

# ENDGAMES

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## CASE REVIEW

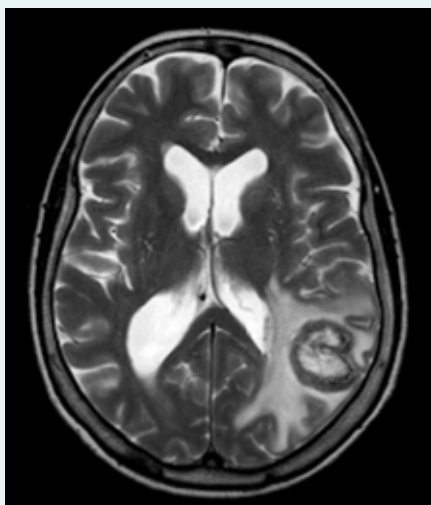
### Tumour biomarkers: diagnostic, prognostic, and predictive

A 63 year old woman presented with a one month history of difficulty in speaking and imbalance. She had been diagnosed with breast cancer two years earlier and had been treated with surgery, chemotherapy, and radiotherapy. This was followed by a year of trastuzumab (Herceptin) and continuous tamoxifen treatment.

Magnetic resonance imaging (figure) of the brain showed that she had a large solitary rounded enhancing mass lesion in the left inferior parietal lobe. It was present at the grey-white interface and there was extensive surrounding vasogenic oedema. The lesion was avidly enhanced after the administration of gadolinium (not shown). The appearances were suspicious of a solitary brain metastasis, but the differential diagnoses included a primary intrinsic malignant brain tumour.

After starting steroids, she underwent neurosurgical craniotomy and a gross total resection was achieved. Histological examination showed extensively necrotic metastatic carcinoma.

On immunohistochemical analysis, the tumour cells were strongly positive for E-cadherin, oestrogen receptors (ERs), and progesterone receptors (PRs). Human epidermal growth factor 2 (Her2) amplification was identified by fluorescence in situ hybridisation.



- 1 What is a tumour biomarker?
- 2 How has the knowledge of biomarkers affected the management of this patient?
- 3 What specific information do the diagnostic biomarkers, E-cadherin and ER, provide?
- 4 What specific information do the prognostic biomarkers, ER and PR, provide?
- 5 What specific information do the predictive biomarkers, ER and Her2, provide?

Submitted by Abigail Shaw, Marcus D Bradley, Sean Elyan, and Kathreena M Kurian  
Patient consent obtained.

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## SPOT DIAGNOSIS

### Plain radiograph in a neonate with abdominal distension

A 2 day old full term boy was referred to our hospital with respiratory distress and abdominal distension. His prenatal examinations had been unremarkable and polyhydramnios had been absent. At physical examination he had tachypnoea and abdominal distension. He was also grunting and cried during abdominal palpation. A plain film was obtained (figure). What is the diagnosis?

Submitted by Hung-Yang Chang, Hung-Chang Lee, Fu-Yuan Huang, and Chien-Yu Lin

Parental consent obtained.

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## STATISTICAL QUESTION

### Multistage sampling

Researchers investigated the views of the British public on the National Cancer Registry's use of personal medical data for public health research and surveillance without individual consent. A cross sectional study with a face to face survey was performed by the Office for National Statistics. Participants were selected using multistage sampling of adults in the United Kingdom during March and April 2015. In each month a sample of postal districts was selected at random, with the probability of selection proportionate to size. Within each district, a sample of private households was chosen at random. During March 2762 households were selected with a further 1819 households in April. At the start of the interview, the interviewer determined the household composition and selected the respondent from among all those aged 16 or more. In households with more than one adult, one person was selected at random. If the person selected was unavailable or declined to be interviewed it was recorded as a non-response. Face to face interviews were carried out with 1703 (62%) adults in March and 1252 (69%) adults in April. The data were combined for analysis.

Of the 2955 respondents, 72% (95% confidence interval 70% to 74%) did not consider any of the following to be an invasion of their privacy by the National Cancer Registry: inclusion of postcode, inclusion of name and address, and the receipt of a letter inviting them to a research study on the basis of inclusion in the registry. It was concluded that most of the British public considers the confidential use of personal, identifiable patient information by the National Cancer Registry for the purposes of public health research and surveillance not to be an invasion of privacy.

Which of the following statements, if any, are true?

- a) The sampling technique constituted a multistage sampling method with three stages
- b) Multistage sampling meant that resources could be concentrated in a limited number of areas of the country
- c) By definition, multistage sampling constitutes probability sampling

Submitted by Philip Sedgwick

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## CASE REVIEW

### Tumour biomarkers: diagnostic, prognostic, and predictive

- 1 Tumour (or cancer) biomarkers are biological molecules that suggest the presence of cancer in a patient. Biomarkers may also be used to characterise known tumours. They are either produced by the tumour itself or by the body in response to the tumour.
- 2 Diagnostic biomarkers helped identify and support the diagnosis, prognostic biomarkers helped estimate prognosis, and predictive biomarkers suggested a possible treatment.
3. The diagnostic biomarkers, ER and E-cadherin, helped determine that the solitary brain lesion was malignant (E-cadherin) and had metastasised from the breast (ER positive).
- 4 Prognostic biomarkers, such as ERs and PRs, indicate the likely outcome of disease. They can provide a more accurate prognosis and may help select patients for treatment, although they do not necessarily predict the response to it. Despite this patient's prognosis being poor because of the late clinical stage (IV), ER and PR positivity improves the chance of survival.
- 5 Predictive biomarkers are used solely to assess whether a certain treatment, such as a chemotherapy agent, may be of potential benefit to a specific patient. Positivity for ER and Her2 suggests that tamoxifen (ER antagonist) and trastuzumab (monoclonal antibody that interferes with Her2 receptors) may be effective in this tumour type.

## SPOT DIAGNOSIS

### Plain radiograph in a neonate with abdominal distension

This plain radiograph shows pneumoperitoneum with several characteristic radiographic findings.

This plain radiograph shows four characteristic radiographic signs of pneumoperitoneum. It shows decreased density of the liver shadow, also known as the hyperlucent liver sign (fig 2A), and the cupola sign, in which the central leaf of the central tendon of the diaphragm is highlighted by gas (fig 2B). The radiograph also shows the double wall sign, or Rigler's sign, which indicates the presence of gas on both sides of the bowel wall (fig 2C). The falciform ligament sign, visible as a linear density, is also visible (fig 2D).

See [thebmj.com](http://thebmj.com) for extended answer and discussion.



## STATISTICAL QUESTION

### Multistage sampling

Statements *a*, *b*, and *c* are all true.