RESEARCH PAPER

RECURRENT URTICARIA WITH ANGIOEDEMA IN A YOUNG WOMAN WITH ANTIPHOSPHOLIPID SYNDROME AND HYPOTHYROIDISM: A CASE REPORT OF OVERLAPPING DRUG-RELATED PROBLEMS

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ABSTRACT

Attributing acute urticaria to a drug is simple when the patient takes one medicine and difficult when several are in use and one of them cannot safely be stopped. A 27-year-old woman with antiphospholipid antibody syndrome on acenocoumarol, hypothyroidism on levothyroxine, obesity and newly recognised pre-diabetes presented with generalised pruritus of one day, giddiness and a single episode of vomiting, having received 100 mg of intravenous hydrocortisone before arrival. An identical episode had occurred fifteen days earlier. She was afebrile and haemodynamically stable, with no residual swelling, no wheeze and a Glasgow Coma Scale score of 15. Her total leucocyte count was 22,600 cells/cumm with 83% polymorphs and 1% eosinophils, drawn within hours of the corticosteroid and read as demargination with steroid-induced eosinopenia rather than sepsis. No antibiotic was given and she recovered within 48 hours. A structured medication review identified six drug-related problems. Anticoagulation was subtherapeutic on both available measurements, the international normalised ratio being 1.04 twenty days before admission and 1.75 on admission; the rise accompanied correction of profound hypothyroidism, thyroid-stimulating hormone falling from 39.97 to 1.61 µIU/ml, which predicts further potentiation and a need to reduce rather than raise the coumarin dose. Nitrofurantoin and levothyroxine each scored 4 on the Naranjo scale, and the first episode preceded the nitrofurantoin course. No suspected agent was recorded anywhere in the file and every drug allergy field was left blank. The case shows what a structured medication review recovers from an admission that otherwise reads as uneventful.

Keywords: Urticaria, Angioedema, Antiphospholipid syndrome, Acenocoumarol, Drug-related problems, Clinical pharmacy.

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INTRODUCTION

Wheals and angioedema arise from mast cell degranulation, and in chronic spontaneous urticaria angioedema accompanies the wheals in roughly 40% of patients; drugs are among the commonest identifiable triggers of an acute episode.[1] Where a single new medicine has been started, attribution is straightforward. Where four or five run concurrently and two changed within the preceding month, it is not.

Antiphospholipid antibody syndrome adds a constraint. The syndrome is defined by persistent antiphospholipid antibodies with vascular thrombosis or defined pregnancy morbidity,[2] and secondary prevention rests on a vitamin K antagonist targeting an international normalised ratio (INR) of 2.0 to 3.0.[3] The anticoagulant is itself a theoretical suspect in any drug eruption, yet also the drug whose interruption carries the greatest immediate hazard. Thyroid status complicates matters again: hypothyroidism slows the catabolism of vitamin K-dependent clotting factors and blunts the coumarin response, while restoring euthyroidism accelerates that turnover and potentiates the same dose,[4,5] so a patient whose levothyroxine has recently been increased is, in anticoagulation terms, a moving target.

We describe a 27-year-old woman with antiphospholipid antibody syndrome, treated hypothyroidism and pre-diabetes, admitted with a second episode of urticaria and angioedema within a fortnight.

CASE

Patient description

A 27-year-old married homemaker weighing 77 kg presented at 22:45 h to the emergency department of a tertiary care teaching hospital in Bagalkot, Karnataka, India, with itching over the whole body which had begun at about 18:00 h the same day and persisted despite initial treatment taken elsewhere. She reported giddiness of one day and one episode

of vomiting, and had received a stat dose of injection hydrocortisone 100 mg at another facility, after which the swelling settled. She was a known case of antiphospholipid antibody syndrome on acenocoumarol 4 mg once daily and of hypothyroidism on levothyroxine, and was P1L1 with a four-year-old child. There was no history of food allergy or of contact with soaps or cosmetics, and no drug allergy had ever been recorded.

Case history

Three outpatient contacts preceded the admission and are central to the case. The sequence was reconstructed from the complete case record, from the outpatient prescriptions of the preceding month through to the discharge summary; day numbering is relative to the index presentation and the chronology appears in Table 1.

Twenty days before admission her thyroid-stimulating hormone (TSH) was 39.97 µIU/ml and her INR 1.04; levothyroxine was increased from 100 µg to 150 µg once daily and cilostazol 100 mg was added. Fifteen days before admission, by her own account, she had an episode of itching and swelling indistinguishable from the index presentation, which settled with corticosteroid; it was recorded in the past history but never investigated, and no suspected agent was entered. Thirteen days before admission she returned with abdominal pain of two to three weeks and burning micturition, was found to have pyuria with marked microscopic haematuria, and was prescribed nitrofurantoin 100 mg once daily for ten days with dicyclomine and paracetamol and potassium citrate syrup. The ultrasound scan and urine culture advised then were absent from the record.

Physical examination

She was conscious, oriented and afebrile, with a Glasgow Coma Scale score of 15 out of 15, blood pressure 110/80 mmHg, pulse 81 to 92 beats per minute and oxygen saturation 96 to 98% on room air. The admitting team described her as morbidly obese; height was not documented, so body mass index could not be calculated. Pallor, icterus, cyanosis, clubbing, lymphadenopathy and pedal oedema were absent, and there was no facial or lip swelling at examination, the angioedema having already responded to the hydrocortisone. Air entry was equal bilaterally with no wheeze, heart sounds were normal without murmur, the abdomen soft and non-tender, and neurological examination normal. There was no stridor, respiratory distress or hypotension, so adrenaline was not indicated.

Investigations

Results appear in Table 2. The complete blood count, drawn within a few hours of the parenteral hydrocortisone, showed a total leucocyte count of 22,600 cells/cumm with 83% polymorphs and 1% eosinophils, haemoglobin 11.2 g/dL and mean corpuscular volume 65.0 fL, giving a Mentzer index of 12.8. Prothrombin time was 22.8 s against a control of 13.0 s, with an INR of 1.75, and the laboratory asked that the count be correlated with clinical details and medication history. Biochemistry was essentially normal apart from a glycated haemoglobin of 6.3%, placing her in the pre-diabetic band. Repeat thyroid function next morning gave a TSH of 1.61 µIU/ml, against 39.97 µIU/ml twenty days earlier. Urine routine was now clear, with pus cells 0 to 2 per high power field and no red cells, in contrast to the specimen of thirteen days before; ketone bodies at 1+ were consistent with reduced oral intake and vomiting. Viral serology was non-reactive.

Treatment plan and hospital course

Treatment was conservative: symptomatic control of an already-responding reaction, observation for recurrence, no antibiotics and no interruption of anticoagulation. She received injection pheniramine maleate 25 mg intravenously twice daily, stopped after the second day, with chronic medication continued and pantoprazole 40 mg daily and metformin 500 mg twice daily added on admission. No corticosteroid was given in hospital, the pre-admission dose having already produced a response, and no antibiotic was prescribed at any stage. Observations stayed stable, with temperature 98 °F, pulse 80 to 88 beats per minute, respiratory rate 21 to 22 per minute, systolic pressure 110 to 126 mmHg and diastolic 70 to 90 mmHg; capillary glucose values were 99, 110, 94, 151, 112 and 108 mg/dL and no insulin was given.

Outcome

The expected outcome was resolution of the eruption within one to two days on an antihistamine alone, with no need for further corticosteroid and no deterioration attributable to the leucocytosis, and that is what occurred. The pruritus settled over 24 hours, no new wheals appeared, and she was discharged on the third hospital day, asymptomatic, with the final diagnosis recorded as hypersensitivity reaction, antiphospholipid antibody syndrome on anticoagulants, and hypothyroidism with pre-diabetes. Discharge medication is listed in Table 1. No suspected drug was named in the discharge summary and the drug allergy field was again left blank.

Causality and drug-related problem assessment

Causality was assessed with the Naranjo probability scale and the World Health Organization–Uppsala Monitoring Centre categories,[6,7] severity with the scale of Hartwig and colleagues[8] and preventability with the criteria of Schumock and Thornton.[9] Nitrofurantoin and levothyroxine, the agents with the clearest temporal relationship, each scored 4 on the Naranjo scale, placing both in the possible category under both systems (Table 3). Severity was Hartwig level 4a, the reaction having caused the admission, and the event was judged probably preventable. Six drug-

related problems were identified and are set out with their recommendations in Table 4.

Written informed consent was obtained from the patient for the use of her anonymised clinical data and for publication, and all identifying particulars have been removed. The work accords with the Declaration of Helsinki, institutional ethics committee acknowledgement was obtained, and the report follows the CARE guidelines.[10]

Table 1: Chronology of clinical events, drug exposures and interventions.

Time point	Clinical event and investigations	Medication action
Day −20	Outpatient review; BP 120/80 mmHg; examination normal. TSH 39.97 µIU/ml; T3 115.49 ng/dl; T4 6.70 µg/dl; RBS 95.6 mg/dL; PT 13.5 s; INR 1.04	Levothyroxine 100 µg increased to 150 µg daily; acenocoumarol 4 mg continued; cilostazol 100 mg added
Day −15	First episode of generalised itching with swelling; settled after corticosteroid elsewhere; not investigated	No agent suspected or withdrawn; drug allergy field blank
Day −13	Revisit for abdominal pain of 2–3 weeks and burning micturition. Urine turbid; protein trace; leucocytes 1+; blood 3+; pus cells 5–10/hpf; RBC >100/hpf; no organisms	Nitrofurantoin 100 mg daily × 10 days; dicyclomine with paracetamol twice daily × 10 days; potassium citrate syrup. USG and urine culture advised; reports untraceable
Day 0, 18:00 h	Second episode: itching over whole body; giddiness of 1 day; one episode of vomiting	Injection hydrocortisone 100 mg stat, at another facility
Day 0, 22:45 h	Emergency arrival; triage yellow; afebrile; PR 92/min; BP 110/70 mmHg; SpO_2 95% on room air; primary survey normal; ECG and capillary glucose done	No further treatment in the emergency department
Day 0, 23:30 h	Admitted for observation; no facial or lip swelling; no wheeze; GCS 15/15	Pheniramine maleate 25 mg intravenously twice daily; chronic medication continued; pantoprazole 40 mg and metformin 500 mg added
Day 1	Pruritus settling; no new wheals; afebrile; BP 110/70 mmHg; moved to female medical ward	Pheniramine stopped after second day; no corticosteroid or antibiotic given in hospital
Day 2	Discharged asymptomatic; BP 126/80 mmHg; PR 86/min; SpO_2 98%; capillary glucose 108 mg/dL	Levothyroxine 150 µg; acenocoumarol 4 mg; pantoprazole 40 mg; cilostazol 100 mg twice daily; metformin SR 500 mg

Day 0 is the day of the index presentation; negative values are days before it. GCS, Glasgow Coma Scale; hpf, high power field; PR, pulse rate; PT, prothrombin time; RBS, random blood sugar; SR, sustained release; USG, ultrasonography.

Table 2: Laboratory investigations, with the reporting laboratory's reference ranges.

Investigation	Day −20	Day −13	Day 0–1	Reference range
Haemoglobin (g/dL); total WBC (cells/cumm); platelets (/cumm)	—	—	11.2; 22,600; 3,76,000	11.5–16.5; 4,000–11,000; 150–400 × 10^3
Differential P / L / E / M / B (%)	—	—	83 / 14 / 01 / 02 / 00	40–75 / 20–50 / 1–6 / 2–10 / 0–1
RBC (× 10^6/µL); MCV (fL) / MCH (pg) / MCHC (%) / RDW (%)	—	—	5.06; 65.0 / 22.2 / 34.2 / 16.0	3.5–5.0; 82–101 / 27.0–32.0 / 32–36 / 12–15
Haematocrit (%); ESR (mm/1st h); blood group	—	—	32.9; 15; O positive	37.0–54.0; 15–20
Prothrombin time / control (s); INR	13.5 / 13.0; 1.04	—	22.8 / 13.0; 1.75	12–16 / 13; 2.0–3.0 target in APS
Random blood sugar (mg/dL); HbA1c (%)	95.6	—	126.5; 6.3	60–140; <6 normal, 6–6.5 pre-diabetic, >6.5

Investigation	Day −20	Day −13	Day 0–1	Reference range
				diabetic
Urea / creatinine (mg/dL); Na / K / Cl (meq/L)	—	—	12.7 / 0.8; 135.0 / 4.8 / 105.0	15–39 / 0.6–1.3; 135–153 / 3.5–5.5 / 95–105
Bilirubin total / direct / indirect (mg%); AST / ALT / ALP (U/L)	—	—	0.5 / 0.2 / 0.3; 14.5 / 10.0 / 81.8	0.2–1.0 / 0.1–0.4 / 0.1–0.6; ≤40 / ≤41 / 35–140
Protein / albumin / globulin; A:G ratio	—	—	6.9 gm% / 4.5 g/dL / 2.4 gm%; 1.8:1	5.5–8.0 / 3.5–5.0 / 1.8–3.0; 1.5:1–2.5:1
T3 (ng/dl) / T4 (µg/dl) / TSH (µIU/ml)	115.49 / 6.70 / 39.97	—	109.32 / 9.10 / 1.61	69–215 / 5.2–12.7 / 0.35–4.5
Urine protein / leucocytes / blood / ketones	—	Trace / 1+ / 3+ / absent	Nil / Nil / Nil / 1+	Nil
Urine pus cells / RBCs (/hpf); HIV, HBsAg, HCV	—	5–10 / >100	0–2 / Nil; non-reactive	Nil; non-reactive

Differential count abbreviations: P, polymorphs; L, lymphocytes; E, eosinophils; M, monocytes; B, basophils. A:G, albumin to globulin ratio; APS, antiphospholipid syndrome; ESR, erythrocyte sedimentation rate; hpf, high power field; RDW, red cell distribution width. The INR entry gives the therapeutic target recommended in antiphospholipid syndrome, not a laboratory range.

Table 3: Item-by-item Naranjo causality assessment for the two principal suspect drugs.

No.	Naranjo question	Nitrofurantoin	Levothyroxine
1	Previous conclusive reports on this reaction?	Yes (+1)	Yes (+1)
2	Event appeared after the drug was administered?	Yes (+2)	Yes (+2)
3	Event improved on withdrawal or specific antagonist?	Yes (+1)	Yes (+1)
4	Event reappeared on readministration?	Not done (0)	Not done (0)
5	Alternative causes able on their own to cause it?	Yes (−1)	Yes (−1)
6	Reaction reappeared on placebo?	Do not know (0)	Do not know (0)
7	Drug detected in blood at toxic concentrations?	Not done (0)	Not done (0)
8	More severe on increasing, or less on decreasing, the dose?	Do not know (0)	Do not know (0)
9	Similar reaction to same or similar drug previously?	Not documented (0)	Not documented (0)
10	Event confirmed by objective evidence?	Yes (+1)	Yes (+1)
	Total score and category	4 — Possible	4 — Possible

Naranjo interpretation: 9 or above, definite; 5 to 8, probable; 1 to 4, possible; 0 or below, doubtful. Item 3 was scored on resolution following parenteral hydrocortisone and antihistamine; neither suspect drug was formally withdrawn.

Table 4: Drug-related problems identified on medication review, with recommendations.

No.	Drug-related problem	Classification	Recommendation
1	INR 1.04 and 1.75 on the only two measurements in three weeks, against a target of 2.0–3.0	Therapeutic failure; dose too low	Repeat INR within one week of discharge and at short intervals until stable; anticipate a rising INR as euthyroidism consolidates and be ready to

No.	Drug-related problem	Classification	Recommendation
			reduce rather than raise the dose
2	No suspected agent identified, recorded or communicated after two episodes; drug allergy field blank throughout	Documentation and monitoring failure	Enter suspected agents in the drug allergy field on all records; issue a patient-held allergy card; file a suspected adverse drug reaction report with the national pharmacovigilance programme
3	First-generation sedating H_1 antihistamine in a patient presenting with giddiness	Inappropriate drug selection	Substitute a second-generation non-sedating H_1 antihistamine such as levocetirizine 5 mg or fexofenadine 180 mg, up-dosed if symptoms persist
4	Pantoprazole started on admission and continued at discharge with no documented indication	Drug without indication	Discontinue unless a documented indication emerges
5	Cilostazol with acenocoumarol, without documented indication or bleeding surveillance	Potential drug interaction; unclear indication	Record the indication; counsel on bleeding; monitor alongside the planned INR surveillance
6	MCV 65.0 fL with Mentzer index 12.8 left unevaluated in a patient with recent haematuria	Untreated indication; incomplete work-up	Serum ferritin, iron studies and high performance liquid chromatography for haemoglobin variants as an outpatient

INR, international normalised ratio; MCV, mean corpuscular volume.

DISCUSSION

Identifying the offending agent in a crowded list

The notes recorded the diagnosis honestly as an urticarial reaction with angioedema, cause uncertain. That uncertainty was reasonable at the bedside, but it should not have survived the admission unchallenged, because the medication history held two documented changes within the relevant window. Nitrofurantoin is a recognised cause of immediate hypersensitivity: such reactions are the most frequently reported spontaneous adverse events for the drug in worldwide post-marketing experience, and pruritus, urticaria, angioedema, anaphylaxis and drug fever are all listed in the product information.[11] The ten-day course begun on Day −13 would have run until about Day −3, placing the exposure within the period of the second episode. An asymmetry in the dates is nevertheless the most discriminating detail in the record: the patient placed her first episode on Day −15, two days before nitrofurantoin was started, so if her recollection is accurate the drug can account for the second episode only. A two-day discrepancy sits within ordinary recall error, so the point cannot be pressed hard; it does direct attention to the one exposure preceding both episodes.

Levothyroxine is the less obvious candidate and the more interesting one. The hormone is endogenous and reactions to it are rare; reactions to excipients and colourants, which differ between tablet strengths and brands, are not. Joseph and colleagues described an Indian patient who developed generalised urticaria and angioedema after starting one brand of levothyroxine, reacted again on rechallenge with a second brand at only 12.5 µg, then tolerated a third, leading the authors to implicate an inactive excipient rather than the active moiety.[12] Our patient's tablet strength changed on Day −20, the first episode followed about five days later, the drug was never withdrawn, and a second episode occurred a fortnight after the first. That sequence does not prove causation, but it is precisely the sequence that ought to be examined. Acenocoumarol is a weaker suspect, in place before the earliest documented contact with no reaction recorded against it, while pantoprazole is excluded outright, having first been given after both reactions.

Causality, severity and preventability

A Naranjo score of 4 for each of two drugs is an uncomfortable result but an accurate one. Three of

the ten items could not be answered for either agent, since no drug was stopped and restarted, no plasma concentrations were measured and no dose–severity relationship was explored; a fourth, the presence of alternative causes, scored negatively for each agent precisely because the other was present. This is the practical limit of causality algorithms under polypharmacy, and it argues for a change in behaviour rather than in instrument: had the first episode been followed by withdrawal of the most recently changed agent and a documented dechallenge, the second admission might not have occurred.[9] That the drug allergy field was blank on every form, that no suspected agent was named anywhere and that no adverse drug reaction report was filed is, after two episodes, the most consequential finding of the admission, because it guarantees the next prescriber will start from zero.

A leucocytosis that was pharmacological rather than infective

A count of 22,600 cells/cumm with 83% polymorphs reliably prompts a search for sepsis and often an empirical antibiotic. Glucocorticoids raise the circulating granulocyte count mainly by demargination of cells already within the vascular compartment, with a contribution from marrow release, and the effect appears within hours of a dose;[13] acute mast cell degranulation, with its catecholamine response, acts by the same mechanism, and the two were additive here. The eosinophil count of 1% is the complementary half of the observation and is easily misread, since corticosteroids produce prompt eosinopenia: a low eosinophil count after a steroid dose carries no weight against an allergic diagnosis, and a serum tryptase would have been far more informative. Withholding antibiotics was supported by the rest of the data rather than by the count: she was afebrile throughout, the erythrocyte sedimentation rate was 15 mm in the first hour, renal and hepatic function were normal, the previously infected urine was now clear, no focus was found, and she recovered fully without antimicrobial treatment. A count of that size is high for demargination alone, which is why infection was excluded not from the count but on the totality of the picture and the subsequent course — the correct order of reasoning.

Anticoagulation quality and the thyroid–coumarin interaction

The most clinically important finding had nothing to do with the rash. Both available INR values were subtherapeutic against the target required in antiphospholipid syndrome,[3] so across the only two measurements in three weeks her time in therapeutic range was nil. For a young woman whose sole reason for taking acenocoumarol is prevention of recurrent thrombosis, this matters more than the urticaria that brought her in. The movement between the two values is instructive: her TSH fell twenty-five-fold over the same interval after the levothyroxine increase, and the INR rose on an essentially unchanged coumarin dose.[4,5] The corollary is anticipatory. Now that she is biochemically euthyroid the full effect of her dose will be expressed and the INR should be expected to go on rising, so she needs measurement within a week of discharge and at close intervals until stable, recognising that a dose inadequate during profound hypothyroidism may prove excessive once euthyroidism is consolidated. The haematuria of Day −13 deserves revisiting in the same light, since more than 100 red cells per high power field in an anticoagulated patient raises the question of over-anticoagulation; an INR of 1.04 disposes of that, and the pyuria with resolution of both findings points to the urinary tract infection. The alternative reading would have prompted a dose reduction in a patient already under-anticoagulated.

Other medication issues

Pheniramine is a first-generation H_1 antagonist, sedating and anticholinergic, whereas current guidance recommends second-generation non-sedating agents as first-line therapy for urticaria, up-dosed where symptoms persist.[1] That is not academic in a patient presenting with giddiness, a symptom such an agent makes harder to interpret and may worsen. Pantoprazole was started on admission and continued at discharge with no documented indication for either treatment or stress ulcer prophylaxis. Cilostazol alongside acenocoumarol deserves attention, since the product information calls for caution and frequent monitoring when a single anticoagulant is co-prescribed, and contraindicates the drug where two or more such agents are taken;[14] the combination here is permissible but should not be left unmonitored, particularly as the INR is expected to rise. The red cell indices also went unaddressed: a Mentzer index of 12.8 favours beta-thalassaemia trait over iron deficiency[15] while a red cell distribution width of 16.0% pulls the other way, and in a young woman with recent haematuria, lifelong anticoagulation and a possible future pregnancy the question is worth settling.

Limitations

No drug was formally withdrawn and none rechallenged, so causality cannot be established beyond the possible category. Serum tryptase, total immunoglobulin E, skin and provocation testing and repeat antiphospholipid titres were all absent, as were the ultrasound scan, urine culture and chest radiograph advised. This is a single patient over a short admission without long-term follow-up, and no inference about frequency or risk can be drawn from it.

CONCLUSION

A two-day admission for an itchy rash reads, on its discharge summary, as an uneventful episode

treated conservatively; a structured medication review found otherwise. Three recommendations follow. Where a hypersensitivity reaction occurs under polypharmacy, the most recently changed agent should be withdrawn and the dechallenge documented, so that the next episode is interpretable. A blood count drawn after parenteral corticosteroid should be read as a pharmacological picture until infection is excluded on other grounds. And thyroid replacement and vitamin K antagonists should be monitored together, since correcting hypothyroidism potentiates the coumarin already prescribed. A reaction treated but never attributed is a reaction waiting to be repeated.

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REFERENCES

1. Zuberbier T, Abdul Latiff AH, Abuzakouk M, Aquilina S, Asero R, Baker D, et al. The international EAACI/GA²LEN/EuroGuiDerm/APAAACI guideline for the definition, classification, diagnosis and management of urticaria. Allergy. 2022;77(3):734-766. DOI: 10.1111/all.15090
2. Miyakis S, Lockshin MD, Atsumi T, Branch DW, Brey RL, Cervera R, et al. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). Journal of Thrombosis and Haemostasis. 2006;4(2):295-306. DOI: 10.1111/j.1538-7836.2006.01753.x
3. Tektonidou MG, Andreoli L, Limper M, Amoura Z, Cervera R, Costedoat-Chalumeau N, et al. EULAR recommendations for the management of antiphospholipid syndrome in adults. Annals of the Rheumatic Diseases. 2019;78(10):1296-1304. DOI: 10.1136/annrheumdis-2019-215213
4. Stephens MA, Self TH, Lancaster D, Nash T. Hypothyroidism: effect on warfarin anticoagulation. Southern Medical Journal. 1989;82(12):1585-1586.
5. Busenbark LA, Cushnie SA. Effect of levothyroxine initiation on warfarin therapy. Annals of Pharmacotherapy. 2006;40(6):1200-1203.
6. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. Clinical Pharmacology and Therapeutics. 1981;30(2):239-245. DOI: 10.1038/clpt.1981.154
7. Zaki SA. Adverse drug reaction and causality assessment scales. Lung India. 2011;28(2):152-153. DOI: 10.4103/0970-2113.80343
8. Hartwig SC, Siegel J, Schneider PJ. Preventability and severity assessment in reporting adverse drug reactions. American Journal of Hospital Pharmacy. 1992;49(9):2229-2232.
9. Schumock GT, Thornton JP. Focusing on the preventability of adverse drug reactions. Hospital Pharmacy. 1992;27(6):538.
10. Gagnier JJ, Kienle G, Altman DG, Moher D, Sox H, Riley D, et al. The CARE guidelines: consensus-based clinical case report guideline development. Journal of Clinical Epidemiology. 2014;67(1):46-51.
11. United States Food and Drug Administration. Nitrofurantoin capsules: prescribing information. Silver Spring: United States Food and Drug Administration. Available from: https://www.accessdata.fda.gov/
12. Joseph A, Cherian KE, Kapoor N, Paul TV. A bizarre complication of levothyroxine therapy. Indian Journal of Endocrinology and Metabolism. 2021;25(2):166-167. DOI: 10.4103/ijem.IJEM_87_21
13. Nakagawa M, Terashima T, D'yachkova Y, Bondy GP, Hogg JC, van Eeden SF. Glucocorticoid-induced granulocytosis: contribution of marrow release and demargination of intravascular granulocytes. Circulation. 1998;98(21):2307-2313.
14. Electronic Medicines Compendium. Cilostazol 100 mg tablets: summary of product characteristics. Leatherhead: Datapharm. Available from: https://www.medicines.org.uk/emc/
15. Mentzer WC Jr. Differentiation of iron deficiency from thalassaemia trait. Lancet. 1973;1(7808):882. DOI: 10.1016/S0140-6736(73)91446-3