POLYCYTHAEMIA ASSOCIATED WITH UTERINE FIBROMYOMATA (MYOMA-ERYTHROCYTOSIS SYNDROME)*

H. GLIETENBERG, M.B., B.CH., DIP. O. & G. (RAND), M.R.C.O.G., F.C.O.G. (S.A.) AND D. C. COMINOS, B.SC., M.B., B.CH., *Department of Obstetrics and Gynaecology, University of the Witwatersrand, Johannesburg*

The association of polycythaemia with uterine fibroids is rare, and surprisingly so, since fibroids is quite a common condition. Because many practitioners are not aware of the association, it may be that the milder forms of polycythaemia are missed, and if a careful watch were to be made on the pre-operative blood findings in future, many more cases might come to light. To date we can find only 14 reported cases in the literature. The first case was reported by Thomson and Marson[1] in 1953, who noted that the polycythaemia disappeared following total abdominal hysterectomy and that there was no recurrence after 22 months. This has been the experience with the other cases, including the one reported here.

CASE REPORT

The patient was a 40-year-old Coloured female, para 5, gravida 5, whose only complaint on admission (22 October 1967) to Coronation Hospital, Johannesburg, was progressive swelling of the abdomen over 9 months and menorrhagia for 4 months. She had missed no periods and had a regular 28-day cycle. She usually bled for 5 days, but during the previous 4 months menstruation had lasted for 10 - 12 days and she had passed large clots. Her last menstrual period started on 29 September 1967. Her past and family history were not relevant.

On examination she seemed in good health, was short (4 ft 6 in.) and plump and had a rather florid appearance. Her blood pressure was 140/90 mm.Hg. Systematic examination of the heart, lungs and central nervous system revealed nothing abnormal.

Abdominal examination revealed an irregular mass arising out of the pelvis and reaching to the level of the xiphisternum. It was firm, dull to percussion and non-tender, with restricted mobility. There was no evidence of ascites. The liver and spleen could not be palpated.

On pelvic examination the whole pelvis was found to be occupied by this mass and the cervix was displaced to the left. The uterus could not be felt apart from the mass, but, by displacing the whole mass upwards with the abdominal hand, the cervix was felt to move with it and the mass was, therefore, considered to be part of the uterus. The adnexa could not be palpated. Rectal examination confirmed that the pouch of Douglas was completely occupied by the mass.

Investigations. The following results were obtained: The haemoglobin level was 18·5 G/100 ml.; the haematocrit was 54%; the white cell count was 5,200/cu.mm. (differential count: neutrophils 55%, eosinophils 8%, lymphocytes 30%, monocytes 1%); and the platelet count was 186,000/cu.mm. The blood urea concentration was 23 mg./100 ml. The electrocardiogram was normal, and X-ray examination of the chest and abdomen was normal. The intravenous pyelogram showed a normal renal pattern and the mass was not related to the renal tract. The urine contained 1+ protein.

Diagnosis. A provisional diagnosis of large uterine fibromyomata was made and it was decided to perform a total abdominal hysterectomy. Laparotomy was performed on 9 November 1967. The abdomen was opened by a vertical midline incision extending to 3 in. above the umbilicus. A very large fibroid uterus was delivered into the wound. Total hysterectomy and bilateral salpingo-oophorectomy was performed. Routine palpation of the other abdominal organs showed no abnormal pathology and the spleen was not enlarged.

Pathology report. The specimen weighed 12 lb. The ovaries and tubes were normal but the cervix showed evidence of chronic cervicitis. The uterus showed gross fibromyomata with no evidence of sarcomatous degeneration. There were scattered areas of adenomysis.

Postoperative progress. The patient's recovery was uneventful. She was discharged on the 10th postoperative day, when the haemoglobin level was 17·5 G/100 ml. and the haematocrit was 52%.

She was instructed to return at monthly intervals until further notice, for routine haemoglobin and haematocrit readings. She lived far away and was unreliable, but we managed to see her on 3 further occasions, when readings were taken (Table I). She had no complaints and felt very well and the wound had healed satisfactorily.

TABLE I. POSTOPERATIVE FOLLOW-UP

Time	*Haemoglobin (G/100 ml.)*	*Haematocrit (%)*
Pre-operative	18·5	54
Postoperative		
10th day	17·5	52
25th day	14·6	43
57th day	12·8	38
118th day	13·4	42

DISCUSSION

The term polycythaemia is used to describe an increase in the number of red cells per unit volume of blood. The increase in the number of red cells is accompanied by an increase in the haemoglobin and packed-cell volume values of the blood. In practice, determination of these values is the most useful method of determining the degree of polycythaemia and of following the response to therapy.

In polycythaemia vera the fundamental abnormality is hyperplasia of the precursors of the red cells, granulocytes and platelets in the bone marrow—a pan-myelopathy. Secondary polycythaemia or erythrocytosis is a true polycythaemia resulting from some known underlying primary disorder. Most cases are due to a disorder which lowers the arterial oxygen saturation of the blood, and a few are due to a disorder which appears to cause erythropoietic factor production with a normal oxygen saturation. The causes of polycythaemia are as follows (after De Gruchy):[2]

True Polycythaemia:

I. Idiopathic polycythaemia vera (erythraemia).

*Date received: 6 June 1969.

II. Secondary polycythaemia (erythrocytosis).
(*a*) Secondary to hypoxia—high altitude; congenital heart disease; chronic pulmonary disease; acquired heart disease; cerebral disorders; obesity; and abnormalities of pigment metabolism.
(*b*) Probably or possibly secondary to increased erythropoietin production—kidney disease (tumours, cysts, hydronephrosis); carcinoma of the liver; cerebellar haemangioblastoma; and uterine myomata.
III. Benign familial polycythaemia.
IV. Miscellaneous—splenic vein thrombosis; visceral syphilis; poisoning with aniline derivatives; pituitary basophilism; and chorea (Whitby and Britton).

Relative Polycythaemia:

Fluid loss; diminished fluid intake; redistribution of body fluids; and polycythaemia of 'stress'.

In secondary polycythaemia resulting from hypoxia, there is a lowering of the arterial oxygen saturation of the blood which acts as a stimulus for increased marrow erythrocyte production. Generally, the degree of polycythaemia is proportional to the degree of reduction in arterial oxygen saturation. Although the tissue tension of oxygen controls the rate of erythropoiesis, it does not do so by direct action on the marrow, but acts through a substance in the plasma produced in the body tissues in response to lack of oxygen. This substance is called erythropoietin, which is a low molecular weight glycoprotein. Erythropoietin cannot be demonstrated in the unconcentrated plasma of normal subjects but it can be demonstrated in concentrated normal human plasma, the level depending upon the rate of production as well as utilization, metabolism and excretion. The level is raised in certain anaemias and in some types of polycythaemia, where there may be an excess production of erythropoietin.

Thus, the production may be increased in certain tumours, such as primary carcinoma of the kidney[3] or liver, cerebellar haemangioblastoma and large uterine myomata, where there is no increase in arterial saturation. In uncomplicated cases the polycythaemia produced by these disorders is not accompanied by leucocytosis, thrombocytosis or palpable splenomegaly.

The significance of the relationship between polycythaemia and myomatous uterus is not clear. It has been reported in nulliparous and multiparous women between the ages of 29 and 59 years.

Most of the tumours have been very large and vascular, reaching to the xiphisternum, and some have been relatively small—the size of a uterus at 14 weeks' gestation (Table II). It has been noted that those tumours situated between the layers of the broad ligament are particularly prone to give rise to this condition. Horwitz and McKelway[8] suggested that the myoma may act as an arteriovenous shunt. This is difficult to accept because a shunt mechanism should produce a rise in the total circulating blood volume rather than in the red cell mass alone, and, furthermore, a pregnant uterus becomes like a large peripheral arteriovenous shunt and polycythaemia does not occur in pregnancy.

It has been suggested that the uterine tumour might produce a humoral erythropoietic factor closely related to, or identical with, erythropoietin. If this were the case, the mechanism of the polycythaemia would be easy to explain. It still remains obscure why, if this is so, erythropoietin should be produced in some tumours and not in most of them. It has also been suggested that this humoral erythropoietic factor might prolong the life-span of the circulating red blood cells or inhibit the reservoir function of the spleen, thereby releasing large quantities of red blood cells into the circulation. This latter theory sounds rather attractive, since many patients showed an immediate, dramatic postoperative response. The theory of erythropoietin production has not received much support from studies made by Van den Berg and Vasu[15] and Penington,[16] although Penington demonstrated the stimulation of iron utilization in rats by crude saline extracts from the tumour.

TABLE II. COMPARISON OF CASE REPORTS

Author	*Age of patient*	*Size of myoma*	*Haemoglobin (G/100 ml.)*	*Hct (%)*
Babuna *et al.*[4]	59	Equal to 4-mth pregnancy	20·0	62
Cohen & Rothenberg[5]	59	3,900 G	17·2	52
Engel & Singer[6]	39	To umbilicus	21·4	61
Fleming & Markley[7]	29	Slightly above umbilicus	19·2	64
Horwitz & McKelway[8]	47	To xiphoid	116%	—
Laurin *et al.*[9]	57	To xiphoid	19·5	78
Menzies (3 cases)[10]	45	To xiphoid, 11¼ lb.	135%	—
	57	Above umbilicus	110%	—
	42	Reaching umbilicus	120%	—
Paranjothy & Vaish[11]	34	Filled the abdomen	21·4	60
Rothman & Rennard[12]	37	28 cm. in diameter	20·4	60
Singmaster[13]	38	Slightly below umbilicus	18·0	—
Thomson & Marson[1]	48	To umbilicus	148%	72
Zilliacus[14]	47	Equal to size of foetal head	17·1	—
Present authors	40	To xiphoid, 12 lb.	18·5	54

There was no follow-up on the last 2 cases of Menzies[10] as they both died, after 48 hours and 6 days, respectively. Horwitz and McKelway[8] also found 2 cases in their records but one of these appears to have been a case of polycythaemia vera as there was no response following hysterectomy.

Cohen and Rothenberg[5] suggested a mechanical-pressure type of vascular impairment to the pelvic bone with consequent marrow hypoxia, but full-term pregnant uteri or large ovarian tumours should have the same effect and polycythaemia does not occur in these cases.

Rothman and Rennard[12] suggested that the myoma may compress the renal vessels and thus impair the circulation to the kidney. This might have an effect on the kidney erythropoietin production similar to that found in non-neoplastic renal disease. Such a possibility might seriously be considered since it is consistent with the fact that the polycythaemia has been found usually in association with large myomas. To date, there has been no mention made that renal arteriography has been done pre-operatively to show if there was any distortion of the renal vessels.

A large abdominal tumour might interfere with pulmonary ventilation, causing hypoxia and consequent stimulation of erythropoiesis by the mechanism described above. This was not so in our case or in any of the other cases described. Furthermore, some of the tumours described had barely reached the level of the umbilicus and this would not cause any respiratory embarrassment. In our particular case one of the presenting symptoms was severe menorrhagia and, in spite of this, her haemoglobin was 18·5 G/100 ml. on admission, so that the degree of polycythaemia was probably masked by this feature. It may be that menorrhagia in fact masks many cases of erythrocytosis. Menzies,[10] re-examining the case records with this in mind, found that of 137 women with fibroids, only 27 had a haemoglobin level of less than 75% (10·8 G/100 ml.). Of the 110 women without gross anaemia, 66 had menorrhagia.

The following facts may be emphasized:

1. The erythrocytosis disappears postoperatively, sometimes dramatically, but definitely over a period of months as shown by monitoring the haemoglobin and

haematocrit values of the blood at regular intervals.

2. The patients complained of no symptoms referable to the polycythaemia. Hypertension was not a constant feature.

3. As opposed to polycythaemia vera, there is no increase in the leucocyte or platelet count and no splenomegaly. This is important from the operative point of view because if there was any evidence of thrombocytosis, the ever-present fear of postoperative thrombosis and consequent pulmonary embolism would be present.

4. Should the condition be recognized pre-operatively, it might be useful—as some authors have done—to bleed the patient pre-operatively, store the blood and administer it again during or after the operation should bleeding become excessive. Menzies[10] is of the opinion that to give whole blood during or immediately after the operation is dangerous. If blood volume has to be restored, plasma transfusion is the method of choice.

SUMMARY

A case of polycythaemia associated with uterine fibroids has been presented. The condition is rare and to date only 14 cases have been reported. The polycythaemia is usually secondary, and differs from polycythaemia vera in that a panmyelopathy does not occur. Various theories regarding the pathogenesis have been put forward. After hysterectomy, the polycythaemia usually disappears.

We wish to thank Dr G. Elliot, Medical Superintendent of Coronation Hospital, for permission to publish.

REFERENCES

1. Thomson, A. P. and Marson, F. G. W. (1953): Lancet, **2**, 759.
2. De Gruchy, G. C. (1964): *Clinical Haematology in Medical Practice*. 2nd ed. Oxford: Blackwell Scientific Publications.
3. Damon, A. and Holub, D. A. (1958): Ann. Intern. Med., **49**, 43.
4. Babuna, C., Gardner, G. H. and Greene, R. R. (1959): Amer. J. Obstet. Gynec., **77**, 424.
5. Cohen, M. and Rothenberg, S. P. (1962): Obstet. and Gynec., **19**, 96.
6. Engel, H. W. and Singer, K. (1955): J. Amer. Med. Assoc., **159**, 190.
7. Fleming, A. R. and Markley, J. C. (1957): Amer. J. Obstet. Gynec., **74**, 677.
8. Horwitz, A. and McKelway, W. P. (1955): J. Amer. Med. Assoc., **158**, 1360.
9. Laurin, J. G., Girard, Y., Gauthier, G. and Leduc, P. E. (1960): Canad. Med. Assoc. J., **83**, 318.
10. Menzies, D. N. (1961): J. Obstet. Gynaec. Brit. Cwlth, **68**, 505.
11. Paranjothy, D. and Vaish, S. K. (1967): *Ibid.*, **74**, 603.
12. Rothman, D. and Rennard, M. (1963): Obstet. and Gynec., **21**, 102.
13. Singmaster, L. (1957): J. Amer. Med. Assoc., **163**, 36.
14. Zilliacus, H. (1959): Acta obstet. gynec. scand., **38**, 737.
15. Van den Berg, A. R. and Vasu, C. M. (1963): J. Amer. Med. Assoc., **185**, 249.
16. Penington, D. G. (1965): Proc. Roy. Soc. Med., **58**, 488.