

PostScript

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Metastasis of solid tumours in bone marrow: a study from Kashmir, India

Between 1935 and 2001, many studies have appeared in the literature from different parts of the world on bone marrow invasion by solid tumours.¹⁻⁴ After lymphoma, the primary tumours that most frequently involve the bone marrow are malignancies of the prostate, breast, lungs, thyroid, kidney, and stomach.⁴ Metastatic deposits of malignant melanoma have also been described.² In many instances, primary tumours remain clinically undetected and are identified only at necropsy.¹

The value of bone marrow aspiration in the diagnosis of malignant neoplasms was confirmed when four of eight cases of malignant melanoma were found to harbour tumour deposits in the bone marrow.³ In a series of 57 patients with known carcinoma of the prostate, five had carcinoma cells in the bone marrow, with no other diagnostic evidence of skeletal system involvement.² The usefulness of such a comparatively simple procedure is emphasised by studies of large series of patients with known malignancies,^{2,3} especially when the primary tumour is known to have a predilection for the skeletal system.

The patients in the abovementioned studies had known primary tumours and at present bone marrow aspiration/biopsy is routinely performed for staging of tumours, but the high incidence of metastatic deposits found in these bone marrows²⁻⁴ emphasises the practicability of routine bone marrow aspiration in patients with suspected malignancy or severe anaemia. It is difficult to determine from the literature the incidence of malignant cells in routine series of unselected bone marrow aspirates, so we investigated the usefulness of routine bone marrow examination for the diagnosis of malignancies.

A one year prospective study covering the year 2001 was conducted in the department of pathology, Government Medical College, Srinagar, Kashmir, India. The bone marrow smears were routinely stained by Leishman's stain and Perl's reaction. Periodic acid Schiff and Sudan black stain were used as and when

required. Of the 318 bone marrow samples studied during the year 2001, eight cases contained metastatic deposits. All of the patients in our present study had pallor (anaemia) as one of the main symptoms, and underwent bone marrow aspiration to determine which type of anaemia they were suffering from. In patients with metastatic deposits the normal haemopoietic cells of the bone marrow are replaced by tumour cells, resulting in myelopathic anaemia, and later on they are liable to develop myeloid metaplasia and myelofibrosis. In most of the cases, the bone marrow was difficult to aspirate, especially in cases of epithelial cell deposits, with mostly cancerous cells obtained in a background of peripheral blood—a fact that has already been reported.⁴

After leukaemia, lymphoma most commonly involves the bone marrow and almost 10% of cases of lymphoma invade the bone marrow. In our present study, lymphoma (non-Hodgkin lymphoma) made up a quarter (two cases) of all the secondary tumours of the bone marrow, along with neuroblastoma (two cases)—a childhood tumour. Neuroblastoma, non-Hodgkin lymphoma, and acute lymphoblastic leukaemia pose a considerable amount of difficulty in diagnosis because all three are round cell tumours with a very similar morphological appearance. In acute lymphoblastic leukaemia, the peripheral blood film examination is of paramount importance because it shows the presence of lymphoblasts, whereas neuroblastoma cells in bone marrow smears tend to form rosettes and may show neural or neurofibrillary differentiation. Non-Hodgkin lymphoma is thought of as a malignancy of old age, although it can be seen at any age; however, childhood lymphomas are mostly of high grade.

In most studies, the incidence of tumour deposits in the bone marrow from gastrointestinal tumours was low, but they made up a quarter of the cases presented here (two cases). This could be explained by the low number of cases in our study, together with the high incidence of gastrointestinal cancers, especially of the oesophagus and stomach, seen in Kashmir.⁵ Deposits from prostate and breast tumours (one case each) are known to have a predilection for skeletal metastasis.

Finally, several features worthy of comment are that the metastatic tumour cells are easily identified in the bone marrow smears because they look foreign within the native bone marrow cell population. These cells are usually identified in groups, even at low power examination, because they are larger than most of the bone marrow cells. Single cells are more difficult to recognise, although they never resemble the normal bone marrow cells. The primary site of the malignant deposits may be extremely difficult to determine on a morphological basis only, but their origin can sometimes be inferred from their morphological appearance, especially in mucous producing carcinoma, squamous carcinoma, some adenocarcinomas, and in many cases of metastatic neuroblastoma or melanoma.

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Fatal water intoxication

Water intoxication can occur in a variety of different clinical settings but is generally not well recognised in the medical literature. The condition may go unrecognised in the early stages when the patient may have symptoms of confusion, disorientation, nausea, and vomiting, but also changes in mental state and psychotic symptoms. Early detection is crucial to prevent severe hyponatraemia, which can lead to seizures, coma, and death.

The patient reported here was a 64 year old woman with a known history of mitral valve disease but no other relevant past history. On the evening before her death, she began compulsively drinking water in vast quantities, estimated at between 30 and 40 glasses, and this was interspersed with episodes of vomiting. She became hysterical and also distressed, shouting that she had not drunk enough water. She declined medical attention but continued to drink water after she had gone to bed. She later fell asleep and died some time later.

A postmortem examination was carried out six hours later. The pituitary and adrenal glands were normal and there was no evidence of a bronchial tumour. There were bilateral pleural effusions of 200 ml on each side and the cut surfaces of the lungs (568 g and 441 g) exuded frothy pink fluid. The heart (461 g) showed evidence of mitral valve disease and left ventricular hypertrophy. Within the stomach there was 800 ml of watery fluid and the intra-abdominal organs were generally wet.

Postmortem toxicology was negative. A sample of vitreous humour showed a sodium concentration of 92 mmol/litre (serum reference range, 132-144). Potassium, urea, and glucose were all within the serum reference ranges. Blood cortisol was raised, excluding an Addisonian crisis.

The cause of death was given as hyponatraemia as a result of acute water intoxication.

Water intoxication provokes disturbances in electrolyte balance, resulting in a rapid decrease in serum sodium concentration and eventual death. The development of acute dilutional hyponatraemia causes neurological symptoms because of the movement of water into the brain cells, in response to the fall in

extracellular osmolality. Symptoms can become apparent when the serum sodium falls below 120 mmol/litre, but are usually associated with concentrations below 110 mmol/litre. Severe symptoms occur with very low sodium concentrations of 90–105 mmol/litre. As the sodium concentration falls, the symptoms progress from confusion to drowsiness and eventually coma. However, the rate at which the sodium concentration falls is also an important factor, and the acute intake of large volumes of water over a short period of time, as occurred in this case, would have produced a rapid drop in serum sodium, which was fatal.

Postmortem serum samples are unsuitable for sodium measurement because concentrations decrease after death and there is considerable individual variation. However, vitreous sodium concentrations are stable in the early postmortem period, and the concentration in vitreous humour is similar to that found in normal serum.¹ Studies have shown that abnormal vitreous humour sodium concentrations had corresponding antemortem hyponatraemia or hypernatraemia.²

Self induced water intoxication is known to psychologists, but there is a paucity of information and little awareness of this life threatening problem in the professional literature.³ The initial symptoms associated with this condition are very similar to psychosis, with inappropriate behaviour, delusions, hallucinations, confusion, and disorientation.⁴ If untreated, the symptoms may progress from mild confusion to acute delirium, seizures, coma, and death, as occurred in this case.

Fatal water intoxication has been described in several different clinical situations. The most common of these is psychogenic polydipsia (compulsive water drinking), which is sometimes associated with either mental illness or mental handicap.^{4,5} The condition has also been described in young army

recruits of good health who developed hyponatraemia after apparent overhydration following heat related injuries.⁶ The most common symptoms suffered by this group were changes in mental status, emesis, nausea, and seizures. Accidental water intoxication has been described as a result of excessive water intake after an episode of gastroenteritis,⁷ and an iatrogenic case has occurred after gastric lavage.⁸ Forced water intoxication is a recognised form of child abuse, which commonly leads to brain damage and is sometimes fatal.⁹

In conclusion, we wish to highlight an unusual cause of death that may go unnoticed without an appropriate clinical history and relevant postmortem biochemical investigations. Both clinicians and pathologists need to be aware of this condition, which may manifest itself as a psychotic illness and so go unrecognised in its early stages. Early detection is crucial to prevent fatal complications.

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CORRECTION

Salivary gland-like tumours of the breast: surgical and molecular pathology. Pia-Foschini M, Reis-Filho JS, Eusebi V, et al. *J Clin Pathol* 2003;**56**:497–506. The name of the first author should have been Foschini MP not Pia-Foschini M.

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J Clin Pathol 2003 56: 803-804

doi: 10.1136/jcp.56.10.803-a

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