CASE REPORT

Chemical Sensitivity Due to Metabolites

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This case is, in many respects, typical of the multiple sensitivities of polysymptomatic patients who react to aeroallergens, foods and chemicals. However, the case has a number of unusual aspects: migraine provoked by pollen, irritable bowel symptoms caused by reactions to a water-soluble metabolite of tetracycline in animal products, and bladder symptoms apparently owing to the excretion of amitriptyline metabolites and of sulphonates in molybdenum deficiency. Sensitivity to drug metabolites was probably acquired by the vaginal route.

Keywords: food intolerance, chemical sensitivity, sulphonates, drug sensitivity, molybdenum, tetracycline, amitriptyline, metabolites, pollen allergy, migraine, irritable bowel syndrome, abacterial cystitis

THE CASE

This is a life history report on a 71-year-old woman, in many ways typical of the patients who suffer from reactions to many different environmental factors and have many different symptoms, but it has several unexpected twists which are of general interest.

HA was a chesty child, with enuresis, nightmares and sleep-walking; her skin became sore if she wore unwashed new clothes. She reacted very strongly to insect bites, developed mild hayfever at about 12 years, and at 14 years old had the first of four severe attacks of a punctate psoriasis, covered almost all over on each occasion, the attacks lasting weeks to months. It is not clear where the psoriasis fits into the story, except that treatment with the usual ointments made her very unwell, and must have provided an additional chemical exposure.

In 1951 while resident in a hospital and under more than usual stress, she had to pass a large bed of wallflowers to get to the mess. After a while she kept arriving for meals with eyes and nose streaming so badly that eating was difficult. It did not happen if she took a route round the back of the hospital. Some years later she developed a bad cold on arriving at a farm for a holiday. She had a young baby so she took great care until her husband found a bed of wallflowers behind the farm, which explained everything. Wallflowers have a heavy pollen and are not a common source of allergies; she has avoided them ever since.

At 30 years old, again under stress from family illness, she started working in cancer immunology research (on immune reactions to chemical carcinogens), received a lecture-ship a few years later and stayed for 25 years, latterly working mostly with patients. In retrospect the laboratory was a very polluted environment—organic solvents and formaldehyde and poor ventilation. Within 10 years she had developed migraine, irritable bowel syndrome (IBS), psoriatic arthritis, recurrent bladder symptoms, insomnia, mood changes, weight gain, and menorrhagia requiring hysterectomy. She creaked on, socially embarrassed by severe IBS, and taking anti-inflammatory drugs for a few days when her fingers became
too clumsy, rarely off sick but often in bed at the weekend with migraine, including some
of the nester variants. For a time her office was off a histology laboratory and she had
constant migraine, finding the repetitive slight sounds from the cutters intolerable, even
through the wall. The migraine was probably due to higher pollution with formaldehyde
and solvents; it stopped when she managed to move offices.

IBS was investigated fully but not helped by the treatment and diets prescribed. Later she
noticed it was worse after pork or chicken but disregarded this in the mistaken supposition
that only one trigger would be responsible. When she read that penicillin and tetracycline
were used as growth promoters in pigs and chickens (as they were at that time) it rang a
bell and she started to avoid pork and chicken and was much better, but had a severe
reaction after eating some ham at a dinner party. She was lucky in having an open-minded
physician who believed the story and told her to avoid milk, eggs and veal as well, with
further improvement. Subsequently her GP wanted to prescribe tetracycline for an infection
and, after initially refusing, she agreed since there was no proof that tetracycline was the
culprit. She was unaffected for 2 days and concluded that her IBS was not due to
tetracycline—and then it hit her. Clearly she was reacting to a metabolite of tetracycline and
it had taken 2 days to make it in sufficient quantity [1]. The metabolite is water-soluble;
dishes made with lard from any source were tolerated but not those made with pork or
chicken stock. Pork from Denmark (whose regulations were stricter than those in the UK)
and from UK pigs scrounging in a wood were tolerated. Tetracycline is not now permitted
as a growth promoter, but is often used to treat infections, which are common in animals
kept in batteries. She now tolerates organic pork, chicken and eggs, but has to avoid
products from batteries. Bulked milks are usually troublesome, presumably because of the
inclusion of milk from one or more cows which have been treated for mastitis, but milk
from a single herd is tolerated for most of the year.

In addition to classical migraine, she developed a constant headache during June, worse
if she went out of doors, and realized that grass pollen and wallflowers now provoked
migraine instead of hay fever. For years she got through the pollen season with difficulty
on antihistamines and ergotamine tartrate, until in June 1975 she was seen by a neurologist
because of severe migraine while in hospital with a fractured ankle; he put her on
amitriptyline prophylaxis. This worked well, but she developed worse trouble with her
bladder, reported on several cystoscopies as inflamed but sterile, which continued until she
stopped taking amitriptyline. Interestingly, before this she had never been treated with either
of these drugs but, at different times, her husband had been treated for prolonged periods
with both tetracycline and amitriptyline, which suggests that sensitization to the metabolites
of each occurred by the vaginal route, a route that is not usually considered.

In 1982 she went to the Department of Health, where she worked for 18 months. Her
allergies were worse in London and before leaving she asked to be referred to someone
interested in migraine as an allergy. Her GP was Professor of General Practice in one of
the London teaching hospitals but knew of no one. He sent her to the Migraine Clinic, who
suggested Dr Jonathan Brostoff. At that time Dr Glenys Scadding was working with him
on neutralization in rhinitis [2], and HA was added to the trial. Migraine was provoked by
nasal challenge with grass pollen and the neutralization endpoint found. While taking the
neutralization vaccine, her tolerance of nasal challenge increased. During the first 2 weeks
of the double-blind randomized phase she was symptom-free even in the garden although
it was June. When she changed tubes severe migraine recurred and after a week she asked
to go back on to the other vaccine, which again proved highly effective.

Jonathan Brostoff had concluded from her history that she also needed to do an
elimination diet and she went to Dr Jonathan Maberly for this as, by this time, she was back
in Yorkshire. She still had all the old symptoms (except the severe IBS), but had also had
lower oesophageal pain that she associated with food (although a gastroenterologist assured
her this was not so), cardiac irregularities with antibiotics and severe migraine on fasting
for operations. She was waiting for a varicose vein operation and had developed typical
FIG. 1. Resting pulse rate before (B), and 20, 40, and 100 minutes after ingesting foods, and symptoms recorded. Examples of positive (upper rows) and negative (bottom row) test results shown.

angina of effort. She was unwell, going a funny green colour if she went into most shops, so her husband did almost all the shopping. She saw Jonathan Maberly, cleaned up her home environment and did a five food elimination diet as instructed, reacting to most of the foods tested. After a fortnight she was very well but afraid she would starve.

Figures 1 and 2 illustrate her responses to challenge. Figure 1 shows plots of pulse rate before and in the hour after challenges; the top two rows show challenges which caused symptoms—each of these also caused pulse rises with the curious exception of coffee, which might have been expected on biochemical grounds. Challenges shown on the
bottom row provoked neither symptoms nor pulse changes. Figure 2 is a plot of body weight morning and evening showing gains after positive challenges. Figure 3 shows an immediate loss of weight at the start of the elimination diet which continued steadily until she reached her normal weight 3 months later, without any control of calories.
remained at this weight without effort for the next 5 years but has gained again recently since she has stopped avoiding foods which cause water retention but no symptoms.

Not long afterwards she started working with Jonathan Maberly, with patients and in research, training with him in the Airedale Allergy Centre, his environmentally controlled unit, which provides a very valuable introduction to this discipline. Patient after patient is admitted with many symptoms, some of them severe, has a nasty withdrawal during the therapeutic fast, and then becomes actively well and often symptom-free. Symptoms recur after some challenges but not others, often to the patient’s great surprise. The investigation is complete within 3 weeks and most patients remain well on discharge, or are at least substantially better [3].

In the last 12 years HA has kept well and worked hard, seeing and treating many patients and writing books [4] and papers. She rebuilt a large rockery single-handed with no angina. Her varicosc veins recovered without an operation and have caused no trouble since. She does not tolerate drugs and has difficulty with supplements but always takes zinc, calcium and magnesium. She had neutralization to some foods, inhalants and chemicals which improved her tolerance.

She is now not affected by pollen and tolerates most foods, but there has been little improvement in her tolerance of chemicals. She avoids polluted buildings and places where people smoke or wear perfumes, foods treated with sulphites and food containing most additives, or soya or unspecified vegetable oil. Some foods she tolerates only if they are organic. She cannot tolerate milk for a few weeks after the cows go out in the spring, or meat from animals slaughtered during the same period, presumably because the grass they have eaten was contaminated by the winter’s accumulation of industrial pollution.

Drugs for cystitis have been a particular difficulty because surgery and abacterial cystitis left her prone to bladder infections. Whichever drug she took, her urine would clear and symptoms disappear but after about 2 days the symptoms would return, worse than ever. She was clearly reacting locally to a metabolite of the drug in urine. Last year she wondered if some of these troubles might be exacerbated by local reactions to sulphite in urine, since she is sulphite sensitive, and sulphites are excreted in molybdenum deficiency [5]. Sure enough, she showed quite high urinary sulphites and bladder symptoms are better if she takes molybdenum. She has had only one infection since then and was able to take a full course of treatment without reacting to the drug. Molybdenum is needed for detoxification processes.

She is now 71, usually symptom-free, remarkably well and still working. Readers will have realized that this is actually a self-report; some of the associations might not have been recognized had this not been so.

REFERENCES