10-minute consultation

Adverse drug event

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This is part of a series of occasional articles on common problems in primary care

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A 72 year old woman on holiday in your area consults you four weeks after starting treatment with a non-steroidal anti-inflammatory drug (NSAID) for her painful knee. She complains of "a reaction" to the drug. She says she has had problems with similar drugs previously, but this drug is new and supposedly has fewer side effects. She says she has been feeling weak and giddy and has developed a widespread itchy skin rash. She tells you, however, that the drug was effective as a pain reliever. You find that she also has angina and high blood pressure.

What issues you should cover

History—Take a detailed history of the presenting complaint. The exact timing of events is important, as 80% of adverse drug reactions (usually type A—that is, pharmacologically predictable) occur in the first month of treatment. Establish whether she had weakness or giddiness to any extent before she began taking the drug. Has she had or does she presently have any intercurrent illness (for example, viral infection)? Has she any symptoms that indicate gastrointestinal, heart, or lung disease? If the rash started within a few days of starting the drug, and she was otherwise well, the chance of a drug reaction is higher. Has she any history of dyspepsia, peptic ulceration, asthma, heart failure, or renal failure? Any of these may be exacerbated by NSAIDs and might result in her non-specific symptoms.

Previous treatment—Has she ever had any similar rash or gastrointestinal bleeding when she has taken any NSAID in the past? Any such history would increase the chance of her present symptoms being a reaction to drugs. Is she taking low dose aspirin for her angina? This will increase the chance of gastrointestinal bleeding.

Examination—All NSAIDs can cause gastrointestinal bleeding, especially in elderly people. Some of these drugs are more dangerous than others, but it is important to exclude such bleeding (palpate the epigastrium, take pulse and blood pressure, and check

Useful reading

British Medical Association, Royal Pharmaceutical Society of Great Britain. *British national formulary*. London: BMA, RPS, 2003 (No 45)

Pirmohamed M, Breckenridge AM, Kitteringham NR, Park BK. Adverse drug reactions. *BMJ* 1998;316:1295-8

Sweetman S, ed. *Martindale. The complete drug reference*. 33rd ed. London: Royal Pharmaceutical Society, 2003

Dukes MNG, Aronson JK, eds. *Meyler's side effects of drugs*. 14th ed. Amsterdam: Elsevier, 2000

for anaemia; rectal examination for melaena may be indicated). Look for any abnormal lung signs, as well as evidence of oedema of the ankle. Consider renal function tests. Rash as a drug reaction can be multifaceted and difficult to diagnose, but the commonest manifestations are probably exanthema, urticaria, and generalised pruritus.

What you should do

- Although her presenting symptoms may not allow a conclusive diagnosis, the risk-benefit analysis of this situation will depend on the clinical assessment of the likelihood of an adverse drug reaction. Adverse drug reactions are commoner in old people and in women. Nearly a quarter of adverse drug reactions officially reported in the United Kingdom are due to NSAIDs. Gastrointestinal bleeding in old people is associated with considerable mortality. Thus, if in doubt it is safer to stop the drug. The clinical result of stopping treatment should be recorded.
- Supply an alternative analgesic if the NSAID is stopped.
- The rash may persist for some time after stopping the drug and may require symptomatic treatment.
- All drug adverse events should be reported through the appropriate channels. These vary from country to country (see box for the UK situation). France, for example, has a system of 31 regional pharmacovigilance centres, each of which collects and records reports of adverse drug events from healthcare professionals. These reports are then collated in a national database. In the United States case reports are sent either to the manufacturer, which forwards the report to the Food and Drug Administration, or to the FDA directly. Most of these systems are voluntary—but they are vital if adverse reactions to drugs already on the market are to be detected before serious damage is done.

Reporting adverse events in the United Kingdom

- Adverse events should be reported on the yellow forms in the back of the *British National Formulary* to the Committee on Safety of Medicines. This is especially important for drugs listed in the formulary with a black triangle next to the drug's name (any new NSAID would carry this symbol). You can get advice from the Medicines Control Agency (tel 0800 7316789).
- If the drug is being monitored by the Drug Safety Research Unit in Southampton you will be sent a green form. You should record all events occurring after start of treatment and return the form to the unit.
- An up to date summary of drugs' characteristics (including adverse events) can be obtained from the medical information department of the manufacturer (contact addresses in the *British National Formulary's* index of manufacturers).