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THROMBOCYTOPENIC PURPURA WITH BRONCHIAL CARCINOMA

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No CASE appears to have been recorded of thrombocytopenia in association with non-metastasising carcinoma, in which the bone marrow megakaryocytes were numerically normal or increased.

The occurrence of leucoerythroblastic anaemia from infiltration of bone marrow with carcinoma cells is well documented (Vaughan, 1936); thrombocytopenia may be a feature (West, Ley and Pearson, 1955), and occasionally may occur alone (Willis, 1942); the marrow megakaryocytes in such cases are usually numerically reduced. There are a few reports in which bone marrow metastases are found with normal numbers of megakaryocytes and thrombocytopenia (Stefanini, 1955; Christenson, Ultmann and Mohos, 1956).

Case Report

A female receptionist, aged 62 years, was admitted to the Royal Infirmary, Sheffield, on the 3rd March, 1965. She had developed a cough with haemoptysis on the 24th February, followed by rapidly progressive purpura, with bleeding into the substance of the tongue and into the lower gastro-intestinal tract.

In the three months prior to admission she had lost 10 kg. in weight; this could be partly attributed to loss of dependent oedema for which she had received oral diuretics at home. Initially she had been treated for "a few weeks" with bendrofluazide 5 mg. b.d.; this was changed to frusemide on the 18th January, starting with 40 mg. daily and increased at intervals to b.d. then t.d.s. Quinidine 200 mg. daily was added at the beginning of February for palpitation.

All drugs were stopped on the day she started to bleed and develop purpura, but as no improvement ensued, she was admitted to hospital eight days later.

Further questioning elicited that she had smoked some twenty cigarettes a day for twenty years.

On examination she was afebrile; there were generalised purpuric lesions in the skin and mucous membranes of the mouth; the tongue was swollen, with ecchymoses on the inferior surface; signs at the base of the left lung were consistent with a pleural

effusion. No lymphadenopathy was noted; pulse rate 120/min., regular; BP 110/80 mm. Hg. Otherwise there were no relevant findings.

Investigations. Chest X-ray demonstrated a large left-sided pleural effusion tracking up the oblique fissure. No bony deposits were seen in dorsal spine, ribs, sternum or clavicles. Hb 45% (6.5 g/100 ml.). WBC 13,000/cu. mm., platelets less than 10,000/cu. mm., ESR (Westergren), 80 mm/hr.

Bone marrow—abnormalities noted were an increase in the megakaryocytes which were of abnormal morphology, with gross maturation arrest; a picture consistent with idiopathic thrombocytopenic purpura.

There was microscopic haematuria.

Group O Rh Positive, Direct Antiglobulin test negative. No red or white cell antibodies were detected.

Tests for complete and incomplete platelet antibodies were negative. These were carried out using the patient's serum alone and also using it in the presence of pharmacological amounts of bendrofluazide, frusemide and quinidine.

No LE cells were seen. Antinuclear factors were not detected.

Urea, electrolytes, plasma proteins were within the normal range.

Treatment was with blood transfusion of packed cells and prednisolone 60 mg/day. Within six days the platelet count had started to rise and on the 22nd March was 200,000/cu. mm.; the purpura had resolved.

Pleural aspiration was performed when the platelet count was within normal limits; the fluid was blood stained and contained malignant cells. Signs of underlying consolidation in the left upper lobe could then be elicited.

Her condition slowly deteriorated and on the 11th April she died; there was no recurrence of the purpura; platelet count four days before death was 300,000/cu. mm.

Necropsy revealed a right-sided pulmonary embolus, and a 6 cm. diameter tumour in the left upper lobe extending into the hilum of the lung and invading the pericardium; microscopy showed it to be a bronchogenic carcinoma of mixed squamous and glandular pattern. No skeletal metastases were

demonstrated macroscopically; the bone marrow in sections from a lumbar vertebra contained normal numbers of megakaryocytes and no carcinoma cells.

Discussion

The negative tests for platelet antibodies make it unlikely that the thrombocytopenia was drug-induced (Bolton and Dameshek, 1956; Ball, 1960). The clinical course too, does not support this; during the eight days following cessation of therapy the bleeding became worse; drug-induced thrombocytopenia usually reverts to normal within seven days of stopping treatment (Schen, 1958).

It would be extremely fortuitous if the bronchial carcinoma and the blood picture consistent with idiopathic thrombocytopenic purpura were in no way related.

There are a few reports, previously mentioned, of thrombocytopenia with normal numbers of megakaryocytes in association with a carcinoma, but marrow infiltration was universal; furthermore as the disease progressed the megakaryocytes diminished in number in each case. The initial cause of the thrombocytopenia was not clear, though in two cases platelet iso- and auto-agglutinins were demonstrated at a time when megakaryocyte numbers were within the normal range (Stefanini, 1955; Christenson and others, 1956).

It is possible that carcinoma cells were present in a patchy manner in the bone marrow of the present case, and were never found; had death been less rapid the progress may therefore have been similar to the cases previously described. The probability is, however, that no metastases occurred, particularly in view of the negative investigations. Even if some carcinoma cells were present in the bone marrow, it is still an unusual feature that the megakaryocytes and platelets were numerically normal at death.

Certainly no antibodies were found to platelets and there was no supporting evidence of an immune process—no LE cells were seen, anti-nuclear factors and Coomb's test were negative, plasma proteins were normal and no red or white cell antibodies were demonstrated.

It is of interest that an increasing number of humoral-secreting bronchogenic carcinomata are being reported (Greenberg, Divertie and Woolner,

1964; Lancet, 1964) and in particular there is evidence that red-cell aplasia may be produced by such a mechanism (Entwistle, Fentem and Jacobs, 1964).

If one element of the bone marrow can be specifically depressed, then it can be postulated that platelet maturation may have been similarly suppressed in the present case.

Summary

A case of non-metastasising bronchogenic carcinoma presented as idiopathic thrombocytopenic purpura; it was unusual in that the megakaryocytes were numerically normal. The possible aetiology is discussed.

Thanks are due to Dr. H. P. Brody, under whose care the patient was admitted, and Dr. E. K. Blackburn, for their helpful advice.

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