STRUMA OVARII WITH MEIGS SYNDROME

(An illustrative approach)

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One hundred and ninety operations were carried out in the Obstetrical and Gynaecological department of the General Hospital of Piraeus during the first semester of 1979 of which 33 concerned common tumors of the ovaries.

Of the above operated cases one concerned the rare tumor "Struma Ovarii".

Struma ovarii is a term named after a dermoid cyst of the ovary which constitutes, almost exclusively, thyroid tissue without other teratomatous elements (Kempers *et al*, 1970). Foci of thyroid tissue may exist in 13% of the dermoid cysts.

These tumors are not common and still continue to present interest due to their rarity on the one hand, especially, when ascites and hydrothorax co-exists as in the author's case, and to the insufficient pathogenetic interpretation on the other, which still constitutes a field of investigation.

It is pointed out that the committee on ovarian tumors, which reviews all the ovarian tumors, of the area of Manchester, has reported only 16 cases of this kind of neoplasm in the last two years (Hasleton *et al*, 1978).

This histopathological ovarian defect has upto the present date been recognized and clearly established; however a clear etiopathogenetic explanation of Meigs syndrome, when accompanied by these tumors, has not yet been given (Harlow *et al*, 1976).

Case Report

A female aged 42 years, with two deliveries in her history, was admitted in the General Hospital of Piraeus on June 5, 1979 complaining of diffuse abdominal pain, weakness, sensation of weight mainly at the lower abdomen, flatulence, dyspnoea and cough of one month's duration.

Patient stated that she had been feeling well a year ago when she started complaining of a sensation of weight at the hypogastrium, acid-like belching and flatulence. The gastrointestinal examination, at the time, was negative for findings.

The clinical examination revealed a diminution of the respiratory sounds at the left semithorax and an alternating abdominal dullness.

The roentgenologic examination revealed a fluid collection at the left semithorax.

The gynecologic examination revealed a hard painful tumor at the left lower pelvis. Palpation of the uterus and right adnexa was difficult and there was fluctuation of the cul-de-sac.

Tapping of the semithorax and abdomen was done and about 2000 ml. of yellow fluid was removed from each tapping.

Laboratory tests did not show any abnormality. The results of the examination of the thoracic and abdominal fluid were as follows:

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Accepted for publication on 8-1-82.

	Abdominal fluid	Thoracic fluid
Specific gravity	1.015	1.021
Rivolta reaction	+	+
Protein	4.5 gm/100 ml	4.16 gm/100 ml
Sugar	96 mg/100 ml	90 mg/100 ml
Pseudo-mucus	—	—
Neoplas-matic cells	—	—

A clinical diagnosis of Meigs syndrome was made (Meigs 1943) and operation was decided. Prior to operation, a radio-immunoassay approach (in addition to the usual serum analyses) was made to detect the presence or absence of proteins or antigens having a relation with the nature of the tumour (Southam and Janovski 1971); Thomson *et al* 1969; Barret 1974; Purves *et al* 1970; Oettgen *et al* 1971).

Thus the radioimmunoassay investigation confirmed the secretion of tri-iodothyronine (T3) and thyroxine (T4) but not carcino-embryonic antigen (CEA) and alpha-feto-protein.

The possbility of hyperfunction or metastasis from an occult carcinoma of the thyroid was suspected but scanning of the thyroid gland did not show any indications of primary tumor and malignancy of the thyroid was thus excluded (Gikas *et al* 1967).

By median incision, a laparotomy was performed and free peritoneal fluid and a solid lobulated tumor, in the left ovary, partly cystic, 15 cm in diameter, with a smooth exterior surface adherent to the uterine fundus and the rectus were discovered. A colloid substance, not very clear, was found in the cystic cavities. Total excision of the uterus with its adnexa and the tumor was carried out.

The post-operative course was normal and there was not any further recurrence of pleuritic or ascitic fluid.

Re-investigation of the patient did not reveal any clinical or laboratory evidence of hyperthyroidism.

The histologic examination showed that the tumor was a benign teratoma and it was beyond doubt, that it absolutely consisted of thyroid tissue, a typical characteristic of embryonal adenoma of the thyroid, termed struma ovarii.. No malignant change was found in the sections.

Staining of the specimen with the immuno-hyperoxidase technic was negative for CEA and alpha-fetoprotein, while on the contrary T4 and T3 were confirmed without difficulty and it was thus established that the tumor was active, producing hormones at the sites of the positive staining (Fox and Langley, 1976).

Comments

According to Wooley and Mortin (1969) the ovary ranks second in what concerns localization of teratomas after the sacrocoxygeal aspect of the spinal column. Struma ovarii is mainly reported only in the ovary and is mostly observed in the period of sexual maturation of the female. In spite of the above, reports for childhood age have also been made (Hossai *et al*, 1977). A special citation perhaps should be accorded to the localization of damage. The left ovary seems to constitute the site of choice, as in the author's case. However, a rate ranging from 8% to 40% with bilateral localization has been reported.

As to the etiopathogenicity, the author concurs that in some site on the interior surface of the ovary a nodule may be observed in most cases, from which a variety of tissues outgrow which arise from all germinative dermas. The missing tissues are: liver, pulmonary tissue, pancreas, kidney, retina and suprarenals (Anderson, 1967).

The most invariable theory which agrees with all the findings admits that the teratomas arise from separated germinations or that they arise from fertilized phyletic cells.

According to the first view the germinations can separate during the early stages of embryonal development, thus remaining in a latent condition for an ample period of time when, for an unknown reason, they begin to differentiate towards

the tissues which they would have normally produced if they had not been separated from the synechia of the remaining germinations but had followed the remaining evolution of the body.

The weak point of this theory however, lies in that it is unexplainable why the ovary is mainly the organ in which such teratomas mostly develop.

The second theory is based on the fact that the ovary normally contains a great number of germinative cells which are able, after special preparatory changes, to produce another human body if they are fertilized.

The incidence of the disease, as results from recent statistical data, remains unchanged in the last decade, and has been found to be 0.3% in a great number of solid ovarian tumors. The present case is added to those few cases of struma ovarii with ascites and hydrothorax which have been reported internationally, and attempts to rationalize and discuss the possible causes of singularity of this formation.

With this presentation the following should be pointed out:

(a) The disease is not easily diagnosed preoperatively because it is asymptomatic, at least in the early stages and, sometimes, in established forms as well. When the disease is suspected, laboratory tests do not usually offer any help whatsoever. A co-existing hyperthyroidism, in a rate of 5-6%, has been reported (Marcus and Marcus, 1961).

According to Anderson (1957), approximately 12% of struma ovarii are functionally active, as the present analysed case, in which the high degree of cytoplasmatic cell staining of the tumor has undoubtably left no thesis that the positive staining represents the localization of T3 and T4 hormones in the cytoplasm or in the colloid.

It has been shown that the awkwardly placed thyroid tissue produces thyroglobulin similar to that of the normal thyroid and thyroid concer and is able to release hormonal substances in the circulation as the case in question (Kempers *et al,* 1970).

However, hyperthyroidism does not usually become an aim of examination until the tumor has been removed, in which case it is already too late. If, however, rigid criteria are used for the diagnosis of hyperthyroidism, the access to determining the source of the disease becomes significant.

This finding is not surprising, due to the histogenetic origin, nevertheless it can introduce a source of diagnostic confusion, except in cases in which thyroglobulin is found in individuals who had been subjected to total thyroidectomy in the past (athyroid patients), in which case it represents a special proteinic index of an existing tumor.

On the contrary, further immunologic control did not present any indication of tumor-antigen formation or other relative proteins in the serum, in which case we have departed from a malignancy of the ovary, a finding in the ovarian neoplasms which has been suggested by several authors (Marchard *et al,* 1975).

The radioimmunoassay control of the serum for alpha fetal protein and cancero-embryonic antigen and thyroglobulin, offers a means for the detection of primary or cancerous change of the ovary, and insinuates the presence of ovarian thyroid tissue which contains and produces thyroglobulin, but which can however introduce a source of diagnostic confusion in non-thyroidectomized patients thus leading to an erroneous diagnosis of thyroid damage.

It can be stated that in this kind of patients, the clinical signs and assessment

of our findings are negligent without a radioimmunoassay control of the serum, because in such cases one is confronted with an open abdomen during the operation and the operator is unprepared while, on the contrary, one faces a correlation between a carinomatous pattern tissue and levels of proteinic derivative of serum, under the prerequisite that the tumor releases such proteinic derivatives.

The author further considers this data important for the re-examination of women with this kind of removed tumors for possible suspicion of cancerous changes and who do not show any other suspicious localization with an allied biochemical activity.

(b) The clinical picture of the disease is mainly the result of hydrothorax and ascites, while the tumor more usually produces the least symptoms due to its relatively small size.

(c) In 1943 Meigs established his syndrome which arises in a similar way as above and defined the following characteristic features:

(1) Fibromuscular benign tumor of the ovary with the co-existence of ascites and hydrothorax (fibroma, thecoma, granulocytic tumor and Brenner's tumor).

(2) Removal of the tumor always brings about the subsidence of ascites and hydrothorax and, in general, cure. However confusion exists up to the present date as to the above definition, because many authors have included various ovarian and malignant tumors in Meigs syndrome, which are associated with ascites and hydrothorax and which do not comply with Meigs initial defined criteria of the tumor pattern (Hammonda, 1967; Aach and Kissani, 1969).

Thus Kawahara proposed two alternative solutions on the initial definition of Meigs syndrome, with whom the author agrees: (1) That the syndrome may include only fibroma of the ovary associated with ascites and hydrothorax as was defined initially. (2) The syndrome should also include all the ovarian tumors (solid, cystic and malignant) with ascites and hydrothorax, because the mechanism of fluid production does not seem to be different, under the condition that there is no evidence of metastasis in the peritoneal and pleural cavity.

(d) The exact mechanism of ascites and hydrothorax production is not known. Various mechanisms have been proposed for the pathogenetic interpretation of these conditions, without however sufficient evidence. Of the various proposed explainable mechanisms concerning the production of ascites, more plausable is, complying also with contemporary views, that ascites is a product of secretion of the tumor per se. The supporters of this view consider the presence of fluid the result of repeated rotations of the pedicle. However in the present case the tumor was firmly immobilized and it was certain that it could not rotate.

In order also to explain ascites in this kind of tumor by the above method, the author refers to Lawson's experiment (1958) who found that tumors placed in dry receptacles excreted great quantities of fluid. Thus it is believed that this kind of tumor is under high interior pressure and is thus the cause of fluid diffusion outwards (although necroses and cystic changes have been found).

Other investigators have attempted to explain the origin of ascites on the basis of the Selye's alarm reaction (1963). The various recent reports of an acute development of ascites and hydrothorax, as a result of ovarian stimulation with human gonadotrophins and clomiphene citrate, are highly significant on the matter in question (Neuwirth *et al*, 1965; Griffin, 1967; Southern *et al*, 1962).

From the resulting findings of such cases, which subsided after ovariectomy, the view was entertained that disruption of venous drainage of the ovaries leads both to the production of fluid from the ovarian surface and in the increased lymphatic drainage from that area. Therefore, the size of the tumor has no relation with the appearance of ascites and hydrothorax, which are connected with conditions of disruption of venous drainage of the ovary (rotation, reduplication of the pedicle etc.).

Schneck and Eis (1939) had moreover proposed an important hypothesis, caused by Selye's alarm reaction with, however, the additional factor of lymphatic hindrance by the compressive reaction of the tumor.

Of course pressure in the lymphatic vessels and in the blood vessels in general, has been shown to constitute a cause. On the contrary, free tumors in the peritoneal cavity are found, and it is obvious that they do not obliterate any drainage. Whatever the cause of ascitic fluid collection, it is rather sure that ascites is produced due to the diminished absorption of the secreted fluid from the tumor itself or from the edema of its pedicle, from the lymphatic vessels of the tumor.

As concerns hydrothorax, it is believed that it arises from ascites, the fluid moving towards the thorax through the lymphatic vessels of the hepato-sickle junction, diaphragm etc., but not adversily (Lemming, 1960).

The above was also demonstrated by Johnston and Loo (1964) by using ^{131}I.

Hodari and Hodgkinson (1968) observed, by means of lymphangiography, that the stain which was used appeared only in the thoracic fluid and not in the ascitic fluid; they thus concluded in the separate pathogenetic mechanism.

In regard to the fact that ascites and hydrothorax do not occur together in in every case and, according to the above lymphographic studies of Hodari, 1968; Aach and Kissane (1969) formulate the view that ascites is mainly the result of fluid liberation from the ovarian surface, while the development of hydrothorax is based on the increase of lymphatic drainage, also taking into account that the lymphatic system is one of the most variable systems of the human body (individual characteristic lymphangitic idiomorphysms).

(e) The differential diagnosis of the syndrome, which is significant for applying the correct treatment, should be made from T.B.C., polyserositis, malignant tumors of intra-abdominal organs, renal failure, ascites of hepatic origin, cardiac failure etc.

(f) Finally, tumors of the struma ovarii type are potentially malignant neoplasms but malignant change is very rare and many cases have thus been characterized diagnostically, without sufficient histologic evidence (Fox and Langley, 1976).

Their prognosis is usually extremely good and surgical removal brings about cure.

Peterson (1957), in a large review of malignant degeneration of dermoid cysts, gives an incidence of occurrence of malignant change of dermoid cysts up to 1.5% of all the ovarian malignancies. Therefore the incidence of occurrence of malignant change in struma ovarii must be less than 1%.

Summary

A case of struma ovarii with ascites and hydrothorax is presented.

A successful immunobiologic approach of the texture of the tumor was achieved by means of new investigational methods with encouraging results which were

established after the examination. Tests and studies by the hyperoxidase technic were also carried out to define the nature of this tumor and also to identify its proteins and antigens.

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