vigilance for the hook effect, and this emphasis reflects a specific view about where the underlying vulnerability in this case actually lay.

This case was ultimately resolved by exactly the kind of individual vigilance -- a laboratory scientist's recognition of a specific, infrequently encountered phenomenon -- that cannot be assumed to occur reliably across every similar case in the future, given that individual staff awareness of any specific infrequent phenomenon varies with experience, training, and chance exposure to a similar case, making a systems-level solution a more reliable long-term safeguard than relying on the same fortunate recognition recurring in future cases.^[7]

Governance Recommendations for Ongoing Monitoring

Implementing the dilution policy and request-form changes recommended throughout this report should be accompanied by ongoing governance arrangements to confirm these measures continue to function as intended over time.

Periodic audit of cases where a clinical-discordance flag prompted dilution testing, tracking how often dilution revealed a materially different result against how often it confirmed the original result, would allow a laboratory to assess whether the triggering criteria for its dilution policy are appropriately calibrated, and to adjust them if the policy is either missing genuine hook effect cases or triggering unnecessary dilution testing too frequently relative to its diagnostic yield.^[6]

A clear local policy document specifying exactly which clinical and laboratory criteria trigger dilution testing, and which staff roles are responsible for recognising and acting on those criteria, would help ensure the lessons of this case translate into durable local practice rather than remaining dependent on individual staff members who happen to recall this specific case report.

Why the Several-Week Delay Occurred Despite a Timely Initial Result

A notable feature of this case is that the initial, misleading CA-125 result was available promptly, without any delay in laboratory turnaround time, yet the overall diagnostic delay still extended to several weeks, illustrating that analytical turnaround speed alone does not guarantee diagnostic timeliness when the result itself is misleading.

The several-week interval reflects the time taken for alternative explanations to be considered clinically, as described in the differential diagnosis discussion earlier in this report, before the clinical-laboratory discordance was specifically escalated and acted upon, underscoring that the most impactful intervention for a case of this kind is not necessarily faster initial testing but faster recognition and resolution of discordance once an unexpected result is received.^[8]

Applicability of This Report's Lessons to Other Rare Immunoassay Interferences

The hook effect is one of several recognised but infrequently encountered immunoassay interference phenomena, alongside heterophilic antibody interference and other cross-reactivity-related artefacts, and the structural recommendations made throughout this report -- clinical-discordance-triggered investigation, structured request form fields, documented local policy -- apply broadly across this wider category of interference phenomena rather than being specific to hook effect alone.^{[4][9]}

A laboratory that implements the systems-level safeguards recommended in this report specifically in response to this hook effect case would, as a secondary benefit, likely also improve its capacity to detect other rare interference phenomena sharing the same fundamental vulnerability -- an infrequent, well-described analytical pitfall whose detection in any individual case has historically depended on incidental staff recognition rather than a systematic safeguard.

Summary of Recommendations for Implementing Laboratories

Implementing laboratories seeking to act on this case's lessons may find it useful to sequence the recommendations made throughout this report roughly in order of implementation ease.

A structured request-form field prompting clinicians to note the strength of clinical suspicion for malignancy, and a reciprocal invitation on the report form for clinicians to flag discordance, can typically be implemented promptly through existing form revision processes; a documented local policy specifying dilution-triggering criteria and responsible staff roles requires somewhat more coordination to establish but remains achievable within existing quality management frameworks; while enabling or acquiring automated two-dilution hook detection capability is necessarily tied to the laboratory's existing analyser platform and procurement cycle.^{[1][6]}

Why This Case Was Reported as a Single Case Rather Than Awaiting a Series

The decision to report this case individually, rather than awaiting accumulation of a larger series of similar hook effect presentations, reflects a judgement that the severity of this particular case -- an undiluted result falling fully within the reference range despite a true concentration over one-hundred-fold higher -- was sufficiently instructive and clinically significant to warrant timely dissemination rather than delayed publication pending a larger accumulated series.

This judgement is consistent with the broader tradition of case report publication in laboratory medicine, where an individual case demonstrating an unusually severe or instructive presentation of a recognised phenomenon is generally considered to carry sufficient independent educational value to warrant publication without needing to await a larger series, particularly for a phenomenon such as hook effect where awareness gaps, rather than uncertainty about the underlying mechanism, are the primary barrier to prevention.^{[5][10]}

Final Reflection on Trust Between Clinicians and Laboratory Results

This case ultimately turned on a clinical team's willingness to continue questioning a normal laboratory result that did not fit the clinical picture, rather than accepting it as definitive simply because it came from an accredited laboratory using a validated assay, and this willingness to question a result in the face of strong contrary clinical evidence is worth reinforcing as a general principle beyond this specific case.

Laboratory results are generally highly reliable, and routine second-guessing of every normal result would be neither practical nor appropriate; but this case illustrates that a sufficiently strong and specific clinical-laboratory discordance warrants active follow-up with the laboratory rather than passive acceptance, a principle that, if more widely internalised by both clinical and laboratory staff, would likely catch future hook effect cases, and other rare interference phenomena, more quickly than this case's several-week delay allowed.^{[2][7]}

Applicability to Laboratories Without Access to Manual Dilution Expertise

Manual dilution and re-assay, as performed in this case, requires a degree of technical expertise and local assay validation to ensure the diluted result remains quantitatively accurate, and not every laboratory, particularly smaller or more remote facilities, necessarily has this capability readily available at the point a discordant result is first identified.

Laboratories without local manual dilution expertise should establish a clear referral pathway to a reference laboratory capable of performing and validating dilution testing promptly when a clinically discordant tumour marker result is identified, rather than either attempting dilution without appropriate validation or, worse, accepting a potentially hook-effect-affected

result as final simply because in-house dilution capability is not available.^[9]

Closing Summary of the Case Timeline

Reviewing the full timeline of this case end to end usefully consolidates the lessons drawn out individually throughout this report.

Initial presentation and strongly suggestive imaging findings were followed by an undiluted CA-125 result within the reference range, producing several weeks of diagnostic uncertainty during which reasonable alternative explanations were considered; a laboratory scientist's recognition of the clinical-laboratory discordance then prompted manual dilution, revealing a true concentration over one-hundred-fold higher and enabling urgent oncology referral, with subsequent imaging and biopsy confirming advanced high-grade serous ovarian carcinoma consistent with the corrected result.^{[3][5]}

Each stage of this timeline up to the point of dilution represents individually reasonable clinical and laboratory practice given the information available at that stage; the recommendations made throughout this report are aimed not at attributing fault to any individual step but at closing the specific systemic gap -- the dependency on incidental staff recognition of an infrequent phenomenon -- that allowed several weeks to elapse before the discordance was specifically identified and acted upon.

Conclusion

A high-dose hook effect produced a falsely normal CA-125 result in a patient with advanced ovarian carcinoma, delaying oncology referral by several weeks until dilution testing, prompted by clinical-laboratory discordance, revealed the true concentration was over one-hundred-fold higher than reported. Laboratories should consider automated hook effect detection where available, or a standing dilution policy for clinically discordant tumour marker results, rather than relying on incidental recognition of the mismatch.

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