

# Gynaecomastia: is one cause enough?

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## ABSTRACT

Gynaecomastia can be detected in between one-third and two-thirds of men. A wide variety of causes of gynaecomastia, some physiological, some very serious, have been identified.

We present a case in which the cause of the gynaecomastia seemed obvious after history taking and physical examination but we finally ended up with a more complex combination of diagnoses. This case stresses the importance of combining history taking and physical examination with additional laboratory testing for the assessment of gynaecomastia.

## INTRODUCTION

Gynaecomastia is an often-encountered entity in clinical practice. True gynaecomastia, a benign enlargement of the glandular component of the male breast, should be distinguished from pseudogynaecomastia, in which fat deposition causes the impression of enlargement of the male breast, and from male breast cancer. Slight gynaecomastia can be detected in between one-third and two-third of adults and even more during normal puberty. Three peaks in the age distribution of gynaecomastia can be identified: the neonatal period, during puberty, and in the adult population, especially from the ages of 50 to 80.<sup>1</sup> Gynaecomastia has a broad range of causes, some of them very serious (table 1). Of all cases, 25% are idiopathic or related to ageing, 25% are classified as persistent after puberty, 10 to 15% are caused by drugs, 10% have a relation with nutritional factors or liver disease, 10% are caused by primary hypo-

Table 1

Causes of gynaecomastia

PHYSIOLOGICAL	
Neonatal	
Pubertal	
Ageing	
PATHOLOGICAL	
Drugs	
Chronic disease	
	Liver disease
	Renal failure
	Malnutrition
Neoplasms	
	Testicular
	Adrenal
	Lung
	Liver
	Kidney
Hyperthyroidism	
Primary or secondary hypogonadism	
Other endocrinological diseases	
Idiopathic	

gonadism, and 3% are due to testicular neoplasms. The remaining cases have their origin in various diseases such as secondary hypogonadism, hyperthyroidism, lung cancer or renal disease.<sup>2</sup>

Gynaecomastia is thought to result from an oestrogen/androgen imbalance at breast tissue level, which can be caused by various pathophysiological mechanisms.<sup>3</sup> Several recommendations have been made for the evaluation of gynaecomastia. Two key articles covering the evaluation of gynaecomastia suggest that careful history taking with specific questions about the use of medication,

drugs, and alcohol in combination with questions about the symptoms of hepatic dysfunction, decreased sexual functioning, pulmonary symptoms suggestive of lung cancer, and hyperthyroidism is sufficient in finding most conditions associated with gynaecomastia.<sup>1,4</sup> In the absence of abnormalities on physical examination, and on laboratory assessment of hepatic, renal, and thyroid function, it has been proposed that further specific evaluation is unlikely to be useful.<sup>1</sup> Neuman, however, added a measurement of testosterone and luteinising hormone (LH) in the evaluation of gynaecomastia.<sup>4</sup>

We present a case in which these recommendations did not suffice. Although the patient's symptoms seemed to lead straight to the diagnosis, he was subsequently diagnosed with a second causative disorder. Our case emphasises the importance of laboratory testing for serious causes of gynaecomastia and the fact that the laboratory results should completely fit the assumed diagnosis.

## CASE REPORT

A 31-year-old previously healthy man was referred because of progressive complaints of headache during the last two months, and because he had noticed that his right eyelid had started hanging. His nipples had become sensitive and slightly enlarged. His libido had not declined. Physical examination including examination of the testicles was normal, except for gynaecomastia and a ptosis at the right side. An ophthalmologist found a temporal vision defect of the right eye.

Laboratory results showed a normal blood cell count, electrolytes, kidney and liver function. Plasma thyroid-stimulating hormone (TSH), free thyroxin, cortisol and insulin-like growth factor-I (IGF-I) were normal. Plasma prolactin was very high (102 U/l, normal <0.5). His luteinising hormone (LH) was immeasurable (normal 1-5 U/l) and follicle-stimulating hormone (FSH) was somewhat low (1.0 U/l). Surprisingly, plasma testosterone was normal (33 nmol/l, normal 10-35). An MRI scan of the brain showed a lesion in the pituitary region with compression of the optic chiasm (*figure 1*).

A diagnosis of macroprolactinoma was made and treatment with an oral dopaminergic drug (cabergoline 1 mg per week) was started. Within three weeks his headache had almost disappeared, his vision returned to normal, and the ptosis was no longer present. After seven weeks, plasma prolactin level had fallen to 7 U/l, LH and FSH were < 1.0 U/l but his plasma testosterone was still 26 nmol/l. A few weeks later he told us he had noticed a painless enlargement of the left testicle; this was confirmed on physical examination. Laboratory testing showed a raised beta human chorionic gonadotropin ( $\beta$ -HCG, 184 U/L, normal <5), and a normal  $\alpha$ -fetoprotein (10  $\mu$ g/l, normal <15) and lactate



**Figure 1**  
*MRI scan shows a pituitary tumour extending to the optic chiasm*

dehydrogenase (LDH, 535 U/l, normal 300-620). A left-sided orchidectomy was performed. Microscopic evaluation showed a nonseminoma testis. A chest X-ray and a CT abdomen did not reveal any metastasis. After the orchidectomy, the  $\beta$ -HCG level became immeasurable and his testosterone level decreased to 2.5 nmol/l. One month after orchidectomy and four months after starting dopaminergic treatment LH, FSH and testosterone levels started climbing and finally reached normal values. His prolactin level had decreased below 0.1 U/l. A second MRI brain scan showed regression of the pituitary lesion. Thirteen months after his initial presentation he was in good health.

## DISCUSSION

Our patient presented with gynaecomastia, ptosis, a temporal vision defect and an elevated serum prolactin. This immediately pointed towards a prolactinoma in the pituitary region which was confirmed by MRI. However, testosterone levels remained normal although LH levels were immeasurable. Initially, this could not be explained and did not completely fit the assumed diagnosis.

Both a testicular tumour and a prolactin-producing tumour are known causes of gynaecomastia. To our great surprise, this patient suffered from both entities at the same time. Hyperprolactinaemia inhibits pituitary release of LH, and may thus lead to hypogonadotropic hypogonadism.<sup>5</sup> Suppression of prolactin release by treatment with dopaminergic agents should lead to resumption of LH and thus testos-

terone secretion.<sup>6</sup> The perplexing combination of immeasurable plasma LH with a 'normal' plasma testosterone was presumably due to testosterone production influenced by the  $\beta$ -HCG from the nonseminoma testis.<sup>7</sup>

Treating prolactinoma with a dopaminergic agent is currently the therapy of choice.<sup>8</sup> In a stage I good prognosis nonseminoma testis, one can suffice with surveillance after orchidectomy. The five-year survival rate in this group is between 89 and 93%.<sup>9,10</sup>

This case illustrates that although the cause of the gynaecomastia may seem obvious after history taking, physical examination, and routine laboratory testing, laboratory testing to investigate serious causes of gynaecomastia is necessary.

In case of nonphysiological gynaecomastia or doubt about physiological gynaecomastia (neonatal, pubertal, ageing/involutional) we would recommend laboratory tests for kidney function, liver function, thyroid stimulating hormone (TSH), free thyroxin (FT<sub>4</sub>),  $\beta$ -human chorionic gonadotropin ( $\beta$ -HCG), luteinising hormone (LH), testosterone and oestradiol.

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